

# Wetenschappelijk jaaroverzicht

2015



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ziekenhuis



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# **Wetenschappelijk Jaaroverzicht 2015**

Onder redactie van:

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Een uitgave van het Catharina Ziekenhuis  
Eindhoven, 2016

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**Scientific advancement should aim to affirm  
and to improve human life  
Nathan Deal (1942)**

## **Algemeen Klinisch Laboratorium**

**Berkel M van**

**Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

Boer AK\*, Kreeftenberg H\*, Bindels A\*, Roos A\*, Houterman S\*, Korsten E\*, van Dijk-van Berkel M\*

Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

*geen abstract beschikbaar*

*impactfactor: --*

**Boer AK**

**Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

Boer AK\*, Kreeftenberg H\*, Bindels A\*, Roos A\*, Houterman S\*, Korsten E\*, van Dijk-van Berkel M\*

Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

*geen abstract beschikbaar*

*impactfactor: --*

**Boer AK**

**Cut-off values to rule out urinary tract infection should be gender-specific**

Geerts N\*, Boonen KJ, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Nov 23;452:173-176

*Voor abstract zie: AKL - Geerts N*

*impactfactor: 2.824*

**Boer AK**

**Subclinical hypothyroidism: a 'laboratory-induced' condition**

Coene KL\*, Demir A, Broeren MA, Verschuure P, Lentjes EG, Boer AK\*

Eur J Endocrinol. 2015 Oct;173(4):499-505. Epub 2015 Jul 28

*Voor abstract zie: AKL - Coene KL*

*impactfactor: 4.069*

**Boer AK**

**Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie: AKL - Geerts N*

*impactfactor: 2.824*

**Boonen KJ**

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Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie: AKL - Geerts N*

*impactfactor: 2.824*

**Coene KL**

**Iatrogenic anemia/Twenty-five million liters of blood into the sewer: comment**

Coene KL\*, Roos AN\*, Scharnhorst V\*

J Thromb Haemost. 2015 Jun;13(6):1160-1

*geen abstract beschikbaar*

*impactfactor:* 5.720

**Coene KL**

**Subclinical hypothyroidism: a 'laboratory-induced' condition**

Coene KL\*, Demir A, Broeren MA, Verschuure P, Lentjes EG, Boer AK\*

Eur J Endocrinol. 2015 Oct;173(4):499-505. Epub 2015 Jul 28

**OBJECTIVE:** In current literature and guidelines there is a tendency to define absolute thyroid stimulating hormone (TSH) concentrations at which patient follow-up or even pharmaceutical intervention should be initiated. As TSH concentrations depend on the analytical method/platform used for TSH quantification, absolute cut-off values may pose threats for uniform clinical decision making. In this study we therefore set out to clarify to what extent the method/platform and the reference values applied for TSH influence the clinical interpretation of thyroid parameters. **DESIGN AND METHODS:** We retrospectively analyzed anonymous TSH results from the Dutch external quality assessment program in relation to reference values advised by different manufacturers. We also examined TSH/free thyroxine (fT4) reference ranges and prevalence of thyroid pathology among different Dutch laboratories, including four cases in which a switch in measuring platform was made. **RESULTS:** Our data show that interpretation of thyroid parameters is not only influenced by between-method/platform variation, but is also substantially affected by the variation in TSH/fT4 reference intervals applied in individual laboratories. Additionally, we show that the transition to a novel analytical method/platform can result in a shift in the prevalence of thyroid pathology, especially for subclinical hypothyroidism. **CONCLUSIONS:** Subclinical hypothyroidism can be a 'laboratory-induced' condition. This is an undesirable situation, regarding the clinical implications such as a diagnosis can have for patients.

*impactfactor:* 4.069

**Geerts N**

**Cut-off values to rule out urinary tract infection should be gender-specific**

Geerts N\*, Boonen KJ, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Nov 23;452:173-176

The diagnosis of urinary tract infection (UTI) by urine culture is an expensive and time-consuming procedure. Using a screening method, to identify negative samples, would improve the procedure and reduce costs. In this study, urine flow cytometry, of over 7000 urine samples, was assessed by retrospective analysis. With a cut-off value of >200bacteria/μl, we obtained a sensitivity of 93.0%, a specificity of 63.5%, and a negative predictive value (NPV) of 96.2%. As a result the culturing of 49% of all samples could be avoided. In addition, the data was retrospectively analyzed to determine if the introduction of gender-specific cut-off values could improve screening results. The obtained receiver operator curves are indeed significantly different when gender specific cut-offs were used. When a NPV of 95% is considered acceptable the unisex cut-off value of >200bacteria/μl can be used for women (NPV 94.9%), but the cut-off value for men could be raised to >400bacteria/μl without diminishing the NPV (NPV 95.0%).

*impactfactor:* 2.824



**Geerts N**

**Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

The diagnosis of urinary tract infection (UTI) by urine culture is a time-consuming and costly procedure. Usage of a screening method, to identify negative samples, would therefore affect time-to-diagnosis and laboratory cost positively. Urine flow cytometers are able to identify particles in urine. Together with the introduction of a cut-off value, which determines if a urine sample is subsequently cultured or not, the number of cultures can be reduced, while maintaining a low level of false negatives and a high negative predictive value. Recently, Sysmex developed additional software for their urine flow cytometers. Besides measuring the number of bacteria present in urine, information is given on bacterial morphology, which may guide the physician in the choice of antibiotic. In this study, we evaluated this software update. The UF1000i classifies bacteria into two categories: 'rods' and 'cocci/mixed'. Compared to the actual morphology of the bacterial pathogen found, the 'rods' category scores reasonably well with 91% chance of classifying rod-shaped bacteria correctly. The 'cocci/mixed' category underperforms, with only 29% of spherical-shaped bacteria (cocci) classified as such. In its current version, the bacterial morphology software does not classify bacteria, according to their morphology, well enough to be of clinical use in this study population.

*impactfactor:* 2.824

**Kerkhof D van de**

**Charcot-Leyden crystals in acute myeloid leukemia**

van de Kerkhof D\*, Scharnhorst V\*, Huysentruyt CJ, Brands-Nijenhuis AV, Ermens AA

Int J Lab Hematol. 2015 Aug;37(4):e100-2

*Geen abstract beschikbaar*

*impactfactor:* 1.819

**Kerkhof D van de**

**Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience**

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*impactfactor:* 1.837

**Scharnhorst V**

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Int J Lab Hematol. 2015 Aug;37(4):e100-2

*Geen abstract beschikbaar*

*impactfactor:* 1.819

## Scharnhorst V

### **Cholesterol in the ICU: a cheap and reliable marker for illness severity?**

Kreeftenberg HG\*, Roos AN\*, Bindels AJ\*, Scharnhorst V\*

Neth J Crit Care 2015;20(2):17-20

Voor abstract zie: *Inwendige geneeskunde - Kreeftenberg HG*

impactfactor: --

## Scharnhorst V

### **Cut-off values to rule out urinary tract infection should be gender-specific**

Geerts N\*, Boonen KJ, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Nov 23;452:173-176

Voor abstract zie: *AKL - Geerts N*

impactfactor: 2.824

## Scharnhorst V

### **Development and validation of a risk score for chronic kidney disease in HIV infection using prospective cohort data from the D:A:D study**

Mocroft A, Lundgren JD, Ross M, Law M, Reiss P, Kirk O, Smith C, Wentworth D, Neuhaus J, Fux CA, Moranne O, Morlat P, Johnson MA, Ryom L; D:A:D study group; Royal Free Hospital Clinic Cohort; INSIGHT study group; SMART study group; ESPRIT study group; collaborator: Scharnhorst V\*

PLoS Med. 2015 Mar 31;12(3):e1001809. eCollection 2015

**BACKGROUND:** Chronic kidney disease (CKD) is a major health issue for HIV-positive individuals, associated with increased morbidity and mortality. Development and implementation of a risk score model for CKD would allow comparison of the risks and benefits of adding potentially nephrotoxic antiretrovirals to a treatment regimen and would identify those at greatest risk of CKD. The aims of this study were to develop a simple, externally validated, and widely applicable long-term risk score model for CKD in HIV-positive individuals that can guide decision making in clinical practice.

**METHODS AND FINDINGS:** A total of 17,954 HIV-positive individuals from the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study with  $\geq 3$  estimated glomerular filtration rate (eGFR) values after 1 January 2004 were included. Baseline was defined as the first eGFR  $> 60$  ml/min/1.73 m<sup>2</sup> after 1 January 2004; individuals with exposure to tenofovir, atazanavir, atazanavir/ritonavir, lopinavir/ritonavir, other boosted protease inhibitors before baseline were excluded. CKD was defined as confirmed ( $>3$  mo apart) eGFR  $\leq 60$  ml/min/1.73 m<sup>2</sup>. Poisson regression was used to develop a risk score, externally validated on two independent cohorts. In the D:A:D study, 641 individuals developed CKD during 103,185 person-years of follow-up (PYFU; incidence 6.2/1,000 PYFU, 95% CI 5.7-6.7; median follow-up 6.1 y, range 0.3-9.1 y). Older age, intravenous drug use, hepatitis C coinfection, lower baseline eGFR, female gender, lower CD4 count nadir, hypertension, diabetes, and cardiovascular disease (CVD) predicted CKD. The adjusted incidence rate ratios of these nine categorical variables were scaled and summed to create the risk score. The median risk score at baseline was -2 (interquartile range -4 to 2). There was a 1:393 chance of developing CKD in the next 5 y in the low risk group (risk score  $< 0$ , 33 events), rising to 1:47 and 1:6 in the medium (risk score 0-4, 103 events) and high risk groups (risk score  $\geq 5$ , 505 events), respectively. Number needed to harm (NNTH) at 5 y when starting unboosted atazanavir or lopinavir/ritonavir among those with a low risk score was 1,702 (95% CI 1,166-3,367); NNTH was 202 (95% CI 159-278) and 21 (95% CI 19-23), respectively, for those with a medium and

high risk score. NNTH was 739 (95% CI 506-1462), 88 (95% CI 69-121), and 9 (95% CI 8-10) for those with a low, medium, and high risk score, respectively, starting tenofovir, atazanavir/ritonavir, or another boosted protease inhibitor. The Royal Free Hospital Clinic Cohort included 2,548 individuals, of whom 94 individuals developed CKD (3.7%) during 18,376 PYFU (median follow-up 7.4 y, range 0.3-12.7 y). Of 2,013 individuals included from the SMART/ESPRIT control arms, 32 individuals developed CKD (1.6%) during 8,452 PYFU (median follow-up 4.1 y, range 0.6-8.1 y). External validation showed that the risk score predicted well in these cohorts. Limitations of this study included limited data on race and no information on proteinuria.

**CONCLUSIONS:** Both traditional and HIV-related risk factors were predictive of CKD. These factors were used to develop a risk score for CKD in HIV infection, externally validated, that has direct clinical relevance for patients and clinicians to weigh the benefits of certain antiretrovirals against the risk of CKD and to identify those at greatest risk of CKD.

*impactfactor:* 14.429

### **Scharnhorst V**

#### **latrogenic anemia/Twenty-five million liters of blood into the sewer: comment**

Coene KL\*, Roos AN\*, Scharnhorst V\*

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### **Scharnhorst V**

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Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie:* AKL - Geerts N

*impactfactor:* 2.824

\* = Werkzaam in het Catharina Ziekenhuis

## **Anesthesiologie**

**Bouwman RA**

**Evaluation of a new double-lumen endobronchial tube with an integrated camera (VivaSight-DL™): a prospective multicentre observational study**

Koopman EM, Barak M, Weber E\*, Valk MJ, de Schepper RT, Bouwman RA\*, Huitink JM  
Anaesthesia. 2015 Aug;70(8):962-8

Voor abstract zie: Anesthesiologie - Weber E

impactfactor: 3.382

**Bouwman RA**

**Phrenic nerve palsy following interscalene brachial plexus block; a long lasting serious complication**

Buise MP\*, Bouwman RA\*, van der Gaag A, Piot V, Korsten HH\*

Acta Anaesthesiol Belg. 2015;66(3):91-4

Voor abstract zie: Anesthesiologie - Buise MP

impactfactor: --

**Bouwman RA**

**Pulmonary blood volume measured by contrast enhanced ultrasound: a comparison with transpulmonary thermodilution**

Herold IH\*, Soliman Hamad MA\*, van Assen HC, Bouwman RA\*, Korsten HH\*, Misch M

Br J Anaesth. 2015 Jul;115(1):53-60

Voor abstract zie: Anesthesiologie - Herold IH

impactfactor: 4.853

**Bouwman RA**

**Reply from the authors. Anaesthetic management during open and percutaneous irreversible electroporation**

Nielsen K, Scheffer HJ, Vieveen JM, van den Tol P, Meijerink MR, Bouwman RA\*

Br J Anaesth. 2015 Sep;115(3):473-4

Geen abstract beschikbaar

impactfactor: 4.853

**Bouwman RA**

**The myth of the difficult airway: airway management revisited**

Huitink JM, Bouwman RA\* Anaesthesia. 2015 Mar;70(3):244-9

Geen abstract beschikbaar

impactfactor: 3.486

**Buise MP**

**Being Overweight Is Associated With Greater Survival in ICU Patients: Results From the Intensive Care Over Nations Audit**

Sakr Y, Alhussami I, Nanchal R, Wunderink RG, Pellis T, Wittebole X, Martin-Loeches I, François B, Leone M, Vincent JL; Intensive Care Over Nations Investigators. Collaborator: Buise MP

Crit Care Med. 2015 Dec;43(12):2623-32

**OBJECTIVE:** To assess the effect of body mass index on ICU outcome and on the development of ICU-acquired infection.

**DESIGN:** A substudy of the Intensive Care Over Nations audit.

**SETTING:** Seven hundred thirty ICUs in 84 countries.

**PATIENTS:** All adult ICU patients admitted between May 8 and 18, 2012, except those admitted for less than 24 hours for routine postoperative monitoring (n = 10,069). In this subanalysis, only patients with complete data on height and weight (measured or estimated) on ICU admission in order to calculate the body mass index were included (n = 8,829).

**INTERVENTIONS:** None.

**MEASUREMENTS AND MAIN RESULTS:** Underweight was defined as body mass index less than 18.5 kg/m, normal weight as body mass index 18.5-24.9 kg/m, overweight as body mass index 25-29.9 kg/m, obese as body mass index 30-39.9 kg/m, and morbidly obese as body mass index greater than or equal to 40 kg/m. The mean body mass index was  $26.4 \pm 6.5$  kg/m. The ICU length of stay was similar among categories, but overweight and obese patients had longer hospital lengths of stay than patients with normal body mass index (10 [interquartile range, 5-21] and 11 [5-21] vs 9 [4-19] d;  $p < 0.01$  pairwise). ICU mortality was lower in morbidly obese than in normal body mass index patients (11.2% vs 16.6%;  $p = 0.015$ ). In-hospital mortality was lower in morbidly obese and overweight patients and higher in underweight patients than in those with normal body mass index. In a multilevel Cox proportional hazard analysis, underweight was independently associated with a higher hazard of 60-day in-hospital death (hazard ratio, 1.32; 95% CI, 1.05-1.65;  $p = 0.018$ ), whereas overweight was associated with a lower hazard (hazard ratio, 0.79; 95% CI, 0.71-0.89;  $p < 0.001$ ). No body mass index category was associated with an increased hazard of ICU-acquired infection.

**CONCLUSIONS:** In this large cohort of critically ill patients, underweight was independently associated with a higher hazard of 60-day in-hospital death and overweight with a lower hazard. None of the body mass index categories was independently associated with an increased hazard of infection during the ICU stay.

*impactfactor:* 6.312

## **Buise MP**

### **Perioperative statin therapy in patients at high risk for cardiovascular morbidity undergoing surgery: a review.**

de Waal BA, Buise MP\*, van Zundert AA

Br J Anaesth. 2015 Jan;114(1):44-52. Epub 2014 Sep 3

Summary Statins feature documented benefits for primary and secondary prevention of cardiovascular disease and are thought to improve perioperative outcomes in patients undergoing surgery. To assess the clinical outcomes of perioperative statin treatment in statin-naïve patients undergoing surgery, a systematic review was performed. Studies were included if they met the following criteria: randomized controlled trials, patients aged  $\geq 18$  yr undergoing surgery, patients not already on long-term statin treatment, reported outcomes including at least one of the following: mortality, myocardial infarction, atrial fibrillation, stroke, and length of hospital stay. The following randomized clinical trials were excluded: retrospective studies, trials without surgical procedure, trials without an outcome of interest, studies with patients on statin therapy before operation, or papers not written in English. The literature search revealed 16 randomized controlled studies involving 2275 patients. Pooled results showed a significant reduction in (i) mortality [risk ratio (RR) 0.53, 95% confidence interval (CI) 0.30-0.94,  $P=0.03$ ], (ii) myocardial infarction (RR 0.54, 95% CI 0.38-0.76,  $P<0.001$ ), (iii) perioperative atrial fibrillation (RR 0.53, 95% CI 0.43-0.66,  $P<0.001$ ),

and (iv) length of hospital stay (days, mean difference -0.58, 95% CI -0.79 to -0.37,  $P < 0.001$ ) in patients treated with a statin. Subgroup analysis in patients undergoing non-cardiac surgery showed a decrease in the perioperative incidence of mortality and myocardial infarction. Consequently, anaesthetists should consider prescribing a standard-dose statin before operation to statin-naïve patients undergoing cardiac surgery. However, there are insufficient data to support final recommendations on perioperative statin therapy for patients undergoing non-cardiac surgery.

*impactfactor:* 4.853

## **Buise MP**

### **Phrenic nerve palsy following interscalene brachial plexus block; a long lasting serious complication**

Buise MP\*, Bouwman RA\*, van der Gaag A, Piot V, Korsten HH\*

Acta Anaesthesiol Belg. 2015;66(3):91-4

Interscalene brachial plexus block (ISBPB) offers good analgesia for painful surgical procedures on the shoulder. We here describe two cases of long-term phrenic palsy following ISBPB that occurred in our practice in a relative short time period and both clearly illustrate the devastating impact of this complication for the patient. We will discuss the benefit of ISBPB in the context of the incidence and significant disability of hemidiaphragm paresis. Anesthesiologists must be aware of this complication and carefully weigh the advantages of ISBPB against the risks of this complication. When ISBPB is considered, the fact that the incidence of prolonged phrenic nerve palsy may be higher than previously expected should be taken into account carefully. A reevaluation on the indication and patient selection of ISBPB may even be warranted.

*impactfactor:* --

## **Buise MP**

### **Postoperative care after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedures**

Rieff EA, Stolker RJ, Koning J, de Hingh IH\*, Buise MP\*

Anaesth Intensive Care. 2015 Jul;43(4):532-3

*geen abstract beschikbaar*

*impactfactor:* 1.296

## **Buise MP**

### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reijnders TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hilgsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

*Voor abstract zie:* Chirurgie - Peters EG

*impactfactor:* 1.731

**Haanschoten MC**

**'Red blood transfusion in patients undergoing cardiac surgery reply'**

Haanschoten MC\*, van Straten AH\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jun;23(6):346

*Geen abstract beschikbaar*

*impactfactor: 1.837*

**Haanschoten MC**

**Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience**

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

**BACKGROUND:** In our institution, we have redefined our criteria for direct availability of red blood cell (RBC) units in the operation room. In this study, we sought to evaluate the safety of applying this new logistical policy of blood transfusion in the first preliminary group of patients.

**METHODS:** In March 2010, we started a new policy concerning the elective availability of RBC units in the operation room. This policy was called: No Elective Red Cells (NERC) program. The program was applied for patients undergoing primary isolated coronary artery bypass grafting (CABG) or single valve surgery. No elective RBC units were preoperatively ordered for these patients. In case of urgent need, blood was delivered to the operating room within 20 min. The present study includes the first 500 patients who were managed according to this policy. Logistic regression analyses were performed to investigate the impact of biomedical variables on fulfilling this NERC program.

**RESULTS:** The majority of patients (n=7409, 81 %) did not receive any RBCs during the hospital stay. In patients who did receive RBCs (n=791, 19 %), 11 patients (2.2 %) received RBCs after 24 h postoperatively. Female gender, left ventricular ejection fraction (LVEF) and EuroSCORE were significant predictors for the need of blood transfusion (OR=3.12; 2.79; 1.17 respectively).

**CONCLUSION:** In a selected group of patients, it is safe to perform cardiac surgery without the immediate availability of RBCs in the operating room. Transfusion was avoided in 81 % of these patients. Female gender, LVEF and EuroSCORE were associated with blood transfusion.

*impactfactor: 1.837*

**Herold IH**

**Automatic indicator dilution curve extraction in dynamic-contrast enhanced imaging using spectral clustering**

Saporito S, Herold IH\*, Houthuizen P\*, van den Bosch HC\*, Korsten HH\*, van Assen HC, Mischi M Phys Med Biol. 2015 Jul 7;60(13):5225-40

Indicator dilution theory provides a framework for the measurement of several cardiovascular parameters. Recently, dynamic imaging and contrast agents have been proposed to apply the method in a minimally invasive way. However, the use of contrast-enhanced sequences requires the definition of regions of interest (ROIs) in the dynamic image series; a time-consuming and operator dependent task, commonly performed manually. In this work, we propose a method for the automatic extraction of indicator dilution curves, exploiting the time domain correlation between pixels belonging to the same region. Individual time intensity curves were projected into a low dimensional subspace



using principal component analysis; subsequently, clustering was performed to identify the different ROIs. The method was assessed on clinically available DCE-MRI and DCE-US recordings, comparing the derived IDCs with those obtained manually. The robustness to noise of the proposed approach was shown on simulated data. The tracer kinetic parameters derived on real images were in agreement with those obtained from manual annotation. The presented method is a clinically useful preprocessing step prior to further ROI-based cardiac quantification

*impactfactor:* 2.761

## **Herold IH**

### **Pulmonary blood volume measured by contrast enhanced ultrasound: a comparison with transpulmonary thermodilution**

Herold IH\*, Soliman Hamad MA\*, van Assen HC, Bouwman RA\*, Korsten HH\*, Mischi M

Br J Anaesth. 2015 Jul;115(1):53-60

**BACKGROUND:** Blood volume quantification is essential for haemodynamic evaluation guiding fluid management in anaesthesia and intensive care practice. Ultrasound contrast agent (UCA)-dilution measured by contrast enhanced ultrasound (CEUS) can provide the UCA mean transit time (MTT) between the right and left heart, enabling the assessment of the intrathoracic blood volume (ITBV(UCA)). The purpose of the present study was to investigate the agreement between UCA-dilution using CEUS and transpulmonary thermodilution (TPTD) in vitro and in vivo.

**METHODS:** In an in vitro setup, with variable flows and volumes, we injected a double indicator, ice-cold saline with SonoVue®, and performed volume measurements using transesophageal echo and thermodilution by PiCCO®. In a pilot study, we assigned 17 patients undergoing elective cardiac surgery for pulmonary blood volume (PBV) measurement using TPTD by PiCCO® and ITBV by UCA-dilution. Correlation coefficients and Bland-Altman analysis were performed for all volume measurements.

**RESULTS:** In vitro, 73 experimental MTT's were obtained using PiCCO® and UCA-dilution. The volumes by PiCCO® and UCA-dilution correlated with true volumes;  $r(s)=0.96$  (95% CI, 0.93-0.97;  $P<0.0001$ ) and  $r(s)=0.97$  (95% CI, 0.95-0.98;  $P<0.0001$ ), respectively. The bias of PBV by PiCCO® and ITBV(UCA) were -380 ml and -42 ml, respectively. In 16 patients, 86 measurements were performed. The correlation between PBV by PiCCO® and ITBV(UCA) was  $r(s)=0.69$  (95% CI 0.55-0.79;  $P<0.0001$ ). Bland-Altman analysis revealed a bias of -323 ml.

**CONCLUSIONS:** ITBV assessment with CEUS seems a promising technique for blood volume measurement, which is minimally-invasive and bedside applicable.

*impactfactor:* 4.853

## **Korsten HH**

### **Automatic indicator dilution curve extraction in dynamic-contrast enhanced imaging using spectral clustering**

Saporito S, Herold IH\*, Houthuizen P\*, van den Bosch HC\*, Korsten HH\*, van Assen HC, Mischi M

Phys Med Biol. 2015 Jul 7;60(13):5225-40

*Voor abstract zie:* Anesthesiologie - Herold IH

*impactfactor:* 2.761

**Korsten HH**

**Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

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Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

*Geen abstract beschikbaar*

*impactfactor:* --

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*impactfactor:* --

**Korsten HH**

**Pulmonary blood volume measured by contrast enhanced ultrasound: a comparison with transpulmonary thermodilution**

Herold IH\*, Soliman Hamad MA\*, van Assen HC, Bouwman RA\*, Korsten HH\*, Mischi M

Br J Anaesth. 2015 Jul;115(1):53-60

*Voor abstract zie: Anesthesiologie - Herold IH*

*impactfactor:* 4.853

**Weber EW**

**Evaluation of a new double-lumen endobronchial tube with an integrated camera (VivaSight-DL<sup>™</sup>): a prospective multicentre observational study**

Koopman EM, Barak M, Weber E\*, Valk MJ, de Schepper RT, Bouwman RA, Huitink JMAnaesthesia. 2015 Aug;70(8):962-8

The VivaSight-DL<sup>™</sup> is a new single-use double-lumen endobronchial tube with an integrated camera. We studied this device in 151 consecutive patients scheduled for elective thoracic surgery in four different hospitals. Endobronchial intubation was successful in 148 patients (98%) (95% CI 94-99%). Median (IQR [range]) endobronchial intubation time was 59 (47-82 [17-932]) s and lung isolation was successfully achieved in 147 (99%) patients (95% CI 96-99%). A fiberoptic bronchoscope was required to assist endobronchial tube placement in 19 (13%) patients (95% CI 8-19%). Sore throat was reported by 37 (25%) patients (95% CI 18-33%), but no major complications were observed. We have reported the successful use of the VivaSight double-lumen tube for endobronchial intubation in a multicentre observational trial.

*impactfactor:* 3.382

**Zundert AA van**

**Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience**

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

Voor abstract zie: *Haanschoten MC - Anesthesiologie*

impactfactor: 1.837

\* = Werkzaam in het Catharina Ziekenhuis

**Apotheek**

Deenen MJ

**Clinical relevance of DPYD variants c.1679T>G, c.1236G>A/HapB3, and c.1601G>A as predictors of severe fluoropyrimidine-associated toxicity: a systematic review and meta-analysis of individual patient data**

Meulendijks D, Henricks LM, Sonke GS, Deenen MJ<sup>∞</sup>, Froehlich TK, Amstutz U, Largiadèr CR, Jennings BA, Marinaki AM, Sanderson JD, Kleibl Z, Kleiblova P, Schwab M, Zanger UM, Palles C, Tomlinson I, Gross E, van Kuilenburg AB, Punt CJ, Koopman M, Beijnen JH, Cats A, Schellens JH

Lancet Oncol. 2015 Dec;16(16):1639-50. Epub 2015 Oct 23

**BACKGROUND:** The best-known cause of intolerance to fluoropyrimidines is dihydropyrimidine dehydrogenase (DPD) deficiency, which can result from deleterious polymorphisms in the gene encoding DPD (DPYD), including DPYD\*2A and c.2846A>T. Three other variants-DPYD c.1679T>G, c.1236G>A/HapB3, and c.1601G>A-have been associated with DPD deficiency, but no definitive evidence for the clinical validity of these variants is available. The primary objective of this systematic review and meta-analysis was to assess the clinical validity of c.1679T>G, c.1236G>A/HapB3, and c.1601G>A as predictors of severe fluoropyrimidine-associated toxicity.

**METHODS:** We did a systematic review of the literature published before Dec 17, 2014, to identify cohort studies investigating associations between DPYD c.1679T>G, c.1236G>A/HapB3, and c.1601G>A and severe (grade ≥3) fluoropyrimidine-associated toxicity in patients treated with fluoropyrimidines (fluorouracil, capecitabine, or tegafur-uracil as single agents, in combination with other anticancer drugs, or with radiotherapy). Individual patient data were retrieved and analysed in a multivariable analysis to obtain an adjusted relative risk (RR). Effect estimates were pooled by use of a random-effects meta-analysis. The threshold for significance was set at a p value of less than 0.0167 (Bonferroni correction).

**FINDINGS:** 7365 patients from eight studies were included in the meta-analysis. DPYD c.1679T>G was significantly associated with fluoropyrimidine-associated toxicity (adjusted RR 4.40, 95% CI 2.08-9.30, p<0.0001), as was c.1236G>A/HapB3 (1.59, 1.29-1.97, p<0.0001). The association between c.1601G>A and fluoropyrimidine-associated toxicity was not significant (adjusted RR 1.52, 95% CI 0.86-2.70, p=0.15). Analysis of individual types of toxicity showed consistent associations of c.1679T>G and c.1236G>A/HapB3 with gastrointestinal toxicity (adjusted RR 5.72, 95% CI 1.40-23.33, p=0.015; and 2.04, 1.49-2.78, p<0.0001, respectively) and haematological toxicity (adjusted RR 9.76, 95% CI 3.03-31.48, p=0.00014; and 2.07, 1.17-3.68, p=0.013, respectively), but not with hand-foot syndrome. DPYD\*2A and c.2846A>T were also significantly associated with severe fluoropyrimidine-associated toxicity (adjusted RR 2.85, 95% CI 1.75-4.62, p<0.0001; and 3.02, 2.22-4.10, p<0.0001, respectively).

**INTERPRETATION:** DPYD variants c.1679T>G and c.1236G>A/HapB3 are clinically relevant predictors of fluoropyrimidine-associated toxicity. Upfront screening for these variants, in addition to the established variants DPYD\*2A and c.2846A>T, is recommended to improve the safety of patients with cancer treated with fluoropyrimidines.

<sup>∞</sup> = Ten tijde van publicatie werkzaam bij: Department of Clinical Pharmacology, Division of Molecular Pathology, Netherlands Cancer Institute, Amsterdam, Netherlands  
impactfactor: 24.690

**Deenen MJ**

**Improved pharmacodynamic assay for dihydropyrimidine dehydrogenase activity in peripheral blood mononuclear cells**

Pluim D, Jacobs BA, Deenen MJ, Ruijter AE, van Geel RM, Burylo AM, Meulendijks D, Beijnen JH, Schellens JH. *Bioanalysis*. 2015;7(5):519-29

**BACKGROUND:** Dihydropyrimidine dehydrogenase (DPD) activity determination in peripheral blood mononuclear cells of DPD deficient patients was hitherto inaccurate due to hemoglobin (Hb) contamination. We developed an improved method for accurate measurement of DPD activity in patients.

**RESULTS:** DPD activity was determined by HPLC with online radioisotope detection using liquid scintillation counting. Hb was determined spectrophotometrically. Method accuracy and precision were significantly improved by using cumulative area of all peaks as IS. Peripheral blood mononuclear cell lysates from DPD deficient patients were highly contaminated with on average 23.3% (range 2.7-51%) of Hb resulting in up to twofold underestimated DPD activity. DPD activities were corrected for Hb contamination. The method was validated and showed good long-term sample stability.

**CONCLUSION:** This method has increased specificity allowing accurate identification of DPD deficient patients.

*∞ = Ten tijde van publicatie werkzaam bij: Rijnstate Ziekenhuis*

*impactfactor: 3.003*

**Deenen MJ**

**Lower Ribavirin Plasma Concentrations in HCV/HIV-Coinfected Patients Than in HCV-Monoinfected Patients Despite Similar Dosage**

Deenen MJ\*, de Kanter CT, Dofferhoff AS, Grintjes-Huisman KJ, van d, V, Fleuren HW, Gisolf EH, Koopmans PP, Drenth JP, Burger DM

*Ther Drug Monit* 2015 December;37(6):751-755

**BACKGROUND:** Hepatitis C virus (HCV)/HIV-coinfected patients respond worse to dual therapy with ribavirin (RBV)/peginterferon compared with HCV-monoinfected patients. Several trials found that lower RBV plasma concentrations are associated with impaired virological response rates. The aim of this study was to determine RBV plasma concentrations in a cohort of HCV-monoinfected and HCV/HIV-coinfected patients. Our hypothesis is that HCV/HIV-coinfected patients have lower RBV plasma concentrations, which may in part explain their inferior response to dual therapy. **METHODS:** A retrospective cohort study was performed in chronic HCV-monoinfected and HCV/HIV-coinfected patients who received peginterferon and weight-based RBV. Plasma RBV concentrations were determined at weeks 4 and 12 by a validated high-performance liquid chromatography assay. RBV concentrations were compared between monoinfected and coinfecting patients. We calculated the proportion of patients with a subtherapeutic RBV plasma concentration defined as <2.0 mg/L.

**RESULTS:** A total of 61 HCV-infected patients were included, of whom 21 (34%) were coinfecting with HIV. Although there was no difference in the weight-based dose of RBV between monoinfected and coinfecting patients, RBV exposure was significantly lower in HCV/HIV-coinfected patients than in HCV-monoinfected patients: the mean  $\pm$  SD RBV plasma concentrations were  $1.82 \pm 0.63$  mg/L versus  $2.25 \pm 0.80$  mg/L ( $P = 0.04$ ) at week 4 and  $2.14 \pm 0.65$  mg/L versus  $2.62 \pm 0.81$  mg/L ( $P = 0.05$ ) at week 12, respectively. The percentage of patients with subtherapeutic plasma concentrations of RBV in coinfecting patients versus monoinfected patients was 62% versus 46% ( $P = 0.240$ ) at week 4 and 50% versus 16% ( $P = 0.01$ ) at week 12 of treatment, respectively.

CONCLUSIONS: HIV/HCV-coinfected patients yield significantly lower plasma concentrations of RBV than HCV-monoinfected patients. This puts them at an increased risk of not achieving sustained virological response.

∞ = Ten tijde van publicatie werkzaam bij: Department of Pharmacy, Radboud University Medical Center, Nijmegen; Department of clinical Pharmacy, Rijnstate Hospital Arnhem  
impactfactor: 2.376

## **Wezel RA**

### **Van Case study on the orientation of phaco hand pieces during steam sterilization processes**

van Doornmalen Gomez Hoyos JP, van Wezel RA\*, van Doornmalen HW J

Hosp Infect. 2015 May;90(1):52-8

BACKGROUND: Steam sterilization is an essential part of infection prevention. The literature shows that sterilization of medical instruments containing channels is not trivial. Phaco hand pieces have a simple configuration: a device contains a channel with a constant radius. No literature was found indicating whether the sterilization conditions on the inner surface of a phaco hand piece are influenced by the orientation of the hand piece.

AIM: To determine whether the orientation of a phaco hand piece influences the results of a sterilization process of this device.

METHODS: A qualitative case study, including experiments, is performed with a protocolled combination of steam sterilizer, process, phaco hand piece, orientation of the phaco hand piece, and wrapping.

FINDINGS: In this specific case, the orientation of the hand piece influenced the result of the steam sterilization process; in vertically (upright) oriented phaco hand pieces with free water drainage, sterilization conditions are reproducibly established. In the same process, in horizontally oriented or vertically oriented hand pieces without free drainage, these conditions are not established in a reproducible way.

CONCLUSION: In the investigated combination of sterilizer, process, load, loading pattern and wrapping, phaco hand pieces have to be oriented vertically (upright) with free water drainage to obtain steam sterilization conditions on the inner surface. It is likely that instruments with comparable configuration and dimensions will yield comparable results. It is therefore recommended that this issue is considered during the development of medical instruments and during performance qualifications of such instruments.

impactfactor: 2.544

## **Wezel RA van**

### **Variability of ATP amount in last rinse water of automated washer-disinfectors demands monitoring of every load**

van Doornmalen Gomez Hoyos JP, van Wezel RA\*, Tessarolo F J

Hosp Infect. 2015 Sep;91(1):87-9.

Geen abstract beschikbaar.

impactfactor: --

\* = Werkzaam in het Catharina Ziekenhuis

## Cardiologie



**Botman CJ**

**Chronic vagal stimulation for the treatment of low ejection fraction heart failure: results of the neural cardiac therapy for heart failure (NECTAR-HF) randomized controlled trial**

Zannad F, De Ferrari GM, Tuinenburg AE, Wright D, Brugada J, Butter C, Klein H, Stolen C, Meyer S, Stein KM, Ramuzat A, Schubert B, Daum D, Neuzil P, Botman C\*, Caste MA, D'Onofrio A, Solomon SD, Wold N, Ruble SB

Eur Heart J. 2015 Feb 14;36(7):425-33. Epub 2014 Aug 31

**AIM:** The neural cardiac therapy for heart failure (NECTAR-HF) was a randomized sham-controlled trial designed to evaluate whether a single dose of vagal nerve stimulation (VNS) would attenuate cardiac remodelling, improve cardiac function and increase exercise capacity in symptomatic heart failure patients with severe left ventricular (LV) systolic dysfunction despite guideline recommended medical therapy.

**METHODS:** Patients were randomized in a 2 : 1 ratio to receive therapy (VNS ON) or control (VNS OFF) for a 6-month period. The primary endpoint was the change in LV end systolic diameter (LVESD) at 6 months for control vs. therapy, with secondary endpoints of other echocardiography measurements, exercise capacity, quality-of-life assessments, 24-h Holter, and circulating biomarkers.

**RESULTS:** Of the 96 implanted patients, 87 had paired datasets for the primary endpoint. Change in LVESD from baseline to 6 months was  $-0.04 \pm 0.25$  cm in the therapy group compared with  $-0.08 \pm 0.32$  cm in the control group ( $P = 0.60$ ). Additional echocardiographic parameters of LV end diastolic dimension, LV end systolic volume, left ventricular end diastolic volume, LV ejection fraction, peak  $\dot{V}O_2$ , and N-terminal pro-hormone brain natriuretic peptide failed to show superiority compared to the control group. However, there were statistically significant improvements in quality of life for the Minnesota Living with Heart Failure Questionnaire ( $P = 0.049$ ), New York Heart Association class ( $P = 0.032$ ), and the SF-36 Physical Component ( $P = 0.016$ ) in the therapy group.

**CONCLUSION:** Vagal nerve stimulation as delivered in the NECTAR-HF trial failed to demonstrate a significant effect on primary and secondary endpoint measures of cardiac remodelling and functional capacity in symptomatic heart failure patients, but quality-of-life measures showed significant improvement.

*impactfactor:* 15.203

**Bracke FA**

**Acute Hemodynamic Effects of Single and Dual Site Left Ventricular Pacing Employing**

van Gelder BM\*, Bracke FA\*

Pacing Clin Electrophysiol. 2015 May;38(5):558-64. Epub 2015 Mar 1

*Voor abstract zie:* Cardiologie - Gelder BM van

*impactfactor:* 1.129

**Bracke FA**

**Extraction of non-functional leads at the time of device upgrade: still unproven benefit compared to abandoning leads**

Bracke FA\*

Heart Rhythm. 2015 Jul;12(7):e65. Epub 2015 Mar 31

*Geen abstract beschikbaar*

*impactfactor:* 5.076

**Bracke FA**

**Inappropriate shock because of triple counting in a patient with a subcutaneous implantable cardioverter defibrillator corrected by initiation of dual site left ventricular pacing**

van Gelder BM\*, Bracke FA\*, Simmers T\*

Circ Arrhythm Electrophysiol. 2015 Feb;8(1):239-40

*Geen abstract beschikbaar*

*impactfactor:* 4.513

**Bracke FA**

**Managing patients with advisory defibrillator leads: what can we learn from published data?**

Bracke FA\*, van Gelder BM\*

Neth Heart J. 2015 Apr;23(4):199-204

Defibrillator lead advisories stir a lot of emotions, both with patients and physicians, and this may influence lead management. We reviewed the literature for a more evidence-based approach to this issue. From the complications of two of the current advisory leads, the Medtronic Sprint Fidelis and St. Jude Riata leads, and the consequences of possible interventions, we can conclude that a restrained approach to premature replacement is appropriate. It may be opportune to replace the leads during a scheduled generator replacement in case of a higher electrical failure rate, in order to prevent future premature interventions. We found no support to extract non-functional advisory leads. In contrast, extraction is often more demanding than anticipated, and the risk substantially exceeds that of simply abandoning the leads.

*impactfactor:* 1.837

**Brueren BR**

**Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie: Cardiologie - van Nunen LX*

*impactfactor:* 3.769

**Brueren BR**

**Trends in the occurrence of new conduction abnormalities after transcatheter aortic valve implantation**

van der Boon RM, Houthuizen P\*, Urena M, Poels TT, van Mieghem NM, Brueren GR\*, Altintas S, Nuis RJ, Serruys PW, van Garsse LA, van Domburg RT, Cabau JR, de Jaegere PP, Prinzen FW

Catheter Cardiovasc Interv. 2015 Apr;85(5):E144-52. Epub 2014 Dec 27

*Voor abstract zie: Cardiologie - Houthuizen P*

*impactfactor:* 2.107

**Brueren BR**

**Uninterrupted oral anticoagulation versus bridging in patients with long-term oral anticoagulation during percutaneous coronary intervention: subgroup analysis from the WOEST trial**

Dewilde WJ, Janssen PW, Kelder JC, Verheugt FW, De Smet BJ, Adriaenssens T, Vrolix M, Brueren GB\*, Vandendriessche T, Van Mieghem C, Cornelis K, Vos J, Breet NJ, Ten Berg JM

EuroIntervention. 2015 Aug;11(4):381-90

**Aims:** To investigate the optimal periprocedural antithrombotic strategy in patients on long-term oral anticoagulation (OAC) who require percutaneous coronary intervention with stenting. **Methods and results:** The WOEST study was a randomised controlled trial which recruited 573 patients on long-term OAC who underwent PCI. The periprocedural treatment strategy was left to the operator's discretion. To assess the safety and feasibility of uninterrupted oral anticoagulation (UAC) and bridging therapy (BT), bleeding complications and MACCE were assessed in patients treated according to UAC (n=241) and BT (n=322) regimen. After 30 days, as well as after one year, there were no significant differences in bleeding complications (HR 0.83, 95% CI: 0.50-1.37, p=0.46, and HR 1.01, 95% CI: 0.71-1.44, p=0.95, respectively) and MACCE. MACCE tended to be less frequent in the UAC group (respectively HR 0.48, 95% CI: 0.15-1.51, p=0.21, and HR 0.72, 95% CI: 0.46-1.14, p=0.16). Additionally, adjustment with a propensity score revealed no significant differences. Periprocedural INR was not associated with bleeding or MACCE. **Conclusions:** In the WOEST study, UAC was not associated with an increase of bleeding or MACCE compared to bridging therapy. This is the largest study up to now to support the current guidelines. The WOEST trial is registered with ClinicalTrials.gov, number NCT00769938.

*impactfactor:* 3.769

**Dantzig JM van**

**No cardiac damage after endurance exercise in cardiologists cycling to the European Society of Cardiology meeting in Barcelona**

Appelman Y, van der Borgh R, van Dantzig JM\*, Mosterd A, Daniels M, Doevendans PA  
Eur J Prev Cardiol. 2015 Sep;22(9):1180-4. Epub 2014 Oct 9

**AIMS:** There are variable results reported for athletes and potential cardiac damage during exercise. In 2009 a group of cardiologists went by bicycle from the Netherlands to the European Society of Cardiology meeting in Barcelona and collected functional and biochemical parameters during this trip in order to evaluate whether cardiac damage was observed in a group of moderately trained amateur cyclists.

**METHODS AND RESULTS:** All of the 20 amateur cyclists (17 men) completed the 1580?km in eight days with an average speed of 27.9?km and an average distance of 190?km/day. Cardiac damage was predefined as wall motion abnormalities detected by echocardiography or an increase of troponin I exceeding three times the upper limit. Although skeletal muscle damage was found in all of the cyclists, no cardiac damage could be detected.

**CONCLUSION:** This long distance bicycle trip performed by moderately trained cardiologists demonstrates that it was safe and feasible and did not lead to cardiac damage although skeletal muscle damage was demonstrated in all participants

*impactfactor:* 3.319

**Dekker LR**

**Broad, broader, broadest**

van Nunen LX\*, Dello SA, Dekker LR\*

Neth Heart J. 2015 May;23(5):285-6, 289

*Geen abstract beschikbaar*

*impactfactor: 1.837*

**Dekker LR**

**Developing a research agenda on ethical issues related to using social media in healthcare**

Adams SA, Van Veghel D\*, Dekker L\*

Camb Q Healthc Ethics. 2015 Jul;24(3):293-302

*Voor abstract zie: Klinische Fysica - Veghel D van*

*impactfactor: 0.682*

**Dekker LR**

**Miniaturized Reveal LINQTM Insertable Cardiac Monitoring (ICM) System: First in Man Experience**

Pürerfellner H, Sanders P, Pokushalov E, Marco DB, Tracy B, Dekker LR\*; for the Reveal LINQ Usability Study Investigators

Heart Rhythm. 2015 Jun;12(6):1113-9. Epub 2015 Feb 26

**BACKGROUND:** The Reveal LINQTM is a miniaturized insertable cardiac monitor (ICM) with wireless telemetry for remote monitoring patients with suspected arrhythmias.

**OBJECTIVE:** The primary objective was to evaluate the Reveal LINQTM system functionality by measuring R-wave sensing and data transmission.

**METHODS:** The Reveal LINQTM Usability study was a non-randomized, prospective, multicenter trial. The study enrolled 30 patients with any indication for an ICM. Data were collected at baseline, implant, and one month follow-up visits and through daily wireless transmissions.

**RESULTS:** Thirty patients were enrolled and implanted with Reveal LINQTM. The mean age was 55±15 years. All patients had a successful implant of the ICM in one of the recommended locations. Ease of implant procedure was rated easy or very easy for 90% of implants. R-wave amplitudes were 0.584±0.325 mV at implant and 0.596±0.336 mV at one month (p=0.8). Automatic transmissions were successful 79.5% (69.5-86.9%) of the time. Transmission failures causing delay in data transfer occurred because of incomplete data reception or patients being out of range in 45% and 42% of instances, respectively. For all patients, transmission failures were followed by successful automated or manual transmission of information on a subsequent day. The devices stored 217 arrhythmic episodes during 30 days of follow-up, identified as AF (111), asystole (95), bradycardia (4), fast VT (1), and VT (6). No serious procedure-related or system-related adverse events occurred during the one month follow-up period.

**CONCLUSION:** The miniaturized Reveal LINQTM ICM supports arrhythmia detection and monitoring, achieving adequate sensing performance without safety issues.

*impactfactor: 5.076*

**Dekker LR**

**Quality of Life in Young Adult Patients with a Cardiogenetic Condition Receiving an ICD for Primary Prevention of Sudden Cardiac Death**

Verkerk AJ, Vermeer AM, Smets EM, Dekker LR, Wilde AA, Van Langen IM, Christiaans, Nieuwkerk PT

Pacing Clin Electrophysiol. 2015 Jul;38(7):870-7

**BACKGROUND:** Prophylactic implantable cardioverter defibrillator (ICD) therapy prevents sudden cardiac death (SCD) among young adults with cardiogenetic conditions, but might reduce quality of life (QoL) due to potential device complications, ongoing medical appointments, and lifestyle restrictions. We investigated QoL in the first year after ICD implantation for the primary prevention of SCD and compared QoL scores with population norms.

**METHODS:** Consecutive patients with cardiogenetic conditions (aged 18-50 years) referred to the Academic Medical Center in Amsterdam to receive ICD therapy for the primary prevention of SCD between 2007 and 2009 were eligible. Patients completed questions about QoL (Short-Form 36 Health Survey; SF-36), depressive symptoms (Center for Epidemiologic Studies Depression scale; CES-D), anxiety (State-Trait Anxiety Inventory; STAI), and the impact of receiving ICD therapy on lifestyle and work, shortly before ICD implantation and after 2 months, 6 months, and 12 months.

**RESULTS:** Thirty-five of 47 eligible patients participated. QoL was significantly reduced shortly before and 2 months after ICD implantation but improved over time and was comparable with population norms at 6 months and 12 months after ICD implantation. Yet, only about half of the patients believed they had a normal life like everyone else, and 28% had lost or changed their job due to their cardiogenetic condition and ICD therapy.

**CONCLUSIONS:** Receiving a diagnosis of a cardiogenetic condition and subsequent ICD implantation was accompanied with a temporarily reduced QoL and a significant negative impact on professional life. Clinicians should inform their patients of the possible QoL consequences when deciding about ICD implantation in primary prevention of SCD in cardiogenetic conditions.

*impactfactor:* 1.129

**El Farissi M\***

**Massive bouncing right cardiac mass as a cause of persistent pulmonary embolism**

Zimmermann FM\*, El Farissi M\*, van Brakel TJ, Lammers J Eur Heart J. 2015 Sep 21;36(36):2472. Epub 2015 Jul 3

*Geen abstract beschikbaar*

*impactfactor:* 15.203

**Gelder BM van**

**Acute Hemodynamic Effects of Single and Dual Site Left Ventricular Pacing Employing**

van Gelder BM\*, Bracke FA\*

Pacing Clin Electrophysiol. 2015 May;38(5):558-64. Epub 2015 Mar 1

**PURPOSE:** We studied the acute hemodynamic effect of left ventricular (LV) pacing from a dual cathodal coronary sinus (CS) lead in a both single and dual site electrode configuration.

**METHODS:** In 17 patients that underwent implantation of a CRT-D system with dual cathodal CS leads LV stimulation was performed from the distal and proximal electrode separately and from both electrodes simultaneously. The acute hemodynamic response (AHR) was evaluated by invasive measurement of LVdP/dtmax. Timing of LV electrical activation time

(LVAT) measured from onset QRS to LV sense during intrinsic rhythm at both electrodes were determined from simultaneous intracardiac recordings. The latter results were compared to those of an additional group of 26 patients in whom no hemodynamic effects were evaluated.

RESULTS: Baseline LVdP/dtmax was  $897 \pm 222$  mmHg/s. Single site LV pacing resulted in a rise of LVdP/dtmax to  $1053 \pm 266$  mmHg/s (+17.4%) taking the best of the 2 sites and  $1020 \pm 254$  mmHg (+13.7%) at the worst site ( $p = 0.0001$ ). In the dual site pacing configuration LVdP/dtmax was  $1026 \pm 243$  mmHg/s (+14.1%). P-value for single best vs. dual site was 0.005, and for dual site vs. worst single site 0.18 (n.s.).

CONCLUSION: Even with a relative small distance of 20-21 mm between stimulation electrodes there is a significant difference in acute hemodynamic effect from the single best and worst site. Dual site LV pacing offers no hemodynamic benefit over the best single pacing site. The short electrode distance may have been a limitation and results may not be applicable to other forms of multisite pacing.

impactfactor: 1.25

#### **Gelder BM van**

##### **Inappropriate shock because of triple counting in a patient with a subcutaneous implantable cardioverter defibrillator corrected by initiation of dual site left ventricular pacing**

van Gelder BM\*, Bracke FA\*, Simmers T\*

Circ Arrhythm Electrophysiol. 2015 Feb;8(1):239-40

Geen abstract beschikbaar

impactfactor: 4.513

#### **Gelder BM van**

##### **Managing patients with advisory defibrillator leads: what can we learn from published data?**

Bracke FA\*, van Gelder BM\* Neth Heart J. 2015 Apr;23(4):199-204

Voor abstract zie: Cardiologie - Bracke FA

impactfactor: 1.837

#### **Houthuizen P**

##### **Automatic indicator dilution curve extraction in dynamic-contrast enhanced imaging using spectral clustering**

Saporito S, Herold IH\*, Houthuizen P\*, van den Bosch HC\*, Korsten HH\*, van Assen HC, Mischi M

Phys Med Biol. 2015 Jul 7;60(13):5225-40

Voor abstract zie: Anesthesiologie - Herold IH

impactfactor: 2.761

## Houthuizen P

### Frequency and prognosis of new bundle branch block induced by surgical aortic valve replacement

Poels TT, Houthuizen P\*, Van Garsse LA\*, Soliman Hamad MA\*, Maessen JG, Prinzen FW, Van Straten AH\*

Eur J Cardiothorac Surg. 2015 Feb;47(2):e47-53

**OBJECTIVES:** Recently, transcatheter aortic valve implantation has been introduced, but one of its complications is left bundle branch block (LBBB), a conduction disturbance that has been associated with increased mortality. We investigated the incidence and fate of both right bundle branch block (RBBB) and LBBB after aortic valve replacement (AVR) using a retrospective analysis. We also studied the predictive value of both disorders for all-cause mortality.

**METHODS:** All patients who underwent AVR, with or without concomitant coronary artery bypass grafting surgery, between 2002 and 2010 in our centre were included. All-cause mortality was compared between patients who did and those who did not develop persistent new bundle branch block (BBB) within 7 days postoperatively. Patients were not eligible if one of their electrocardiogram (ECG) recordings prior to AVR showed a BBB or pacemaker activity. A postoperative period of 3-12 months was used to collect follow-up ECGs.

**RESULTS:** Of the 2279 AVR patients, 2033 patients were eligible for analysis. After excluding patients lacking baseline or follow-up ECG (n = 269), 1764 patients remained for analysis. Early LBBB and RBBB occurred in 71 (4.0%) and 92 (5.2%) patients, respectively. At follow-up, LBBB was persistent in 29 patients (1.6%) and RBBB in 74 patients (4.2%). During a median follow-up of 4.5 (2.4-6.5) years, the mortality rate was 16.3% (n = 271) in patients without BBB, 24.1% (n = 7) in patients with persistent LBBB and 18.9% (n = 14) in patients with persistent RBBB (log-rank P = 0.49). Though, in univariate analysis, the hazard ratio for mortality was 1.54 and 1.10 for LBBB and RBBB, respectively, the small numbers precluded identifying AVR-induced LBBB and RBBB as a predictor of mortality.

**CONCLUSIONS:** In the current practice of AVR, persistent postoperative LBBB and RBBB occur infrequently (~5% of cases), a percentage less than half of that in current transcatheter aortic valve implantation procedures. Given the adverse effects of LBBB, the lower prevalence of procedure-induced LBBB in AVR should be taken into account while deciding which valve replacement procedure is chosen for a patient.

*impactfactor:* 3.304

## Houthuizen P

### Long-term follow-up of 82 patients after surgical excision of atrial myxomas

Vroomen M\*, Houthuizen P\*, Khamooshian A\*, Soliman Hamad MA\*, van Straten AH\*

Interact Cardiovasc Thorac Surg. 2015 Aug;21(2):183-8. Epub 2015 May 13

*Voor abstract zie:* Cardiothoracale chirurgie - Vroomen M

*impactfactor:* 1.155

## Houthuizen P

### **Trends in the occurrence of new conduction abnormalities after transcatheter aortic valve implantation**

van der Boon RM, Houthuizen P\*, Urena M, Poels TT, van Mieghem NM, Brueren GR\*, Altintas S, Nuis RJ, Serruys PW, van Garsse LA\*, van Domburg RT, Cabau JR, de Jaegere PP, Prinzen FW

Catheter Cardiovasc Interv. 2015 Apr;85(5):E144-52. Epub 2014 Dec 27

**OBJECTIVES:** The aim of the study was to investigate trends over time in the occurrence of left bundle branch block (LBBB) and permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI) with the Medtronic CoreValve System (MCS) and Edwards SAPIEN Valve (ESV). Background: TAVI-induced conduction abnormalities (TAVI-CAs) such as LBBB and the need for PPI are frequent postoperative complication. New techniques, procedural refinements, and increased awareness are focused on the reduction of these abnormalities.

**METHODS:** Electrocardiograms of 549 patients without preprocedural LBBB and/or pacemaker were assessed to determine the frequency and nature of TAVI-CAs. To study the effect of experience, patients were subdivided per center into tertiles based on the number of procedures. Univariate and multivariate logistic regression was used to study predictors of TAVI-induced LBBB (TAVI-LBBB) and PPI.

**RESULTS:** TAVI-LBBB occurred in 185 patients (33.7%) and significantly decreased over time, from 42.6% to 27.3% ( $P=0.006$ ). This effect was only significant after implantation of the MCS (59.6% vs. 46.5% vs. 31.1%,  $P=0.001$ , ESV: 22.6% vs. 13.1% vs. 24.8%,  $P=0.11$ ). Between tertiles there was no difference in the frequency of PPI after TAVI ( $n=73$ , 13.1% vs. 14.8% vs. 12%,  $P=0.74$ ). Multivariate analysis revealed that, independent from valve type, depth of implantation was the only significant predictor of TAVI-LBBB (OR [95% C.I.]: 1.16 [1.10-1.24],  $P<0.001$ ). In case of PPI pre-existing RBBB (OR [95% C.I.]: 7.22 [3.28-15.88],  $P<0.001$ ) was the only significant predictor.

**CONCLUSIONS:** Over time the frequency of LBBB after TAVI decreased significantly, especially in patients undergoing TAVI with the MCS. Experience and the subsequent reduction in depth of implantation seem responsible for this reduction. Contrary to TAVI-LBBB, the incidence of PPI remained unchanged over time and was not affected by experience. Although experience has led to a decrease in new CAs after TAVI, elucidation of pathophysiologic mechanisms underlying these CAs and subsequent changes in patient stratification, valve design and the procedure are needed to further reduce this complication.

*impactfactor:* 2.107

## Koolen JJ

### **Appropriate use of bioresorbable vascular scaffolds in percutaneous coronary interventions: a recommendation from experienced users : A position statement on the use of bioresorbable vascular scaffolds in the Netherlands**

Everaert B, Felix C, Koolen J\*, den Heijer P, Henriques J, Wykrzykowska J, van der Schaaf R, de Smet B, Hofma S, Diletti R, Van Mieghem N, Regar E, Smits P, van Geuns RJ  
Neth Heart J. 2015 Mar;23(3):161-5

Percutaneous coronary interventions (PCI) have become a reliable revascularisation option to treat ischaemic coronary artery disease. Drug-eluting stents (DES) are widely used as first choice devices in many procedures due to their established good medium to long term outcomes. These permanent implants, however, do not have any residual function after



vascular healing following the PCI. Beyond this initial healing period, metallic stents may induce new problems, resulting in an average rate of 27% reinterventions per year. To eliminate this potential late limitation of permanent metallic DES, bioresorbable coronary stents or 'vascular scaffolds' (BVS) have been developed. In a parallel publication in this journal, an overview of the current clinical performance of these scaffolds is presented. As these scaffolds are currently CE marked and commercially available in many countries and as clinical evidence is still limited, recommendations for their general usage are needed to allow successful clinical introduction.

*impactfactor:* 1.837

## **Koolen JJ**

### **Bioresorbable vascular scaffold treatment induces the formation of neointimal cap that seals the underlying plaque without compromising the luminal dimensions: a concept based on serial optical coherence tomography data**

Bourantas CV, Serruys PW, Nakatani S, Zhang YJ, Farooq V, Diletti R, Ligthart J, Sheehy A, van Geuns RJ, McClean D, Chevalier B, Windecker S, Koolen J\*, Ormiston J, Whitbourn R, Rapoza R, Veldhof S, Onuma Y, Garcia-Garcia HM

EuroIntervention. 2015 Nov 22;11(8):746-56

**Aims:** To evaluate the implications of an Absorb bioresorbable vascular scaffold (Absorb BVS) on the morphology of the superficial plaques. **Methods and results:** Forty-six patients who underwent Absorb BVS implantation and 20 patients implanted with bare metal stents (BMS) who had serial optical coherence tomographic examination at baseline and follow-up were included in this analysis. The thin-capped fibroatheromas (TCFA) were identified in the device implantation regions and in the adjacent native coronary segments. Within all regions, circumferential locations of TCFA and calcific tissues were identified, and the neointimal thickness was measured at follow-up. At six to 12-month follow-up, only 8% of the TCFA detected at baseline were still present in the Absorb BVS and 27% in the BMS implantation segment ( $p=0.231$ ). Sixty percent of the TCFA in native segments did not change their phenotype at follow-up. At short-term follow-up, significant reduction in the lumen area of the BMS was noted, which was higher compared to that reported in the Absorb BVS group ( $-2.11\pm 1.97$  mm<sup>2</sup> vs.  $-1.34\pm 0.99$  mm<sup>2</sup>,  $p=0.026$ ). In Absorb BVS, neointima tissue continued to develop at midterm follow-up ( $2.17\pm 0.48$  mm<sup>2</sup> vs.  $1.38\pm 0.52$  mm<sup>2</sup>,  $p<0.0001$ ) and covered the underlying tissues without compromising the luminal dimensions ( $5.93\pm 1.49$  mm<sup>2</sup> vs.  $6.14\pm 1.49$  mm<sup>2</sup>,  $p=0.571$ ) as it was accommodated by the expanded scaffold ( $8.28\pm 1.74$  mm<sup>2</sup> vs.  $7.67\pm 1.28$  mm<sup>2</sup>,  $p<0.0001$ ). **Conclusions:** Neointimal tissue develops following either Absorb BVS or BMS implantation and shields lipid tissues. The neointimal response in the BMS causes a higher reduction of luminal dimensions compared to the Absorb BVS. Thus, Absorb BVS may have a value in the invasive re-capping of high-risk plaques.

*impactfactor:* 3.769

**Koolen JJ**

**Three-year clinical outcome in the Primary Stenting of Totally Occluded Native Coronary Arteries III (PRISON III) trial: a randomised comparison between sirolimus-eluting stent implantation and zotarolimus-eluting stent implantation for the treatment of total coronary occlusions**

Teeuwen K, Van den Branden BJ, Koolen JJ\*, van der Schaaf RJ, Henriques JP, Tijssen JG, Kelder JC, Vermeersch PH, Rensing BJ, Suttorp MJ

EuroIntervention. 2015 Mar;10(11):1272-5

Aims: Sirolimus-eluting stents (SES) have been shown to be superior to Endeavor zotarolimus-eluting stents (ZES) and comparable to Resolute ZES at eight-month angiography in patients treated for total coronary occlusions (TCO). This study investigated clinical outcome at three-year follow-up. Methods and results: The PRISON III trial investigated the efficacy and safety of SES against ZES (Endeavor and Resolute) in two study phases. In the first phase, 51 patients were randomised to receive SES and 46 to Endeavor ZES. In the second phase, 103 and 104 patients were randomised to SES or Resolute ZES, respectively. Between one and three years there were only a few additional clinical events in all groups. As a result, the rates of target lesion revascularisation 12.2% vs. 19.6%,  $p=0.49$ , target vessel failure 14.3% vs. 19.6%,  $p=0.68$ , and definite or probable stent thrombosis 4.1% vs. 2.2% were comparable between SES and Endeavor ZES at three years. In the second study phase, the rates of target lesion revascularisation 10% vs. 5.9%,  $p=0.42$ , target vessel failure 10% vs. 7.9%,  $p=0.79$  and definite or probable stent thrombosis 1.0% vs. 0% were similar between SES and Resolute ZES. Conclusions: The present study demonstrated a low incidence of clinical events between one- and three-year follow-up with either SES compared to Endeavor ZES or SES versus Resolute ZES in patients treated for total coronary occlusions.

*impactfactor:* 3.758

**Lenders G**

**Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie:* Cardiologie - van Nunen LX

*impactfactor:* 3.769

## **Lenders G**

### **The impact of downstream coronary stenosis on fractional flow reserve assessment of intermediate left main coronary artery disease: human validation**

Fearon WF, Yong AS, Lenders G\*, Toth GG, Dao C, Daniels DV, Pijls NH\*, De Bruyne  
BJACC Cardiovasc Interv. 2015 Mar;8(3):398-403

**OBJECTIVES:** The aim of this study was to determine the impact of downstream coronary stenosis in the left anterior descending coronary artery (LAD) or left circumflex coronary artery (LCx) on the assessment of fractional flow reserve (FFR) across an intermediate left main coronary artery (LMCA) stenosis in humans with the pressure wire positioned in the nondiseased downstream vessel.

**BACKGROUND:** Accurate assessment of intermediate LMCA disease is critical for guiding decisions regarding revascularization. In theory, FFR across an intermediate LMCA stenosis will be affected by downstream disease, even if the pressure wire is positioned in the nondiseased downstream vessel.

**METHODS:** After percutaneous coronary intervention of the LAD, LCx, or both, an intermediate LMCA stenosis was created with a deflated balloon catheter. FFR was measured in the LAD and LCx coronary arteries before and after creation of downstream stenosis by inflating an angioplasty balloon within the newly placed stent. The true FFR (FFR<sub>true</sub>) of the LMCA, measured in the nondiseased downstream vessel in the absence of stenosis in the other vessel, was compared with the apparent FFR (FFR<sub>app</sub>) measured in the presence of stenosis.

**RESULTS:** In 25 patients, 91 pairs of measurements were made, 71 with LAD stenosis and 20 with LCx stenosis. FFR<sub>true</sub> of the LMCA was significantly lower than FFR<sub>app</sub> ( $0.81 \pm 0.08$  vs.  $0.83 \pm 0.08$ ,  $p < 0.001$ ), although the numerical difference was small. This difference correlated with the severity of the downstream disease ( $r = 0.35$ ,  $p < 0.001$ ). In all cases in which FFR<sub>app</sub> was  $>0.85$ , FFR<sub>true</sub> was  $>0.80$ .

**CONCLUSIONS:** In most cases, downstream disease does not have a clinically significant impact on the assessment of FFR across an intermediate LMCA stenosis with the pressure wire positioned in the nondiseased vessel.

*impactfactor:* 7.345

## **Meijer A**

### **Low inappropriate shock rates in patients with single and dual/triple chamber ICDs using a novel suite of detection algorithms: PainFree SST Trial Primary Results**

Auricchio A, Schloss EJ, Kurita T, Meijer A\*, Gerritse B, Zweibel S, AlSmadi FM, Leng CT, Sterns LD; On behalf of the PainFree SST Investigators

Heart Rhythm. 2015 May;12(5):926-36. Epub 2015 Jan 28

**BACKGROUND:** The benefits of implantable cardioverter defibrillators (ICDs) have been well demonstrated in many clinical trials and ICD shocks for ventricular tachyarrhythmias save lives. However, inappropriate and unnecessary shock delivery remains a significant clinical issue with considerable consequences for patients and healthcare system.

**OBJECTIVE:** The PainFree SmartShock Technology (SST) study investigated a new generation ICDs to reduce inappropriate and unnecessary shocks through novel discrimination algorithms with modern programming strategies.

**METHODS:** This prospective, multicentre clinical trial enrolled 2,790 patients with approved indication for ICD implantation (79% male, mean age 65 years, 69% primary prevention indication, 27% single chamber ICD, 33% replacement or upgrade). Patients were followed for a minimum of 12 months and the mean follow-up was 22 months. The primary endpoint of the study was the percentage of patients remaining free of inappropriate shocks at 1 year

post implant, analysed separately for dual/triple-chamber (N=2,019) and single-chamber (N=751) ICDs.

**RESULTS:** The inappropriate shock rate at 1 year was 1.5% for patients with dual/triple chamber ICDs and 2.5% for patients with single chamber devices. Two years post implant, the inappropriate shock rate was 2.8% for patients with dual/triple chamber and 3.7% for those with single chamber ICD. The most common cause of an inappropriate shock in both groups was atrial fibrillation or flutter.

**CONCLUSION:** In a large patient cohort receiving ICDs for primary or secondary prevention, the adoption of novel enhanced detection algorithms in conjunction with routine implementation of modern programming strategies led to a very low inappropriate shock rate.

*impactfactor:* 5.076

### **Nunen LX van**

#### **Broad, broader, broadest**

van Nunen LX\*, Dello SA, Dekker LR\*

Neth Heart J. 2015 May;23(5):285-6, 289

*Geen abstract beschikbaar*

*impactfactor:* 1.837

### **Nunen LX van**

#### **Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial**

Zimmermann FM\*, Ferrara A, Johnson NP, van Nunen LX\*, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR, van Schaardenburgh P, Bech GJ, De Bruyne B, Pijls NH\*

Eur Heart J. 2015 Dec 1;36(45):3182-8. Epub 2015 Sep 23

*Voor abstract zie: Cardiologie - Zimmermann FM*

*impactfactor:* 15.203

### **Nunen LX van**

#### **Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial**

van Nunen LX\*, Zimmermann FM\*, Tonino PA\*, Barbato E, Baumbach A, Engstrøm T, Klauss V, McCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M\*, Fearon WF, De Bruyne B, Pijls NH\*; FAME Study Investigators

Lancet. 2015 Nov 7;386(10006):1853-60. Epub 2015 Aug 30

**BACKGROUND:** In the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study, fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) improved outcome compared with angiography-guided PCI for up to 2 years of follow-up. The aim in this study was to investigate whether the favourable clinical outcome with the FFR-guided PCI in the FAME study persisted over a 5-year follow-up.

**METHODS:** The FAME study was a multicentre trial done in Belgium, Denmark, Germany, the Netherlands, Sweden, the UK, and the USA. Patients (aged  $\geq 18$  years) with multivessel coronary artery disease were randomly assigned to undergo angiography-guided PCI or FFR-guided PCI. Before randomisation, stenoses requiring PCI were identified on the angiogram. Patients allocated to angiography-guided PCI had revascularisation of all identified stenoses.

Patients allocated to FFR-guided PCI had FFR measurements of all stenotic arteries and PCI was done only if FFR was 0.80 or less. No one was masked to treatment assignment. The primary endpoint was major adverse cardiac events at 1 year, and the data for the 5-year follow-up are reported here. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00267774.

**FINDINGS:** After 5 years, major adverse cardiac events occurred in 31% of patients (154 of 496) in the angiography-guided group versus 28% (143 of 509 patients) in the FFR-guided group (relative risk 0.91, 95% CI 0.75-1.10;  $p=0.31$ ). The number of stents placed per patient was significantly higher in the angiography-guided group than in the FFR-guided group (mean 2.7 [SD 1.2] vs 1.9 [1.3],  $p<0.0001$ ).

**INTERPRETATION:** The results confirm the long-term safety of FFR-guided PCI in patients with multivessel disease. A strategy of FFR-guided PCI resulted in a significant decrease of major adverse cardiac events for up to 2 years after the index procedure. From 2 years to 5 years, the risks for both groups developed similarly. This clinical outcome in the FFR-guided group was achieved with a lower number of stented arteries and less resource use. These results indicate that FFR guidance of multivessel PCI should be the standard of care in most patients.

*impactfactor:* 45.217

#### **Nunen LX van**

##### **Fractional flow reserve, maximum hyperemia, adenosine, and regadenoson**

Pijls NH\*, van Nunen LX\*

Cardiovasc Revasc Med. 2015 Jul-Aug;16(5):263-5

Comment on: Pooled comparison of regadenoson versus adenosine for measuring fractional flow reserve and coronary flow in the catheterization laboratory. [Cardiovasc Revasc Med. 2015]

*Geen abstract beschikbaar*

*impactfactor:* 1.411

#### **Nunen LX van**

##### **Intra-aortic balloon counterpulsation reduces mortality in large anterior myocardial infarction complicated by persistent ischaemia: a CRISP-AMI substudy**

van Nunen LX\*, van 't Veer M\*, Schampaert S\*, Rutten MC, van de Vosse FN, Patel MR, Pijls NH\*

EuroIntervention. 2015 Jul;11(3):286-92

**Aims:** This substudy investigated IABP support in large STEMI complicated by persistent ischaemia within the original CRISP-AMI trial. **Methods and results:** Patients were included if the ECG at admission showed summed ST deviation (SST-D)  $\geq 15$  mm and the ECG post PCI showed poor ST resolution ( $<50\%$ ). Endpoints evaluated were all-cause mortality at six months and the composite endpoint of death, cardiogenic shock or new or worsening heart failure at six months. One hundred and forty-nine patients had SST-D  $\geq 15$  mm (mean SST-D  $24 \pm 8$  mm). Of these patients, 36 (24%) showed poor ST resolution (15 patients in the IABP group; 21 patients in the control group). Mean age was  $55 \pm 11$  years, 89% were male. Mean systolic and diastolic blood pressures were  $135 \pm 31$  mmHg and  $83 \pm 22$  mmHg, respectively. The left anterior descending coronary artery was the infarct-related artery in all cases, primary PCI was successful in 94%. At six months, zero patients in the IABP group died versus five patients in the control group (0% versus 24%;  $p=0.046$ ). There was a trend towards statistical significance in the composite endpoint (one patient [7%] versus seven patients

[33%];  $p=0.06$ ). Conclusions: In this substudy, use of IABP was associated with decreased six-month mortality in large STEMI complicated by persistent ischaemia after PCI.

*impactfactor:* 3.769

#### **Nunen LX van**

##### **Intra-Aortic Balloon Pump Support in the Isolated Beating Porcine Heart in Nonischemic and Ischemic Pump Failure**

Schampaert S\*, van Nunen LX\*, Pijls NH\*, Rutten MC, van Tuijl S, van de Vosse FN, van 't Veer M\*

Artif Organs. 2015 Nov;39(11):931-8

*Voor abstract zie: Cardiologie - Schampaert S*

*impactfactor:* 2.050

#### **Nunen LX van**

##### **Reply**

van Nunen LX, Tonino PA

Herz. 2015 May;40(3):453-4.

Comment on: Recent insights into the treatment of stable CAD : FFR-guided PCI vs. medical therapy. [Herz. 2013]

Noninvasive fractional flow reserve measurement in stable CAD. [Herz. 2015]

*Geen abstract beschikbaar*

*impactfactor:* 0.690

#### **Nunen LX van**

##### **Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

**Aims:** The aim of this study was to compare the hyperaemic effect of a single bolus regadenoson injection to a central venous adenosine infusion for inducing hyperaemia in the measurement of fractional flow reserve (FFR). **Methods and results:** One hundred patients scheduled for FFR measurement were enrolled. FFR was first measured by IV adenosine (140 µg/kg/min), thereafter by IV bolus regadenoson injection (400 µg), followed by another measurement by IV adenosine and bolus injection of regadenoson. The regadenoson injections were randomised to central or peripheral intravenous. Hyperaemic response and duration of steady state maximum hyperaemia were studied, central versus peripheral venous regadenoson injections were compared, and safety and reproducibility of repeated injections were investigated. Mean age was 66±8 years, 75% of the patients were male. The target stenosis was located in the LM, LAD, LCX, and RCA in 7%, 54%, 20% and 19%, respectively. There was no difference in FFR measured by adenosine or by regadenoson (?FFR=0.00±0.01,  $r=0.994$ ,  $p<0.001$ ). Duration of maximum hyperaemia after regadenoson was variable (10-600 s). No serious side effects of either drug were observed. **Conclusions:** Maximum coronary hyperaemia can be achieved easily, rapidly, and safely by one single intravenous bolus of regadenoson administered either centrally or peripherally. Repeated regadenoson injections are safe. The hyperaemic plateau is variable.

*impactfactor:* 3.769

**Nunen LX van**

**Variability of fractional flow reserve according to the methods of hyperemia induction**

Lim WH, Koo BK, Nam CW, Doh JH, Park JJ, Yang HM, Park KW, Kim HS, Takashima H, Waseda K, Amano T, Kato D, Kurita A, Oi M, Toyofuku M, van Nunen L\*, Pijls NH\*

Catheter Cardiovasc Interv. 2015 May;85(6):970-6. Epub 2014 Dec 2

**OBJECTIVES:** We performed this study to evaluate the variability of fractional flow reserve (FFR) values which were measured from various methods of hyperemia induction.

**BACKGROUND:** Concerns have been raised regarding the variability of FFR due to different routes for hyperemic agent administration and different hyperemic agents targeting different receptors to induce maximal hyperemia.

**METHODS:** A total of 656 intermediate coronary lesions from 628 patients with coronary artery disease were analyzed. Among them, 238 lesions underwent FFR measurement with hyperemia induced by both intravenous (IV) and intracoronary (IC) adenosine administration, 318 by IV adenosine/adenosine triphosphate (ATP) and IC nicorandil injection, and 100 by IV adenosine and regadenoson infusion.

**RESULTS:** Excellent correlation and close classification agreement ( $\text{FFR} = 0.80$ ) were observed between IV vs. IC adenosine ( $r = 0.980$ ,  $\text{CA} = 92.9\%$ , Cohen's Kappa  $= 0.887$ ,  $P < 0.001$ ), between IV adenosine/ATP vs. IC nicorandil ( $r = 0.962$ ,  $\text{CA} = 91.2\%$ , Cohen's Kappa  $= 0.817$ ,  $P < 0.001$ ), and between IV adenosine vs. regadenoson ( $r = 0.990$ ,  $\text{CA} = 100\%$ , Cohen's Kappa  $= 1.000$ ,  $P < 0.001$ ). When changes in blood pressure ( $\Delta\text{BP}$ ) or heart rate ( $\Delta\text{HR}$ ) were compared with changes in FFR ( $\Delta\text{FFR}$ ) between IV adenosine/ATP and IC nicorandil administration, there were no significant correlations between  $\Delta\text{BP}$  and  $\Delta\text{FFR}$  nor between  $\Delta\text{HR}$  and  $\Delta\text{FFR}$  ( $r = -0.122$ ,  $P = 0.076$ ;  $r = 0.036$ ,  $P = 0.605$ , respectively).

**CONCLUSIONS:** This study suggests that the measurement of FFR is reproducible regardless of the hemodynamic changes, hyperemic agents used, or the route of administration.

*impactfactor:* 2.107

**Peels CH**

**Uncertainties in insurances for adults with congenital heart disease**

Sluman MA, Apers S, Bouma BJ, van Melle JP, Peels CH\*, Post MC, Waskowsky WM, Moons P, Mulder BJ

Int J Cardiol. 2015;186:93-5. Epub 2015 Mar 18

*Geen abstract beschikbaar*

*impactfactor:* 4.036

**Pijls NH**

**Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial**

Zimmermann FM\*, Ferrara A, Johnson NP, van Nunen LX\*, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR, van Schaardenburgh P, Bech GJ, De Bruyne B, Pijls NH\*

Eur Heart J. 2015 Dec 1;36(45):3182-8. Epub 2015 Sep 23

*Voor abstract zie: Cardiologie - Zimmermann FM*

*impactfactor:* 15.203

**Pijls NH**

**Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial**

van Nunen LX\*, Zimmermann FM\*, Tonino PA\*, Barbato E, Baumbach A, Engstrøm T, Klauss V, MacCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M\*, Fearon WF, De Bruyne B, Pijls NH\*; FAME Study Investigators  
Lancet. 2015 Nov 7;386(10006):1853-60. Epub 2015 Aug 3

Voor abstract zie: *Cardiologie - Nunen LX van*  
impactfactor: 45.217

**Pijls NH**

**Fractional flow reserve, maximum hyperemia, adenosine, and regadenoson**

Pijls NH\*, van Nunen LX\*

Cardiovasc Revasc Med. 2015 Jul-Aug;16(5):263-5

Comment on: Pooled comparison of regadenoson versus adenosine for measuring fractional flow reserve and coronary flow in the catheterization laboratory. [Cardiovasc Revasc Med. 2015]

Geen abstract beschikbaar  
impactfactor: 1.411

**Pijls NH**

**Intra-aortic balloon counterpulsation reduces mortality in large anterior myocardial infarction complicated by persistent ischaemia: a CRISP-AMI substudy**

van Nunen LX\*, van 't Veer M\*, Schampaert S\*, Rutten MC, van de Vosse FN, Patel MR, Pijls NH\*

EuroIntervention. 2015 Jul;11(3):286-92

Voor abstract zie: *Cardiologie - van Nunen LX*  
impactfactor: 3.769

**Pijls NH**

**Intra-Aortic Balloon Pump Support in the Isolated Beating Porcine Heart in Nonischemic and Ischemic Pump Failure**

Schampaert S\*, van Nunen LX\*, Pijls NH\*, Rutten MC, van Tuijl S, van de Vosse FN, van 't Veer M\*

Artif Organs. 2015 Nov;39(11):931-8

Voor abstract zie: *Cardiologie - Schampaert S*  
impactfactor: 2.050

**Pijls NH**

**Noninvasive Fractional Flow Reserve Derived From Coronary CT Angiography: Clinical Data and Scientific Principles**

Min JK, Taylor CA, Achenbach S, Koo BK, Leipsic J, Nørgaard BL, Pijls NJ\*, De Bruyne B  
JACC Cardiovasc Imaging. 2015 Oct;8(10):1209-22

Fractional flow reserve derived from coronary computed tomography angiography enables noninvasive assessment of the hemodynamic significance of coronary artery lesions and coupling of the anatomic severity of a coronary stenosis with its physiological effects. Since



its initial demonstration of feasibility of use in humans in 2011, a significant body of clinical evidence has developed to evaluate the diagnostic performance of coronary computed tomography angiography-derived fractional flow reserve compared with an invasive fractional flow reserve reference standard. The purpose of this paper was to describe the scientific principles and to review the clinical data of this technology recently approved by the U.S. Food and Drug Administration.

*impactfactor:* 7.188

## **Pijls NH**

### **Rationale and design of the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) 3 Trial: A comparison of fractional flow reserve-guided percutaneous coronary intervention and coronary artery bypass graft surgery in patients with multivessel coronary artery disease**

Zimmermann FM\*, De Bruyne B, Pijls NH\*, Desai M, Oldroyd KG, Park SJ, Reardon MJ, Wendler O, Woo J, Yeung AC, Fearon WF

Am Heart J. 2015 Oct;170(4):619-626.e2

**Abstract:** Guidelines recommend coronary artery bypass graft (CABG) surgery over percutaneous coronary intervention (PCI) for the treatment of 3-vessel coronary artery disease (3-VD). The inferior results of PCI demonstrated by previous large randomized trials comparing PCI and CABG might be explained by the use of suboptimal stent technology and by the lack of fractional flow reserve (FFR) guidance of PCI.

**TRIAL DESIGN:** The objective of this investigator-initiated, multicenter, randomized clinical trial is to investigate whether FFR-guided PCI with new-generation stents is noninferior to CABG in patients with 3-VD, not including the left main coronary artery. Eligible patients must have ≥50% coronary stenoses in all 3 major epicardial vessels or major side branches. Patients with a nondominant right coronary artery may be included only if the left anterior descending artery and left circumflex have ≥50% stenoses. Consecutive patients who meet all of the inclusion criteria and none of the exclusion criteria will be randomized in a 1:1 fashion to either CABG or FFR-guided PCI. Coronary artery bypass graft will be performed based on the angiogram as per clinical routine. Patients assigned to FFR-guided PCI will have FFR measured in each diseased vessel and only undergo stenting if the FFR is ≤0.80. The primary end point of the study is a composite of major adverse cardiac and cerebrovascular events, including death, myocardial infarction, repeat coronary revascularization, and stroke at 1 year. Key secondary end point will be a composite of death, myocardial infarction, and stroke at 3-year follow-up. Other secondary end points include the individual adverse events, cost-effectiveness, and quality of life at 2-year, 3-year, with up to 5-year follow-up.

**CONCLUSION:** The FAME 3 study will compare in a multicenter, randomized fashion FFR-guided PCI with contemporary drug-eluting stents to CABG in patients with 3-VD.

*impactfactor:* --

## **Pijls NH**

### **Repeatability of Fractional Flow Reserve Despite Variations in Systemic and Coronary Hemodynamics**

Johnson NP, Johnson DT, Kirkeeide RL, Berry C, De Bruyne B, Fearon WF, Oldroyd KG, Pijls NH\*, Gould KL

JACC Cardiovasc Interv. 2015 Jul;8(8):1018-27

**OBJECTIVES:** This study classified and quantified the variation in fractional flow reserve (FFR) due to fluctuations in systemic and coronary hemodynamics during intravenous adenosine

infusion.

**BACKGROUND:** Although FFR has become a key invasive tool to guide treatment, questions remain regarding its repeatability and stability during intravenous adenosine infusion because of systemic effects that can alter driving pressure and heart rate.

**METHODS:** We reanalyzed data from the VERIFY (VERification of Instantaneous Wave-Free Ratio and Fractional Flow Reserve for the Assessment of Coronary Artery Stenosis Severity in Everyday Practice) study, which enrolled consecutive patients who were infused with intravenous adenosine at 140 µg/kg/min and measured FFR twice. Raw phasic pressure tracings from the aorta (Pa) and distal coronary artery (Pd) were transformed into moving averages of Pd/Pa. Visual analysis grouped Pd/Pa curves into patterns of similar response. Quantitative analysis of the Pd/Pa curves identified the "smart minimum" FFR using a novel algorithm, which was compared with human core laboratory analysis.

**RESULTS:** A total of 190 complete pairs came from 206 patients after exclusions. Visual analysis revealed 3 Pd/Pa patterns: "classic" (sigmoid) in 57%, "humped" (sigmoid with superimposed bumps of varying height) in 39%, and "unusual" (no pattern) in 4%. The Pd/Pa pattern repeated itself in 67% of patient pairs. Despite variability of Pd/Pa during the hyperemic period, the "smart minimum" FFR demonstrated excellent repeatability (bias - 0.001, SD 0.018, paired  $p = 0.93$ ,  $r(2) = 98.2\%$ , coefficient of variation = 2.5%). Our algorithm produced FFR values not significantly different from human core laboratory analysis (paired  $p = 0.43$  vs. VERIFY;  $p = 0.34$  vs. RESOLVE).

**CONCLUSIONS:** Intravenous adenosine produced 3 general patterns of Pd/Pa response, with associated variability in aortic and coronary pressure and heart rate during the hyperemic period. Nevertheless, FFR - when chosen appropriately - proved to be a highly reproducible value. Therefore, operators can confidently select the "smart minimum" FFR for patient care. Our results suggest that this selection process can be automated, yet comparable to human core laboratory analysis.

*impactfactor: 7.345*

## **Pijls NH**

### **Reply: True Fractional Flow Reserve of Left Main Coronary Artery Stenosis in the Presence of Downstream Coronary Stenoses**

Fearon WF, Yong AS, Lenders G, Toth GG, Dao C, Daniels DV, Pijls NH\*, De Bruyne B  
JACC Cardiovasc Interv. 2015 Aug 17;8(9):1273

Comment on: True Fractional Flow Reserve of Left Main Coronary Artery Stenosis in the Presence of Downstream Coronary Stenoses. [JACC Cardiovasc Interv. 2015]

The impact of downstream coronary stenosis on fractional flow reserve assessment of intermediate left main coronary artery disease: human validation. [JACC Cardiovasc Interv. 2015]

*Geen abstract beschikbaar*

*impactfactor: 7.345*

**Pijls NH**

**Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie: Cardiologie - van Nunen LX*

*impactfactor: 3.769*

**Pijls NH**

**The impact of downstream coronary stenosis on fractional flow reserve assessment of intermediate left main coronary artery disease: human validation**

Fearon WF, Yong AS, Lenders G\*, Toth GG, Dao C, Daniels DV, Pijls NH\*, De Bruyne B

JACC Cardiovasc Interv. 2015 Mar;8(3):398-403

*Voor abstract zie: Cardiologie - Lenders G*

*impactfactor: 7.345*

**Pijls NH**

**The impact of left ventricular ejection fraction on fractional flow reserve: Insights from the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) trial**

Kobayashi Y, Tonino PA\*, De Bruyne B, Yang HM, Lim HS, Pijls NH\*, Fearon WF; FAME Study Investigators

Int J Cardiol. 2015 Nov 27;204:206-210.

*Voor abstract zie: Cardiologie - Tonino WA*

*impactfactor: 4.036*

**Pijls NH**

**The Impact of Processes of Care on Myocardial Infarct Size in Patients With ST-Segment Elevation Myocardial Infarction: Observations From the CRISP-AMI Trial**

Jones WS, Clare RM, Chiswell K, Perera D, French JK, Kumar AS, Blaxill J, Pijls N\*, Mills J, Ohman EM, Patel MR

Clin Cardiol. 2015 Jan;38(1):25-31. Epub 2014 Dec 8

**BACKGROUND:** Primary percutaneous coronary intervention (PCI) is the most common method of reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) in the United States. The intersection between processes of care and performance measures such as door-to-balloon (D2B) times and clinical trials evaluating novel therapies for STEMI has not been fully investigated.

**HYPOTHESIS:** Processes of STEMI care, incorporating clinical trial enrollment and randomization, in patients undergoing reperfusion with primary PCI in the Counterpulsation Reduces Infarct Size Pre-Percutaneous Coronary Intervention Acute Myocardial Infarction trial (CRISP-AMI) will conform to current standards of care.

**METHODS:** Patients enrolled in CRISP-AMI were included in the current analysis. Processes of care during reperfusion were recorded prospectively and compared between groups.

**RESULTS:** A total of 337 patients with anterior STEMI without cardiogenic shock were randomized in CRISP-AMI. Complete processes-of-care data were available for 303 patients

(89.9%). In this cohort, 68.0% of patients underwent reperfusion within 90 minutes of hospital contact, and the median D2B time was 71 minutes. Time from hospital contact to informed consent was significantly different across different regions (North America, 45 minutes; India, 35 minutes; Europe, 20 minutes).

**CONCLUSIONS:** In CRISP-AMI, reperfusion was accomplished in a timely fashion while incorporating informed consent and randomization among patients with anterior myocardial infarction. Further study of patients' comprehension and preferences during the informed-consent process in STEMI patients is warranted so that innovative drugs and devices can be safely and ethically tested.

*impactfactor:* 2.151

## **Pijls NH**

### **Variability of fractional flow reserve according to the methods of hyperemia induction**

Lim WH, Koo BK, Nam CW, Doh JH, Park JJ, Yang HM, Park KW, Kim HS, Takashima H, Waseda K, Amano T, Kato D, Kurita A, Oi M, Toyofuku M, van Nunen L\*, Pijls NH\*

Catheter Cardiovasc Interv. 2015 May;85(6):970-6.Epub 2014 Dec 2

**OBJECTIVES:** We performed this study to evaluate the variability of fractional flow reserve (FFR) values which were measured from various methods of hyperemia induction.

**BACKGROUND:** Concerns have been raised regarding the variability of FFR due to different routes for hyperemic agent administration and different hyperemic agents targeting different receptors to induce maximal hyperemia.

**METHODS:** A total of 656 intermediate coronary lesions from 628 patients with coronary artery disease were analyzed. Among them, 238 lesions underwent FFR measurement with hyperemia induced by both intravenous (IV) and intracoronary (IC) adenosine administration, 318 by IV adenosine/adenosine triphosphate (ATP) and IC nicorandil injection, and 100 by IV adenosine and regadenoson infusion.

**RESULTS:** Excellent correlation and close classification agreement (FFR?=0.80) were observed between IV vs. IC adenosine ( $r=0.980$ ,  $CA=92.9\%$ , Cohen's Kappa?=0.887,  $P<0.001$ ), between IV adenosine/ATP vs. IC nicorandil ( $r=0.962$ ,  $CA=91.2\%$ , Cohen's Kappa?=0.817,  $P<0.001$ ), and between IV adenosine vs. regadenoson ( $r=0.990$ ,  $CA=100\%$ , Cohen's Kappa?=1.000,  $P<0.001$ ). When changes in blood pressure (?BP) or heart rate (?HR) were compared with changes in FFR (?FFR) between IV adenosine/ATP and IC nicorandil administration, there were no significant correlations between ?BP and ?FFR nor between ?HR and ?FFR ( $r=-0.122$ ,  $P=0.076$ ;  $r=0.036$ ,  $P=0.605$ , respectively).

**CONCLUSIONS:** This study suggests that the measurement of FFR is reproducible regardless of the hemodynamic changes, hyperemic agents used, or the route of administration.

*impactfactor:* 2.107

## **Ponten JE**

### **A consecutive series of 235 epigastric hernias**

Ponten JE\*, Leenders BJ, Charbon JA, Nienhuijs SW\*

Hernia. 2015 Oct;19(5):821-5. Epub 2014 Feb 12

**BACKGROUND:** Epigastric herniation is a common, though not always symptomatic condition. It is likely, that in accordance to the tension-free principles for other hernias, epigastric hernia repair should be mesh based.

**METHODS:** Patients from two large hospitals were investigated retrospectively if they were operated on an epigastric hernia for the past 6 years. Follow-up was completed with a postal questionnaire.

RESULTS: A total of 235 patients (50 % male) were operated. Sixty-eight patients were operated with mesh and 167 patients with suture repair. Forty-six patients were loss-to follow-up (19.6 %). In the mesh operated patients the recurrence rate was 10.9 % (n = 6) compared to 14.9 % (n = 20) in the suture repair group. Cox-regression analysis showed an increased risk for recurrence in the suture repair group (odds ratio 1.43; 95 % CI 0.56-3.57; p = 0.44). Operation time for mesh repair (47 min) was significantly longer compared to suture repair (29 min) (p < 0.0001). Thirty-seven patients had previous or other anterior wall hernias. A total of 51 patients smoked and 14 patients had diabetes mellitus. Fourteen patients used steroids and 22 patients suffered from a chronic lung disease. Subgroup analysis showed a significant difference for pain in patients in which re-operation for a recurrence occurred (p = 0.004).

CONCLUSIONS: This is one of the largest reported series on solely epigastric hernias. A recurrence occurred more often after sutured repair compared to mesh repair. No differences in chronic pain was seen between mesh and suture repaired patients. Male:female ratio of 1:1, which is different from the 3:1 ratio found in previous older smaller studies, could be more reliable.

impactfactor: 2.050

## Ponten JE

### Hiatal Hernia

Castelijns B\*, Ponten JE\*, Van de Poll MC, Nienhuijs SW\*, Smulders JF\*, Hu ZW, Wu JM, Wang ZG, Idani H, Asami S, Nakano K, Miyake S, Harano M, Miyoshi H, Araki H, Ogawa T, Takahashi K, Shiozaki S, Ninomiya M, Prasad A, Todkar J, Asti E, Lovece A, Sironi A, Bonavina , Wright , Wurst H, Zhang C, Li HL, Ke LM, Loi K12, Hua R, Yao QY, Chen H, Okinyi W, Odende K, Ndungu B, Ndonga A, Kiragu P, Kelimu A, Alimujiang M, Tian W, Bing M

Hernia. 2015 Apr;19 Suppl 1:S13-7

Geen abstract beschikbaar

impactfactor: 2.050

## Ponten JE

### Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruyt PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22.

Voor abstract zie: Chirurgie - Nienhuijs SW

impactfactor: 45.217

## Ponten JE

### Topic: Rare and Special Cases, The Real "Strange Cases".

Zarrinkhoo E, Miller J, Walker A, Weisman M, Towfigh S, Tushev R, Petkov I, Tsutsumi G, Leija C, Castillo E, Moncada F, Mendoza M, Morua AG, Bravo R, Azcarate A, Zavala H, Coman IS, Radu EV, David OI, Stoian AR, Strambu VE, Iancu C, Gheorghiu LI, Grigorean VT, Sinescu DR, Plesa E, Lupascu C, Straja DN, Iacobini MA, Ponten J, Luyer M,

Nienhuijs S, Permekerlis A, Petousis S, Miroforidis A, Miliadis K, Kouridakis P, Park J, Kim D, Nakata R, Chihara N, Suzuki H, Watanabe M, Uchida E, Nakanaga H, Irie S, Endo Y, Sonoda H, Minamimura K, Kobayashi T, Hirata T, Mafune K, Milosevic P, Babovic M, Sorat D, Light D, Aawsaj Y, Horgan L, Latham L, Ceriani I, Livraghi L, Berselli M, Gambitta B, Galvanin J, Cotronea C, Pagano G, Farassino L, Ambrosoli A, Crespi A, Coccozza E, Kulic V, Matkovic M, Percevic G, Katayama T, Kumata Y, Ogawa E, Horikawa M, Yaguchi Y, Inaba T, Fukushima R, Jaroszewski D, Johnson K, Harold K, Mori M, Kumata M, Guarnieri F, Smaldone W, Gaspard M, Bomben F, Ceranto S, Gamarra MF, Soria MP, Olivero CF, Martinez MJ, Contin MP, Gómez JC, Jiménez-Valladolid D, Torres García A, Descloux A, Pohle S, Schramm B, Schneider U, Nocito A, Navarrete MC, Solis A, Ortega N, Bergamini S, Semeraro C, Armengol M, Cano ML, Torrecilla NO, Cavallaro G, Iorio O, Avallone M, Ruscio S, Rizzello M, Silecchia G, Butron T, Rubio E, Passas J, Sopeña R, Lagaron E, Silan F, Garcia V, Bernal J, Ortiz M, Guadarrama J, Shirai K, Lomas M, Shah BB, Degloorkar SS.

Hernia. 2015 Apr;19 Suppl 1:S317-27

*geen abstract beschikbaar*

*impactfactor:* 2.050

## Schampaert S

### **Intra-aortic balloon counterpulsation reduces mortality in large anterior myocardial infarction complicated by persistent ischaemia: a CRISP-AMI substudy**

van Nunen LX\*, van 't Veer M\*, Schampaert S\*, Rutten MC, van de Vosse FN, Patel MR, Pijls NH\*

EuroIntervention. 2015 Jul;11(3):286-92

*Voor abstract zie: Cardiologie - van Nunen LX*

*impactfactor:* 3.769

## Schampaert S

### **Intra-Aortic Balloon Pump Support in the Isolated Beating Porcine Heart in Nonischemic and Ischemic Pump Failure**

Schampaert S\*, van Nunen LX\*, Pijls NH\*, Rutten MC, van Tuijl S, van de Vosse FN, van 't Veer M\*

Artif Organs. 2015 Nov;39(11):931-8

The blood pressure changes induced by the intra-aortic balloon pump (IABP) are expected to create clinical improvement in terms of coronary perfusion and myocardial oxygen consumption. However, the measured effects reported in literature are inconsistent. The aim of this study was to investigate the influence of ischemia on IABP efficacy in healthy hearts and in shock. Twelve slaughterhouse porcine hearts (hearts 1-12) were connected to an external circulatory system, while physiologic cardiac performance was restored. Different clinical scenarios, ranging from healthy to cardiogenic shock, were simulated by step-wise administration of negative inotropic drugs. In hearts 7-12, severe global myocardial ischemia superimposed upon the decreased contractile states was created. IABP support was applied in all hearts under all conditions. Without ischemia, the IABP induced a mild increase in coronary blood flow and cardiac output. These effects were strongly augmented in the presence of persisting ischemia, where coronary blood flow increased by  $49 \pm 24\%$  ( $P < 0.01$ ) and cardiac output by  $17 \pm 6\%$  ( $P < 0.01$ ) in case of severe pump failure. As expected, myocardial oxygen consumption increased in case of ischemia

( $21\pm 17\%$ ;  $P<0.01$ ), while it slightly decreased without ( $-3\pm 6\%$ ;  $P<0.01$ ). In case of progressive pump failure due to persistent myocardial ischemia, the IABP increased hyperemic coronary blood flow and cardiac output significantly, and reversed the progressive hemodynamic deterioration within minutes. This suggests that IABP therapy in acute myocardial infarction is most effective in patients with viable myocardium, suffering from persistent myocardial ischemia, despite adequate epicardial reperfusion.

*impactfactor:* 2.050

## **Schampaert S**

### **Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie:* van Nunen LX – Cardiology

*impactfactor:* 3.769

## **Simmers TA**

### **Early performance of a miniaturized leadless cardiac pacemaker: the Micra Transcatheter Pacing Study**

Ritter P, Duray GZ, Steinwender C, Soejima K, Omar R, Mont L, Boersma LV, Knops RE, Chinitz L, Zhang S, Narasimhan C, Hummel J, Lloyd M, Simmers TA\*, Voigt A, Laager V, Stromberg K, Bonner MD, Sheldon TJ, Reynolds D; Micra Transcatheter Pacing Study Group

Eur Heart J. 2015 Oct 1;36(37):2510-9. Epub 2015 Jun 4

**AIMS:** Permanent cardiac pacing is the only effective treatment for symptomatic bradycardia, but complications associated with conventional transvenous pacing systems are commonly related to the pacing lead and pocket. We describe the early performance of a novel self-contained miniaturized pacemaker.

**METHODS AND RESULTS:** Patients having Class I or II indication for VVI pacing underwent implantation of a Micra transcatheter pacing system, from the femoral vein and fixated in the right ventricle using four protractible nitinol tines. Prespecified objectives were  $>85\%$  freedom from unanticipated serious adverse device events (safety) and  $<2$  V 3-month mean pacing capture threshold at 0.24 ms pulse width (efficacy). Patients were implanted ( $n = 140$ ) from 23 centres in 11 countries (61% male, age  $77.0 \pm 10.2$  years) for atrioventricular block (66%) or sinus node dysfunction (29%) indications. During mean follow-up of  $1.9 \pm 1.8$  months, the safety endpoint was met with no unanticipated serious adverse device events. Thirty adverse events related to the system or procedure occurred, mostly due to transient dysrhythmias or femoral access complications. One pericardial effusion without tamponade occurred after 18 device deployments. In 60 patients followed to 3 months, mean pacing threshold was  $0.51 \pm 0.22$  V, and no threshold was  $\approx 2$  V, meeting the efficacy endpoint ( $P < 0.001$ ). Average R-wave was  $16.1 \pm 5.2$  mV and impedance was  $650.7 \pm 130$  ohms.

**CONCLUSION:** Early assessment shows the transcatheter pacemaker can safely and effectively be applied. Long-term safety and benefit of the pacemaker will further be evaluated in the trial.

*impactfactor:* 15.203

### **Simmers TA**

#### **Inappropriate shock because of triple counting in a patient with a subcutaneous implantable cardioverter defibrillator corrected by initiation of dual site left ventricular pacing**

van Gelder BM\*, Bracke FA\*, Simmers T\*

Circ Arrhythm Electrophysiol. 2015 Feb;8(1):239-40

*Geen abstract beschikbaar*

*impactfactor:* 4.513

### **Tonino WA**

#### **Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial**

van Nunen LX\*, Zimmermann FM\*, Tonino PA\*, Barbato E, Baumbach A, Engstrøm T, Klauss V, MacCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M\*, Fearon WF, De Bruyne B, Pijls NH\*; FAME Study Investigators

Lancet. 2015 Nov 7;386(10006):1853-60. Epub 2015 Aug 3

*Voor abstract zie: Cardiologie - Nunen LX van*

*impactfactor:* 45.217

### **Tonino WA**

#### **Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie: van Nunen LX – Cardiologie*

*impactfactor:* 3.769

### **Tonino WA**

#### **The impact of left ventricular ejection fraction on fractional flow reserve: Insights from the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) trial**

Kobayashi Y, Tonino PA\*, De Bruyne B, Yang HM, Lim HS, Pijls NH\*, Fearon WF; FAME Study Investigators

Int J Cardiol. 2015 Nov 27;204:206-210

**BACKGROUND:** Fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) significantly improves outcomes compared with angio-guided PCI in patients with multivessel coronary artery disease. However, there is a theoretical concern that in patients with reduced left ventricular ejection fraction (EF) FFR may be less accurate and FFR-guided PCI less beneficial.

**METHODS:** From the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) trial database, we compared FFR values between patients with reduced EF (both =40%, n=90 and =50%, n=252) and preserved EF (>40%, n=825 and >50%, n=663) according to the angiographic stenosis severity. We also compared differences in 1year outcomes between FFR- vs. angio-guided PCI in patients with reduced and preserved EF.



RESULTS: Both groups had similar FFR values in lesions with 50-70% stenosis ( $p=0.49$ ) and with 71-90% stenosis ( $p=0.89$ ). The reduced EF group had a higher mean FFR compared to the preserved EF group across lesions with 91-99% stenosis (0.55 vs. 0.50,  $p=0.02$ ), although the vast majority of FFR values remained  $\geq 0.80$ . There was a similar reduction in the composite end point of death, nonfatal myocardial infarction, and repeat revascularization with FFR-guided compared to angio-guided PCI for both the reduced (14.5% vs. 19.0%, relative risk=0.76,  $p=0.34$ ) and the preserved EF group (13.8 vs. 17.0%, relative risk=0.81,  $p=0.25$ ). The results were similar with an EF cutoff of 40%.

CONCLUSION: Reduced EF has no influence on the FFR value unless the stenosis is very tight, in which case a theoretically explainable, but clinically irrelevant overestimation might occur.

As a result, FFR-guided PCI remains beneficial regardless of EF.

impactfactor: 4.036

#### **Veer M van 't**

##### **Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial.**

van Nunen LX\*, Zimmermann FM\*, Tonino PA\*, Barbato E, Baumbach A, Engstrøm T, Klauss V, McCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M\*, Fearon WF, De Bruyne B, Pijls NH\*; FAME Study Investigators

Lancet. 2015 Nov 7;386(10006):1853-60. Epub 2015 Aug 3

Voor abstract zie: *Cardiologie - Nunen LX van*

impactfactor: 45.217

#### **Veer M van 't**

##### **Intra-aortic balloon counterpulsation reduces mortality in large anterior myocardial infarction complicated by persistent ischaemia: a CRISP-AMI substudy**

van Nunen LX\*, van 't Veer M\*, Schampaert S\*, Rutten MC, van de Vosse FN, Patel MR, Pijls NH\*

EuroIntervention. 2015 Jul;11(3):286-92

Voor abstract zie: *van Nunen LX – Cardiologie*

impactfactor: 3.769

#### **Veer M van 't**

##### **Intra-Aortic Balloon Pump Support in the Isolated Beating Porcine Heart in Nonischemic and Ischemic Pump Failure**

Schampaert S\*, van Nunen LX\*, Pijls NH\*, Rutten MC, van Tuijl S, van de Vosse FN, van 't Veer M\*

Artif Organs. 2015 Nov;39(11):931-8

Voor abstract zie: *Cardiologie - Schampaert S*

impactfactor: 2.050

**Veer M van 't**

**Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie: van Nunen LX – Cardiologie*

*impactfactor: 3.769*

**Veghel D van**

**Developing a research agenda on ethical issues related to using social media in healthcare**

Adams SA, Van Veghel D\*, Dekker L\*

Camb Q Healthc Ethics. 2015 Jul;24(3):293-302

The consequences of using publicly available social media applications specifically for healthcare purposes are largely unaddressed in current research. Where they are addressed, the focus is primarily on issues of privacy and data protection. We therefore use a case study of the first live Twitter heart operation in the Netherlands, in combination with recent literature on social media from other academic fields, to identify a wide range of ethical issues related to using social media for health-related purposes. Although this case reflects an innovative approach to public education and patient centeredness, it also illustrates the need for institutions to weigh the various aspects of use and to develop a plan to deal with these on a per case basis. Given the continual development of technologies, researchers may not yet be able to oversee and anticipate all of the potential implications. Further development of a research agenda on this topic, the promotion of guidelines and policies, and the publication of case studies that reveal the granularity of individual situations will therefore help raise awareness and assist physicians and institutions in using social media to support existing care services.

*impactfactor: 0.682*

**Vermeulen Windsant IC**

**Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S\*, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

*Voor abstract zie: Inwendige geneeskunde - Bie AJ de*

*impactfactor: 1.969*

**Vervaat FE**

**Is it possible to differentiate between Takotsubo cardiomyopathy and acute anterior ST-elevation myocardial infarction?**

Vervaat FE<sup>∞</sup>, Christensen TE, Smeijers L, Holmvang L, Hasbak P, Szabó BM, Widdershoven JW, Wagner GS, Bang LE, Gorgels AP.

J Electrocardiol. 2015 Jul-Aug;48(4):512-9. Epub 2015 Feb 20

INTRODUCTION: Several studies have investigated the ability of the twelve-lead electrocardiogram (ECG) to reliably distinguish Takotsubo cardiomyopathy (TC) from an

acute anterior ST-segment elevation myocardial infarction (STEMI). In these studies, only ECG changes were required - ST-segment deviation and/or T-wave inversion - in TC whereas in acute anterior STEMI, ECGs had to meet STEMI criteria. In the majority of these studies, patients of both genders were used even though TC predominantly occurs in women. The aim of this study is to see whether TC can be distinguished from acute anterior STEMI in a predominantly female study population where all patients meet STEMI-criteria.

**METHODS:** Retrospective analysis of the ST-segment changes was done on the triage ECGs of 37 patients with TC (34 female) and was compared to the triage ECGs of 103 female patients with acute anterior STEMI. The latter group was divided into the following subgroups: 46 patients with proximal, 47 with mid and 10 with distal LAD occlusion. Three ST-segment based ECG features were investigated: (1) Existing criterion for differentiating anterior STEMI from TC: ST-segment depression  $>0.5\text{mm}$  in lead aVR+ST-segment elevation  $\geq 1\text{mm}$  in lead V1, (2) frontal plane ST-vector and (3) mean amplitude of ST-segment deviation in each lead. **RESULTS:** The existing ECG criterion was less accurate (76%) than in the original study (95%), with a large difference in sensitivity (26% vs. 91%). Only a frontal plane ST-vector of  $60^\circ$  could significantly distinguish TC from all acute anterior STEMI subgroups ( $p<0.01$ ) with an overall diagnostic accuracy of 81%. The mean amplitude in inferior leads II and aVF was significantly higher for patients with TC compared to all patients with acute anterior STEMI ( $p<0.01$  and  $p<0.05$  respectively) and the mean amplitude in the precordial leads V1 and V2 was significantly lower compared to proximal and mid LAD occlusion ( $p<0.01$ ).

**CONCLUSIONS:** Given the consequences of missing the diagnosis of an acute anterior STEMI the diagnostic accuracy of the ECG criteria investigated in this retrospective study were insufficient to reliably distinguish patients with TC from patients with an acute anterior STEMI. To definitely exclude the diagnosis of an acute anterior STEMI coronary angiography, which remains the gold standard, will need to be performed.

$\infty$  = Ten tijde van publicatie werkzaam bij: Department of Cardiology, Maastricht University Medical Centre, the Netherlands.

impactfactor: 1.361

## Vervaat FE

### Using the triage twelve-lead electrocardiogram to differentiate between Takotsubo cardiomyopathy and acute anterior ST-elevation myocardial infarction

Vervaat FE\*

J Electrocardiol. 2015 Sep-Oct;48(5):916-7. Epub 2015 Jun 19

geen abstract beschikbaar

impactfactor: 1.361

## Voort PH van der

### Time Course of Atrial Fibrillation in Patients with Congenital Heart Defects

Teuwen CP, Ramdjan TT, Götte M, Brundel BJ, Evertz R, Vriend JW, Molhoek SG, Dorman HG, van Opstal JM, Konings TC, van der Voort P\*, Delacrétaz E, Houck C, Yaksh A, Jansz LJ, Witsenburg M, Roos-Hesselink JW, Triedman JK, Bogers AJ, de Groot NM  
Circ Arrhythm Electrophysiol. 2015 Oct;8(5):1065-72

**BACKGROUND:** -The incidence of atrial fibrillation (AF) is rising in the aging patients with congenital heart disease (CHD). However, studies reporting on AF in CHD patients are scarce. The aim of this multicenter study was to examine in a large cohort of patients with a variety of CHD 1) the age of onset and initial treatment of AF, co-existence of atrial tachyarrhythmia 2) progression of paroxysmal to (long-standing) persistent/permanent AF during long-term follow-up.

**METHODS AND RESULTS:** -Patients (N=199) with 15 different CHD and documented AF episodes were studied. AF developed at 49±17 years. Regular atrial tachycardia (AT) co-existing with AF occurred in 65 (33%) patients; 65% initially presented with regular AT. At the end of a follow-up period of 5 (0-24) years, the ECG showed AF in 81 patients (41%). In a subgroup of 114 patients, deterioration from paroxysm of AF to (long-standing) persistent/permanent AF was observed in 29 patients (26%) after only 3 (0-18) years of the first AF episode. Cerebrovascular accidents/transient ischemic attacks occurred in 26 patients (13%), although a substantial number (N=16) occurred before the first documented AF episode.

**CONCLUSIONS:** -Age at development of AF in CHD patients is relative young compared to patients without CHD. Co-existence of episodes of AF and regular AT occurred in a considerable number of patients; most of them initially presented with regular AT. The fast and frequent progression from paroxysmal to (long-standing) persistent or permanent AF episodes justifies close follow-up and early, aggressive therapy of both AT and AF.

*impactfactor:* 4.513

### **Wijnbergen I**

#### **Single bolus intravenous regadenoson injection versus central venous infusion of adenosine for maximum coronary hyperaemia in fractional flow reserve measurement**

van Nunen LX\*, Lenders GD\*, Schampaert S\*, van 't Veer M\*, Wijnbergen I\*, Brueren GR\*, Tonino PA\*, Pijls NH\*

EuroIntervention. 2015 Dec 22;11(8):905-13

*Voor abstract zie:* Cardiologie - van Nunen LX

*impactfactor:* 3.769

### **Zimmermann FM**

#### **Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial**

Zimmermann FM\*, Ferrara A, Johnson NP, van Nunen LX\*, Escaned J, Albertsson P, Erbel R, Legrand V, Gwon HC, Remkes WS, Stella PR, van Schaardenburgh P, Bech GJ, De Bruyne B, Pijls NH\*

Eur Heart J. 2015 Dec 1;36(45):3182-8. Epub 2015 Sep 23

**AIMS:** Stenting an angiographically intermediate but functionally non-significant stenosis is controversial. Nevertheless, it has been questioned if deferral of a functionally non-significant lesion on the basis of fractional flow reserve (FFR) measurement, is safe, especially on the long term. Five-year follow-up of the DEFER trial showed that outcome after deferral of percutaneous coronary intervention (PCI) of an intermediate coronary stenosis based on FFR = 0.75 is excellent and was not improved by stenting. The aim of this study was to investigate the validity of this position on the very long term.

**METHODS AND RESULTS:** In 325 patients scheduled for PCI of an intermediate stenosis, FFR was measured just before the planned intervention. If FFR was ≥0.75, patients were randomly assigned to deferral (Defer group; n = 91) or performance (Perform group; n = 90) of PCI. If FFR was <0.75, PCI was performed as planned (Reference group; n = 144). Clinical follow-up was 15 years. There were no differences in baseline clinical characteristics between the randomized groups. Complete 15-year follow-up was obtained in 92% of patients. After 15 years of follow-up, the rate of death was not different between the three groups: 33.0% in the Defer group, 31.1% in the Perform group, and 36.1% in the Reference

group (Defer vs. Perform, RR 1.06, 95% CI: 0.69-1.62, P = 0.79). The rate of myocardial infarction was significantly lower in the Defer group (2.2%) compared with the Perform group (10.0%), RR 0.22, 95% CI: 0.05-0.99, P = 0.03.

CONCLUSION: Deferral of PCI of a functionally non-significant stenosis is associated with a favourable very long-term follow-up without signs of late 'catch-up' phenomenon.

impactfactor: 15.203

### **Zimmermann FM**

#### **Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial**

van Nunen LX\*, Zimmermann FM\*, Tonino PA\*, Barbato E, Baumbach A, Engstrøm T, Klauss V, McCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M\*, Fearon WF, De Bruyne B, Pijls NH\*; FAME Study Investigators

Lancet. 2015 Nov 7;386(10006):1853-60. Epub 2015 Aug 30

Voor abstract zie: *Cardiologie - Nunen LX van*

impactfactor: 45.217

### **Zimmermann FM**

#### **Massive bouncing right cardiac mass as a cause of persistent pulmonary embolism**

Zimmermann FM\*, El Farissi M\*, van Brakel TJ, Lammers J

Eur Heart J. 2015 Sep 21;36(36):2472. Epub 2015 Jul 3

Geen abstract beschikbaar

impactfactor: 15.203

### **Zimmermann FM**

#### **Rationale and design of the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) 3 Trial: A comparison of fractional flow reserve-guided percutaneous coronary intervention and coronary artery bypass graft surgery in patients with multivessel coronary artery disease**

Zimmermann FM\*, De Bruyne B, Pijls NH\*, Desai M, Oldroyd KG, Park SJ, Reardon MJ, Wendler O, Woo J, Yeung AC, Fearon WF

Am Heart J. 2015 Oct;170(4):619-626.e2

Abstract: Guidelines recommend coronary artery bypass graft (CABG) surgery over percutaneous coronary intervention (PCI) for the treatment of 3-vessel coronary artery disease (3-VD). The inferior results of PCI demonstrated by previous large randomized trials comparing PCI and CABG might be explained by the use of suboptimal stent technology and by the lack of fractional flow reserve (FFR) guidance of PCI.

TRIAL DESIGN: The objective of this investigator-initiated, multicenter, randomized clinical trial is to investigate whether FFR-guided PCI with new-generation stents is noninferior to CABG in patients with 3-VD, not including the left main coronary artery. Eligible patients must have ≥50% coronary stenoses in all 3 major epicardial vessels or major side branches. Patients with a nondominant right coronary artery may be included only if the left anterior descending artery and left circumflex have ≥50% stenoses. Consecutive patients who meet all of the inclusion criteria and none of the exclusion criteria will be randomized in a 1:1 fashion to either CABG or FFR-guided PCI. Coronary artery bypass graft will be performed based on the angiogram as per clinical routine. Patients assigned to FFR-guided PCI will have

FFR measured in each diseased vessel and only undergo stenting if the FFR is  $\leq 0.80$ . The primary end point of the study is a composite of major adverse cardiac and cerebrovascular events, including death, myocardial infarction, repeat coronary revascularization, and stroke at 1 year. Key secondary end point will be a composite of death, myocardial infarction, and stroke at 3-year follow-up. Other secondary end points include the individual adverse events, cost-effectiveness, and quality of life at 2-year, 3-year, with up to 5-year follow-up. CONCLUSION: The FAME 3 study will compare in a multicenter, randomized fashion FFR-guided PCI with contemporary drug-eluting stents to CABG in patients with 3-VD.

*impactfactor:* 4.463

## **Cardiothoracale Chirurgie**

**Berrekouw E****Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience**

de Jonge M\*, van Boxtel A\*, Soliman Hamad M\*, Mokhles M, Bramer S, Osnabrugge R, van Straten A\*, Berrekouw E\*

Perfusion. 2015 Apr;30(3):243-9. Epub 2014 Jun 26

Voor abstract zie: *Cardiothoracale Chirurgie - de Jonge M*

impactfactor: 0.935

**Boxtel AG van****Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience**

de Jonge M\*, van Boxtel A\*, Soliman Hamad M\*, Mokhles M, Bramer S, Osnabrugge R, van Straten A\*, Berrekouw E\*

Perfusion. 2015 Apr;30(3):243-9. Epub 2014 Jun 26

Voor abstract zie: *Cardiothoracale Chirurgie - de Jonge M*

impactfactor: 0.935

**Garsse AF van****Frequency and prognosis of new bundle branch block induced by surgical aortic valve replacement**

Poels TT, Houthuizen P\*, Van Garsse LA\*, Soliman Hamad MA\*, Maessen JG, Prinzen FW, Van Straten AH\*

Eur J Cardiothorac Surg. 2015 Feb;47(2):e47-53

Voor abstract zie: *Cardiologie – Houthuizen P*

impactfactor: 3.304

**Garsse AF van****Trends in the occurrence of new conduction abnormalities after transcatheter aortic valve implantation**

van der Boon RM, Houthuizen P\*, Urena M, Poels TT, van Mieghem NM, Brueren GR\*, Altintas S, Nuis RJ, Serruys PW, van Garsse LA\*, van Domburg RT, Cabau JR, de Jaegere PP, Prinzen FW

Catheter Cardiovasc Interv. 2015 Apr;85(5):E144-52

Voor abstract zie: *Cardiologie - Houthuizen P*

impactfactor: 2.107

**Jonge M de****Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience**

de Jonge M\*, van Boxtel A\*, Soliman Hamad M\*, Mokhles M, Bramer S, Osnabrugge R, van Straten A\*, Berrekouw E\*

Perfusion. 2015 Apr;30(3):243-9

OBJECTIVES: This study analyzes the efficacy in myocardial protection of two types of cardioplegia solutions, namely, blood and crystalloid cardioplegia, both given intermittently in patients undergoing coronary artery bypass grafting (CABG).

METHODS: Adult patients undergoing primary isolated coronary artery bypass grafting



between January 1998 and January 2011 with cardiopulmonary bypass, using either blood or crystalloid cardioplegia, were identified in our database. Propensity score matching was performed to create comparable patient groups. Multivariate logistic regression analysis was performed to identify independent risk factors for perioperative myocardial damage. The primary endpoint of the study was the maximum creatine kinase-MB (CK-MB) value within 5 days postoperatively with a cut-off point of 100 U/L. Early mortality and perioperative low cardiac output syndrome in both groups were compared. RESULTS: The study included 7138 CABG patients: 3369 patients using crystalloid cardioplegia and 3769 using blood cardioplegia. After propensity score matching, 2585 patients per study group remained for the analysis. Wilcoxon signed-rank test revealed significantly higher CK-MB levels in patients operated with the use of blood cardioplegia. Multivariate regression analysis identified blood cardioplegia as an independent risk factor for elevated CK-MB levels. However, it was associated with lower aspartate aminotransferase (AST) levels. The type of cardioplegia had no influence on early mortality, postoperative low cardiac output syndrome or intensive care unit stay. CONCLUSIONS: Blood cardioplegia was identified as an independent risk factor for elevated levels of CK-MB after CABG, but was associated with lower AST levels. The authors conclude that the type of cardioplegia had no significant influence on clinical outcome.

*impactfactor:* 0.935

## **Jonge M de**

### **PICSO: from myocardial salvage to tissue regeneration**

Mohl W, Gangl C, Jusic A, Aschacher T, De Jonge M\*, Rattay F

Cardiovasc Revasc Med. 2015 January - February;16(1):36-46

Despite advances in primary percutaneous interventions (PPCI), management of microvascular obstructions in reperfused myocardial tissue remains challenging and is a high-risk procedure. This has led to renewed interest in the coronary venous system as an alternative route of access to the myocardium. This article reviews historical data describing therapeutic options via cardiac veins as well as discussing the clinical potential and limitations of a catheter intervention: pressure controlled intermittent coronary sinus occlusion (PICSO). Collected experimental and clinical information suggest that PICSO also offers the potential for tissue regeneration beyond myocardial salvage. A meta-analysis of observer controlled pICSO application in animal studies showed a dose dependent reduction in infarct size of 29.3% ( $p<0.001$ ). Additionally, a 4-fold increase of hemeoxygenase-1 gene expression ( $p<0.001$ ) in the center of infarction and a 2.5 fold increase of vascular endothelial growth factor (VEGF) ( $p<0.002$ ) in border zones suggest that molecular pathways are initiating structural maintenance. Early clinical evidence confirmed significant salvage and event free survival in patients with acute myocardial infarction and risk reduction for event free survival 5years after the acute event ( $p<0.0001$ ). This experimental and clinical evidence was recently corroborated using modern PICSO technology in PPCI showing a significant reduction of infarct size, when compared to matched controls ( $p<0.04$ ). PICSO enhances redistribution of flow towards deprived zones, clearing microvascular obstruction and leading to myocardial protection. Beyond salvage, augmentation of molecular regenerative networks suggests a second mechanism of PICSO involving the activation of vascular cells in cardiac veins, thus enhancing structural integrity and recovery.

*impactfactor:* --

**Khamooshian A**

**Long-term follow-up of 82 patients after surgical excision of atrial myxomas**

Vroomen M\*, Houthuizen P\*, Khamooshian A\*, Soliman Hamad MA\*, van Straten AH\*  
Interact Cardiovasc Thorac Surg. 2015 Aug;21(2):183-8

Voor abstract zie: *Cardiothoracale Chirurgie - Vroomen M*

*impactfactor:* 1.155

**Salah K**

**Are Changes in Serum Potassium Levels During Admissions for Acute Decompensated Heart Failure Irrelevant for Prognosis: The End of the Story?**

Kok W, Salah K\*, Stienen S Am J Cardiol. 2015 Sep 1;116(5):825

Comment in Reply: Are Changes in Serum Potassium Levels During Admissions for Acute Decompensated Heart Failure Irrelevant for Prognosis: The End of the Story? [Am J Cardiol. 2015]

Comment on: Changes in serum potassium levels during hospitalization in patients with worsening heart failure and reduced ejection fraction (from the EVEREST trial). [Am J Cardiol. 2015]

*impactfactor:* 3.276

**Salah K**

**Challenging the two concepts in determining the appropriate pre-discharge N-terminal pro-brain natriuretic peptide treatment target in acute decompensated heart failure patients: absolute or relative discharge levels?**

Stienen S, Salah K\*, Eurlings LW, Bettencourt P, Pimenta JM, Metra M, Bayes-Genis A, Verdiani V, Bettari L, Lazzarini V, Tijssen JP, Pinto YM, Kok WE  
Eur J Heart Fail. 2015 Sep;17(9):936-44

AIMS: NT-proBNP is a strong predictor for readmissions and mortality in acute decompensated heart failure (ADHF) patients. We assessed whether absolute or relative NT-proBNP levels should be used as pre discharge treatment target.

METHODS AND RESULTS: Our study population was assembled from seven ADHF cohorts. We defined absolute (<1500, <3000, <5000, and <15 000 ng/L) and relative NT-proBNP targets (>30, >50, and >70%). Population attributable risk fraction (PARF) is the proportion of all-cause 6-month mortality in the population that would be reduced if all patients attain the NT-proBNP target. PARF was determined for each target as well as the percentage of patients attaining the NT-proBNP target. Attainability was investigated by logistic regression analysis. A total of 1266 patients [age 74 (64-80), 60% male] was studied. For every absolute NT-proBNP level, a corresponding percentage reduction was found that resulted in similar PARFs. The highest PARF (~60-70%) was observed for <1500 or >70%, but attainability was low (27% and 22%, respectively). The strongest predictor for not attaining these targets was admission NT-proBNP. In admission NT-proBNP tertiles, PARFs were significantly different for absolute, but not for relative targets.

CONCLUSION: In an ADHF population, pre-discharge absolute or relative NT-proBNP targets may both be useful as they have similar effects on PARF. However, depending on admission NT-proBNP, absolute targets show varying PARFs, while PARFs for relative targets were similar. A relative target is predicted to reduce mortality consistently across the whole spectrum of ADHF patients, while this is not the case using a single absolute target.

*impactfactor:* 6.526

Salah K

### **Competing Risk of Cardiac Status and Renal Function During Hospitalization for Acute Decompensated Heart Failure**

Salah K\*, Kok WE, Eurlings LW, Bettencourt P, Pimenta JM, Metra M, Verdiani V, Tijssen JG, Pinto YM JACC Heart Fail. 2015 Oct;3(10):751-61

**OBJECTIVES:** The aim of this study was to analyze the dynamic changes in renal function in combination with dynamic changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients hospitalized for acute decompensated heart failure (ADHF).

**BACKGROUND:** Treatment of ADHF improves cardiac parameters, as reflected by lower levels of NT-proBNP. However this often comes at the cost of worsening renal parameters (e.g., serum creatinine, estimated glomerular filtration rate [eGFR], or serum urea). Both the cardiac and renal markers are validated indicators of prognosis, but it is not yet clear whether the benefits of lowering NT-proBNP are outweighed by the concomitant worsening of renal parameters.

**METHODS:** This study was an individual patient data analysis assembled from 6 prospective cohorts consisting of 1,232 patients hospitalized for ADHF. Endpoints were all-cause mortality and the composite of all-cause mortality and/or readmission for a cardiovascular reason within 180 days after discharge. **RESULTS:** A significant reduction in NT-proBNP was not associated with worsening of renal function (WRF) or severe WRF (sWRF). A reduction of NT-proBNP of more than 30% during hospitalization determined prognosis (all-cause mortality hazard ratio [HR]: 1.81; 95% confidence Interval [CI]: 1.32 to 2.50; composite endpoint: HR: 1.36, 95% CI: 1.13 to 1.64), regardless of changes in renal function and other clinical variables.

**CONCLUSIONS:** When we defined prognosis, NT-proBNP changes during hospitalization for treatment of ADHF prevailed over parameters for worsening renal function. Severe WRF is a measure of prognosis, but is of lesser value than, and independent of the prognostic changes induced by adequate NT-proBNP reduction. This suggests that in ADHF patients it may be warranted to strive for an optimal decrease in NT-proBNP, even if this induces WRF.

*impactfactor:* --

Salah K

### **N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) Measurements Until a 30% Reduction Is Attained During Acute Decompensated Heart Failure Admissions and Comparison With Discharge NT-proBNP Levels: Implications for In-Hospital Guidance of Treatment**

Stienen S, Salah K\*, Dickhoff C, Carubelli V, Metra M, Magrini L, Di Somma S, Tijssen JP, Pinto YM, Kok WE

J Card Fail. 2015 Nov;21(11):930-4

**BACKGROUND:** A >30% N-terminal pro-B-type natriuretic peptide (NT-proBNP) reduction at discharge in acute decompensated heart failure (ADHF) predicts a favorable prognosis. To study the feasibility of guiding ADHF treatment by measuring NT-proBNP well before discharge, we assessed at which moment during hospitalization patients attain a NT-proBNP reduction of >30% (target) and whether this target is still attained at discharge. **METHODS:** Twenty-five consecutive ADHF patients with NT-proBNP >1,700 ng/L were included (original cohort). NT-proBNP was measured daily until the target was attained, at clinical stability, and at discharge and was analyzed as percentages of patients on target. For comparison purposes, the same analysis was performed in individual patient data from 2

other ADHF cohorts (42 and 111 patients, respectively), in which NT-proBNP was measured from admission to day 3 and at discharge.

**RESULTS:** In the original cohort of 25 patients (median age 70 years, 40% male), the cumulative percentage of patients attaining the target increased gradually during admission to 22 patients (88%) in a median of 3 days (interquartile range 2-5). In the comparison cohorts, a similar course was observed in patients attaining the target before discharge. Compared with levels measured at days 2 and 3, rebound NT-proBNP increases to levels off-target at discharge were seen in up to 33% of patients in the original and comparison cohorts. **CONCLUSION:** A target >30% NT-proBNP reduction is gradually attained before discharge, and rebound NT-proBNP increases to levels off-target occur in up to 33% of ADHF patients who initially attained target early during admission.

*impactfactor:* 3.051

### **Salah K**

#### **Serum potassium decline during hospitalization for acute decompensated heart failure is a predictor of 6-month mortality, independent of N-terminal pro-B-type natriuretic peptide levels: An individual patient data analysis**

Salah K\*, Pinto YM, Eurlings LW, Metra M, Stienen S, Lombardi C, Tijssen JG, Kok WE  
Am Heart J. 2015 Sep;170(3):531-542.e1

**BACKGROUND:** Limited data exist for the role of serum potassium changes during hospitalization for acute decompensated heart failure (ADHF). The present study investigated the long-term prognostic value of potassium changes during hospitalization in patients admitted for ADHF.

**METHODS:** Our study is a pooled individual patient data analysis assembled from 3 prospective cohorts comprising 754 patients hospitalized for ADHF. The endpoint was all-cause mortality within 180 days after discharge. Serum potassium levels and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were measured at admission and at discharge.

**RESULTS:** A percentage decrease >15% in serum potassium levels occurred in 96 (13%) patients, and an absolute decrease of >0.7 mmol/L in serum potassium levels occurred in 85 (12%) patients; and both were predictors of poor outcome independent of admission or discharge serum potassium. After the addition of other strong predictors of mortality-a 30% change in NT-proBNP during hospitalization, discharge levels of NT-proBNP, renal markers, and other relevant clinical variables-the multivariate hazard ratio of serum potassium percentage reduction of >15% remained an independent predictor of 180-day mortality (hazard ratio 2.06, 95% CI 1.14-3.73).

**CONCLUSIONS:** A percentage serum potassium decline of >15% is an independent predictor of 180-day all-cause mortality on top of baseline potassium levels, NT-proBNP levels, renal variables, and other relevant clinical variables. This suggest that patients hospitalized for ADHF with a decline of >15% in serum potassium levels are at risk and thus monitoring and regulating of serum potassium level during hospitalization are needed in these patients.

*impactfactor:* 4.463

### **Soliman Hamad MA**

#### **Frequency and prognosis of new bundle branch block induced by surgical aortic valve replacement** Poels TT, Houthuizen P\*, Van Garsse LA\*, Soliman Hamad MA\*, Maessen JG, Prinzen FW, Van Straten AH\*

Eur J Cardiothorac Surg. 2015 Feb;47(2):e47-53.

*Voor abstract zie:* Cardiologie – Houthuizen P

*impactfactor:* 3.304

**Soliman Hamad MA**

**Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience**

de Jonge M\*, van Boxtel A\*, Soliman Hamad M\*, Mokhles M, Bramer S, Osnabrugge R, van Straten A\*, Berreklouw E\*

Perfusion. 2015 Apr;30(3):243-9. Epub 2014 Jun 26

Voor abstract zie: *Cardiothoracale Chirurgie - de Jonge M*

impactfactor: 0.935

**Soliman Hamad MA**

**Long-term follow-up of 82 patients after surgical excision of atrial myxomas**

Vroomen M\*, Houthuizen P\*, Khamooshian A\*, Soliman Hamad MA\*, van Straten AH\*

Interact Cardiovasc Thorac Surg. 2015 Aug;21(2):183-8. Epub 2015 May 13

Voor abstract zie: *Cardiothoracale Chirurgie - Vroomen M*

impactfactor: 1.155

**Soliman Hamad MA**

**Pulmonary blood volume measured by contrast enhanced ultrasound: a comparison with transpulmonary thermodilution**

Herold IH\*, Soliman Hamad MA\*, van Assen HC, Bouwman RA\*, Korsten HH\*, Mischi M Br J Anaesth. 2015 Jul;115(1):53-60

Voor abstract zie: *Anesthesiologie - Herold IH*

impactfactor: 4.853

**Soliman Hamad MA**

**'Red blood transfusion in patients undergoing cardiac surgery reply'**

Haanschoten MC\*, van Straten AH\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jun;23(6):346

Geen abstract beschikbaar

impactfactor: 1.837

**Soliman Hamad MA**

**Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience**

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

Voor abstract zie: *Anesthesiologie - Haanschoten MC*

impactfactor: 1.837

**Straten AH van****Frequency and prognosis of new bundle branch block induced by surgical aortic valve replacement**

Poels TT, Houthuizen P\*, Van Garsse LA\*, Soliman Hamad MA\*, Maessen JG, Prinzen FW, Van Straten AH\*

Eur J Cardiothorac Surg. 2015 Feb;47(2):e47-53

Voor abstract zie: *Cardiologie – Houthuizen P*

impactfactor: 3.304

**Straten AH van****Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience**

de Jonge M\*, van Bortel A\*, Soliman Hamad M\*, Mokhles M, Bramer S, Osnabrugge R, van Straten A\*, Berreklouw E\*

Perfusion. 2015 Apr;30(3):243-9. Epub 2014 Jun 26

Voor abstract zie: *Cardiothoracale Chirurgie - de Jonge M*

impactfactor: 0.935

**Straten AH van****Long-term follow-up of 82 patients after surgical excision of atrial myxomas**

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Voor abstract zie: *Cardiothoracale Chirurgie - Vroomen M*

impactfactor: 1.155

**Straten AH van****'Red blood transfusion in patients undergoing cardiac surgery reply'**

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Neth Heart J. 2015 Jun;23(6):346

Geen abstract beschikbaar.

impactfactor: 1.837

**Straten AH van****Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience**

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

Voor abstract zie: *Anesthesiologie - Haanschoten MC*

impactfactor: 1.837

**Tan ME****Clinical and haemodynamic outcomes in 804 patients receiving the Freedom SOLO stentless aortic valve: results from an international prospective multicentre study†**

Grubitzsch H, Wang S, Matschke K, Glauber M, Heimansohn D, Tan E\*, Francois K, Thalmann M

Eur J Cardiothorac Surg. 2015 Mar;47(3):e97-104

**OBJECTIVES:** The Freedom SOLO™ valve (Sorin Group, Italy) is a stentless aortic bioprosthesis designed for simplified implantation. The present multicentre study is the largest prospective evaluation of this prosthesis. Herein, we report on outcomes at 3-year follow-up.

**METHODS:** From March 2009 to February 2013, a total of 804 consecutive patients (mean age  $74.9 \pm 6.3$  years; 45.1% females) underwent aortic valve replacement with the Freedom SOLO™ valve at 33 centres. Concomitant procedures (70.2% coronary artery bypass grafting) were performed in 376 patients. The cumulative follow-up included 1100 patient-years (mean  $16.5 \pm 10.8$  months; range: 0-40.5 months).

**RESULTS:** Sixty-four patients died (14 early, 50 late); 12 deaths (1 early, 11 late) were valve-related. Operative mortality (30 days) was 1.7%. At 3 years, overall survival was 82.6% [95% confidence interval (CI) 75.5-87.8%] and freedom from valve-related death was 95.5% (95% CI 89.2-98.2%). Linearized late event rates were 0.82%/patient-years for non-structural valve dysfunction, 0.55%/patient-years for structural valve deterioration, 1.55%/patient-years for endocarditis, 3.64%/patient-years for thromboembolism and 3.18%/patient-years for bleeding. In total, there were 22 reinterventions [19 valve explants, 2 refixations, 1 transcatheter aortic valve intervention (TAVI)] for endocarditis (11), non-structural dysfunction (9) and structural valve deterioration (2). Freedom from reintervention was 95.2% (95% CI 91.2-97.4%) at 3 years. There were no instances of valve thrombosis or haemolysis. At 1, 2 and 3 years, 97.0, 95.5 and 91.4% of patients were in NYHA class I or II. Between discharge and 3 years after surgery, mean transvalvular gradients exhibited a non-significant increase ( $6.5 \pm 4.3$  vs  $8.7 \pm 6.5$  mmHg), whereas effective orifice area index remained stable ( $0.9 \pm 0.2$  vs  $0.8 \pm 0.3$  cm<sup>2</sup>/m<sup>2</sup>). At 3 years, no patient presented with more than mild aortic regurgitation. Left ventricular mass index decreased significantly between discharge and 1 year after surgery ( $139.4 \pm 40.9$  vs  $122.4 \pm 35.3$  g/m<sup>2</sup>,  $P < 0.001$ ) and remained unchanged thereafter. Left ventricular size and function did not change over time.

**CONCLUSIONS:** The Freedom SOLO™ valve is a unique stentless pericardial bioprosthesis whose design favours haemodynamic performance and thus facilitates left ventricular reverse remodelling. In terms of survival, morbidity and functional status, it is associated with beneficial outcomes up to 3 years after surgery. Ongoing follow-up will assess the valve at the long-term course.

*impactfactor: 3.304*

## **Tan ME**

### **Effects of cell-saving devices and filters on transfusion in cardiac surgery: a multicenter randomized study**

Vermeijden WJ, van Klarenbosch J, Gu YJ, Mariani MA, Buhre WF, Scheeren TW, Hagens JA, Tan ME\*, Haenen JS, Bras L, van Oeveren W, van den Heuvel ER, de Vries AJ

Ann Thorac Surg. 2015 Jan;99(1):26-32

**BACKGROUND:** Cell-saving devices (CS) are frequently used in cardiac surgery to reduce transfusion requirements, but convincing evidence from randomized clinical trials is missing. Filtration of salvaged blood in combination with the CS is widely used to improve the quality of retransfused blood, but there are no data to justify this approach.

**METHODS:** To determine the contribution of CS and filters on transfusion requirements, we performed a multicenter factorial randomized clinical trial in two academic and four nonacademic hospitals. Patients undergoing elective coronary, valve, or combined surgical procedures were included. The primary end point was the number of allogeneic blood products transfused in each group during hospital admission.

RESULTS: From 738 included patients, 716 patients completed the study (CS+filter, 175; CS, 189; filter, 175; neither CS nor filter, 177). There was no significant effect of CS or filter on the total number of blood products (fraction [95% confidence interval]: CS, 0.96 [0.79, 1.18]; filter, 1.17 [0.96, 1.43]). Use of a CS significantly reduced red blood cell transfusions within 24 hours (0.75 [0.61,0.92]), but not during hospital stay (0.86 [0.71, 1.05]). Use of a CS was significantly associated with increased transfusions of fresh frozen plasma (1.39 [1.04, 1.86]), but not with platelets (1.25 [0.93, 1.68]). Use of a CS significantly reduced the percentage of patients who received any transfusion (odds ratio [95% confidence interval]: 0.67 [0.49, 0.91]), whereas filters did not (0.92 [0.68, 1.25]).

CONCLUSIONS: Use of a CS, with or without a filter, does not reduce the total number of allogeneic blood products, but reduces the percentage of patients who need blood products during cardiac surgery.

impactfactor: 3.849

## Verstappen F

### Reducing the immediate availability of red blood cells in cardiac surgery, a single-centre experience

Haanschoten MC\*, van Straten AH\*, Verstappen F\*, van de Kerkhof D\*, van Zundert AA\*, Soliman Hamad MA\*

Neth Heart J. 2015 Jan;23(1):28-32. Epub 2014 Oct 18

Voor abstract zie: Haanschoten MC - Anesthesiologie

impactfactor: 1.837

## Vroomen M

### Long-term follow-up of 82 patients after surgical excision of atrial myxomas

Vroomen M\*, Houthuizen P\*, Khamooshian A\*, Soliman Hamad MA\*, van Straten AH\*

Interact Cardiovasc Thorac Surg. 2015 Aug;21(2):183-8. Epub 2015 May 13

OBJECTIVES: Literature reporting on large patient groups with the long-term follow-up is limited due to the low incidence of myxomas. This single-centre, retrospective study reports on the long-term follow-up (e.g. complications, recurrence and survival) of a substantial patient group operated for cardiac myxomas.

METHODS: Patients were retrospectively selected from a prospectively obtained database comprising patients who had undergone cardiac surgery in the Catharina Hospital from 1990 onwards. Baseline characteristics and perioperative data were obtained from the database. In case of insufficient information, medical reports were analysed. The echocardiogram and clinical follow-up data were collected at outpatient clinics.

RESULTS: Eighty-two patients were included, of which 48 were females with a mean age of 61.3 years ( $\pm 13.8$ ). The main presenting symptom was dyspnoea (29.3%), followed by chest pain (24.4%), palpitations (19.5%) and embolism (15.9%). Atrial fibrillation was the most frequent complication; directly postoperative (22%) and at the long-term follow-up (26.3%). The follow-up was completed in 95.1%, with a mean echocardiographic follow-up time of 72 months and with a longest follow-up of almost 23 years. There were no myxoma recurrences. Thirteen patients (16.5%) deceased during the follow-up, with a mean time of 9 years after surgery.

CONCLUSIONS: Myxomas carry the risk of severe complications. Surgical excision is the only option of treatment and gives excellent early and long-term results. Recurrence rates are low in case of non-hereditary myxomas, even in case of irradical excision. The echocardiographic follow-up therefore could be called into question.

impactfactor: 1.155



**Woorst FJ ter**

**Preoperative exercise therapy in lung surgery patients: A systematic review**

Pouwels S\*, Fiddelaers J, Teijink JA\*, Woorst JF\*, Siebenga J, Smeenk FW\*

Respir Med. 2015 Dec;109(12):1495-504. Epub 2015 Aug 15

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: *3.086*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Chirurgie**

## **Bakens M**

### **Hospital of diagnosis and likelihood of surgical treatment for pancreatic cancer**

Bakens MJ\*, van Gestel YR, Bongers M, Besselink MG, Dejong CH, Molenaar IQ, Busch OR, Lemmens VE, de Hingh IH\*; Dutch Pancreatic Cancer Group

Br J Surg. 2015 Dec;102(13):1670-5. Epub 2015 Oct 5

**BACKGROUND:** Surgical resection for pancreatic cancer offers the only chance of cure. Assessment of the resectability of a pancreatic tumour is therefore of great importance. The aim of the study was to investigate whether centre of diagnosis influences the likelihood of surgery and whether this affects long-term survival.

**METHODS:** Patients diagnosed with non-metastasized pancreatic cancer (M0) between 2005 and 2013 in the Netherlands were selected from the Netherlands Cancer Registry. Hospitals were classified as a pancreatic centre (at least 20 resections/year) or a non-pancreatic centre (fewer than 20 resections/year). The relationship between centre of diagnosis and likelihood of surgery was analysed by multivariable logistic regression. Influence of centre on overall survival was assessed by means of multivariable Cox regression analysis.

**RESULTS:** Some 8141 patients were diagnosed with non-metastasized pancreatic cancer, of whom 3123 (38.4 per cent) underwent surgery. Of the 2712 patients diagnosed in one of 19 pancreatic centres, 52.4 per cent had exploratory laparotomy compared with 31.4 per cent of 5429 patients diagnosed in one of 74 non-pancreatic centres ( $P < 0.001$ ). A pancreatectomy was performed in 42.8 and 24.6 per cent of the patients respectively ( $P < 0.001$ ). Multivariable analysis revealed that patients diagnosed in a pancreatic centre had a higher chance of undergoing surgery (odds ratio 2.21, 95 per cent c.i. 1.98 to 2.47). Centre of diagnosis was not associated with improved long-term survival (hazard ratio 0.95, 95 per cent c.i. 0.91 to 1.00).

**CONCLUSION:** Patients with non-metastasized pancreatic cancer had a greater likelihood of having surgical treatment when the diagnosis was established in a pancreatic centre.

*impactfactor:* 5.542

## **Bakens M**

### **Implementing an enhanced recovery program after pancreaticoduodenectomy in elderly patients: is it feasible?**

Coolsen MM, Bakens M\*, van Dam RM, Olde Damink SW, Dejong CH

World J Surg. 2015 Jan;39(1):251-8

**BACKGROUND:** An enhanced recovery after surgery (ERAS) program aims to reduce the stress response to surgery and thereby accelerate recovery. It is unclear whether these programs can be safely implemented for elderly patients, especially in highly complex surgery such as pancreaticoduodenectomy (PD). The objective of this study was to evaluate the feasibility of an ERAS program in elderly patients undergoing PD.

**METHODS:** Implementation of the ERAS protocol was studied prospectively in a consecutive series of patients undergoing PD between January 2009 and August 2013. Patients were divided into two groups:  $\geq 65$  years and  $< 70$  years. Endpoints were length of stay (LOS), readmissions, morbidity, mortality, and compliance with ERAS targets.

**RESULTS:** Of a total of 110 patients, 55 were  $\geq 65$  years (median 57) and 55  $< 70$  years (median 77). Median LOS was 14 days in both groups. In patients without complications median LOS was 9 days. Both mortality and readmissions did not differ between groups (mortality  $n = 3$  (5.5 %) in younger versus  $n = 6$  (10.9 %) in older patients,  $p = 0.49$ , readmissions:  $n = 11$  (20 %) versus  $n = 7$  (12.7 %),  $p = 0.44$ ). CT-drainage and relaparotomy-rates were not different between groups, nor was overall morbidity ( $n = 31$  (56.3 %) in the

older versus  $n = 35$  (63.3 %) in the younger group,  $p = 0.44$ ). There were no differences in compliance with elements of the ERAS protocol between groups.

#### CONCLUSION:

An ERAS program seems feasible and safe for patients = 70 years of age undergoing PD.

*impactfactor:* 2.642

#### **Berghuis KA**

#### **Technology-based interventions in the treatment of overweight and obesity: A systematic review**

Raaijmakers LC\*, Pouwels S\*, Berghuis KA\*, Nienhuijs SW\*

*Appetite.* 2015 Jul 10;95:138-151

*Voor abstract zie: Chirurgie - Raaijmakers LC*

*impactfactor:* 2.691

#### **Berkelmans G**

#### **Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy**

Berkelmans GH\*, Kouwenhoven EA, Smeets BJ\*, Weijs TJ\*, Silva Corten LC, van Det MJ, Nieuwenhuijzen GA\*, Luyer MD\*

*World J Gastroenterol.* 2015 Aug 14;21(30):9118-25

**AIM:** To investigate the value of elevated drain amylase concentrations for detecting anastomotic leakage (AL) after minimally invasive Ivor-Lewis esophagectomy (MI-ILE).

**METHODS:** This was a retrospective analysis of prospectively collected data in two hospitals in the Netherlands. Consecutive patients undergoing MI-ILE were included. A Jackson-Pratt drain next to the dorsal side of the anastomosis and bilateral chest drains were placed at the end of the thoracoscopic procedure. Amylase levels in drain fluid were determined in all patients during at least the first four postoperative days. Contrast computed tomography scans and/or endoscopic imaging were performed in cases of a clinically suspected AL. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis on endoscopy, re-operation, radiographic investigations, post mortal examination or when gastro-intestinal contents were found in drain fluid. Receiver operator characteristic curves were used to determine the cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value, risk ratio and overall test accuracy were calculated for elevated drain amylase concentrations.

**RESULTS:** A total of 89 patients were included between March 2013 and August 2014. No differences in group characteristics were observed between patients with and without AL, except for age. Patients with AL were older than were patients without AL ( $P = 0.01$ ). One patient (1.1%) without AL died within 30 d after surgery due to pneumonia and acute respiratory distress syndrome. Anastomotic leakage that required any intervention occurred in 15 patients (16.9%). Patients with proven anastomotic leakage had higher drain amylase levels than patients without anastomotic leakage [median 384 IU/L (IQR 34-6263) vs median 37 IU/L (IQR 26-66),  $P = 0.003$ ]. Optimal cut-off values on postoperative days 1, 2, and 3 were 350 IU/L, 200 IU/L and 160 IU/L, respectively. An elevated amylase level was found in 9 of the 15 patients with AL. Five of these 9 patients had early elevations of their amylase levels, with a median of 2 d (IQR 2-5) before signs and symptoms occurred.

**CONCLUSION:** Measurement of drain amylase levels is an inexpensive and easy tool that may be used to screen for anastomotic leakage soon after MI-ILE. However, clinical validation of this marker is necessary.

*impactfactor:* 2.369

**Berkelmans G**

**Routes for early enteral nutrition after esophagectomy. A systematic review**

Weijs TJ\*, Berkelmans GH\*, Nieuwenhuijzen GA\*, Ruurda JP, Hillegersberg RV, Soeters PB, Luyer MD\*

Clin Nutr. 2015 Feb;34(1):1-6. Epub 2014 Aug 1

Voor abstract zie: *Chirurgie - Weijs TJ*

impactfactor: 4.476

**Bode AS**

**Hemodialysis vascular access management in the Netherlands**

Tordoir JH, van Loon MM, ter Meer M, van Laanen J, Bode AS, Weijmer MC, Peppelenbosch NJ

Vasc Access. 2015;16 Suppl 9:S11-5

**PURPOSE:** In the Netherlands, 86% of patients start renal replacement therapy with chronic intermittent hemodialysis (HD). Guidelines do indicate predialysis care and maintenance of a well-functioning vascular access (VA) as critical issues in the management of the renal failure patient. Referral to the surgeon and time to VA creation are important determinants of the type and success of the VA and HD treatment.

**METHODS AND RESULTS:** Data from a national questionnaire showed that time from referral to the surgeon and actual access creation is <4 weeks in 43%, 4 to 8 weeks in 30% and >8 weeks in 27% of the centers. Preoperative ultrasonography and postoperative access flowmetry are the diagnostic methods in the majority of centers (98%). Most facilities perform rope-ladder cannulation with occasionally the buttonhole technique for selected patients in 87% of the dialysis units. Endovascular intervention for thrombosis is practiced by 13%, surgical thrombectomy by 21% and either endovascular or surgery by 66% of the centers. Weekly multidisciplinary meetings are organized in 57% of the units. Central vein catheters are inserted by radiologists (36%), nephrologists and surgeons (32%).

**CONCLUSIONS:** We conclude that guidelines implementation has been successful in particular regarding issues as preoperative patient assessment for VA creation and postoperative surveillance in combination with (preemptive) endovascular intervention, leading to very acceptable VA thrombosis rates.

impactfactor: 0.846

**Bode AS**

**Preferred Strategy for Hemodialysis Access Creation in Elderly Patients**

Tordoir JH, Bode AS\*, van Loon MM

Eur J Vasc Endovasc Surg. 2015 Jun;49(6):738-743

**BACKGROUND:** Adequate functioning vascular access is the key to successful hemodialysis. The use of an autologous arteriovenous fistula (AVF) is advised because of good long-term patency and a low incidence of complications. However, the number of patients with AVFs is declining because of the change in the demography of the dialysis population, with increasing numbers of very old patients with multiple comorbidities.

**METHODS:** In this vignette an elderly patient is described with calcified distal arteries and a small cephalic vein who is referred at a late stage for access creation. The results and performance of different types of vascular access (AVF; arteriovenous graft; central vein catheter), in relation to late referral and patient demographics, are described. In addition, patient morbidity and mortality versus the type of access are discussed.

**CONCLUSIONS:** The patient described in this vignette appears to be unsuitable for the creation of a forearm AVF because of calcified distal arteries and a small cephalic vein. The risk of non-maturing autologous AVFs is high in elderly patients and this observation might justify the use of early stick grafts. High risk patients may benefit from permanent central vein catheters.

*impactfactor:* 3.490

## **Bransen J**

### **Costs of Leaks and Bleeding After Sleeve Gastrectomies**

Bransen J\*, Gilissen LP\*, van Rutte PW, Nienhuijs SW\*

Obes Surg. 2015 Oct;25(10):1767-71

**BACKGROUND:** Leaks and bleeding are serious postoperative complications after a sleeve gastrectomy (SG). The objective of the present study was to evaluate the costs of leaks and bleeding after SG.

**METHODS:** A retrospective analysis was conducted of a prospective cohort of primary SGs between August 2006 and September 2013 in a bariatric center. All SGs were performed consistently without reinforcement of the staple line. Abscesses adjacent to the staple line were also regarded as leaks. Data were collected on all diagnostic and therapeutic measures necessary to manage leaks or bleeding, days of hospitalization and parenteral feeding, number of blood products, antibiotics, and additional outpatient department visits.

**RESULTS:** One thousand two hundred sixty one patients underwent a SG. Leaks occurred in 32 (2.5 %) and bleeding in 27 (2.1 %) patients. Median additional costs for leaks were <euro>9284 (range <euro>1748-125,684) and <euro>4267 (range <euro>1524-40,022) for bleeding. Prolonged hospitalization in the ward and ICU accounted for the majority of costs, 50.3 and 31.4 %, respectively, for leaks and 42.0 and 34.8 % for bleeding.

**CONCLUSIONS:** These data provide insight into the costs of major complications after SG. A wide range is seen especially due to prolonged hospitalization in the ward and ICU. High costs are an additional argument to reduce complication rate. These data should be considered when analyzing the cost-effectiveness of staple line reinforcement.

*impactfactor:* 3.747

## **Broos PP**

### **Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair**

Broos PP\*, Stokmans RA\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*; ENGAGE

Investigators J Endovasc Ther. 2015 Oct;22(5):770-7

**PURPOSE:** To examine outcomes of endovascular aortic aneurysm repair (EVAR) using general, regional, or local anesthesia.

**METHODS:** From March 2009 to April 2011, patients were enrolled from 79 sites in 30 countries worldwide and treated with an Endurant Stent Graft System. Data were compared among 3 groups based on the method of anesthesia: general anesthesia (GA) was used in 785 (62%) patients, regional anesthesia (RA) in 331 (27%) patients, and local anesthesia (LA) in 145 (11%) patients. Multivariate logistic regression analysis was performed to adjust for possible confounding factors; outcomes are presented as the odds ratio and 95% confidence interval.

**RESULTS:** There were intercontinental differences in the distribution of type of anesthesia used for EVAR. Higher ASA (American Society of Anesthesiologists) classification was associated with predominant use of GA. Procedure time was reduced in LA (80.4±40.0 minutes) compared with RA (94.2±41.6 min, adjusted p=0.001) and GA (105.3±46.0 minutes,

adjusted  $p < 0.001$ ). Intensive care unit (ICU) admission was less frequent for RA than for GA (adjusted OR 0.71, 95% CI 0.53 to 0.97,  $p = 0.030$ ) and LA (adjusted OR 0.51, 95% CI 0.33 to 0.79,  $p = 0.002$ ). Postoperative hospital stay was significantly shorter for RA and LA compared with GA (adjusted  $p = 0.003$  and  $p = 0.010$ , respectively). There were no significant differences in systemic and surgical complications. Mortality rates within 30 days did not differ among the groups.

**CONCLUSION:** Type of anesthesia used during EVAR has no influence on perioperative mortality and morbidity. The use of local or regional anesthesia during EVAR appeared to be beneficial concerning procedure time, ICU admission, and postoperative hospital stay.

*impactfactor:* 2.826

## **Broos PP**

### **Endovascular Treatment of Ruptured Abdominal Aortic Aneurysms with Hostile Aortic Neck Anatomy**

Broos PP\*, 't Mannelte YW\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Sep;50(3):313-9. Epub 2015 May 28

**OBJECTIVE:** To compare the mid-term results of endovascular aortic aneurysm repair (EVAR) for ruptured abdominal aortic aneurysms (RAAAs) in patients with favourable aortic neck anatomy (FNA) and hostile aortic neck anatomy (HNA).

**METHODS:** Patients treated for a RAAA in a high volume endovascular centre in the Netherlands between February 2009 and January 2014 were identified retrospectively and divided into two groups based on aortic neck anatomy, FNA and HNA. HNA was defined as RAAA with a proximal neck of  $< 10$  mm, or a proximal neck of 10-15 mm with a suprarenal angulation ( $\alpha$ )  $> 45^\circ$  and/or an infrarenal angulation ( $\beta$ )  $> 60^\circ$ , or a proximal neck of  $> 15$  mm combined with a  $> 60^\circ$  and/or  $\beta > 75^\circ$ . Patient demographics, procedure details, 30 day and 1 year outcomes were recorded.

**RESULTS:** Of 39 included patients, 17 (44%) had HNA. Technical success was 100% for FNA and 88% for HNA ( $p = .184$ ). There were no type IA endoleaks on completion angiography in either group; however, more adjunctive procedures were necessary for intra-operative type IA endoleaks in the HNA group (24% vs. 0%,  $p = .029$ ). Thirty day mortality rates were comparable, FNA 14% vs. HNA 12% ( $p = 1.000$ ). There were no statistically significant differences at 1 year follow up in type I endoleaks, secondary endovascular procedures, or all cause mortality.

**CONCLUSION:** Emergency EVAR provides excellent results for treatment of RAAA patients with both FNA and HNA. EVAR in RAAAs with HNA is technically feasible and safe in experienced endovascular centres. Article history.

*impactfactor:* 3.490

## **Broos PP**

### **Performance of the Endurant stent graft in challenging anatomy**

Broos PP\*, Stokmans RA\*, van Sterkenburg SM, Torsello G, Vermassen F, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

J Vasc Surg. 2015 Aug;62(2):312-8

**OBJECTIVE:** This study aimed to compare perioperative and postoperative outcomes after endovascular repair of abdominal aortic aneurysms (AAAs) in patients with various neck morphologic features.

**METHODS:** Data from the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE) were used for the analyses. Patients were categorized into three different groups according to proximal aortic neck anatomy: regular (REG), intermediate (INT), and

challenging (CHA). REG was defined as AAAs with a proximal neck  $\leq 15$  mm combined with a suprarenal angulation ( $\alpha$ )  $\leq 45$  degrees and an infrarenal neck angulation ( $\beta$ )  $\leq 60$  degrees. INT was defined as AAAs with a proximal neck of 10 to 15 mm combined with a  $\alpha \leq 45$  degrees and  $\beta \leq 60$  degrees or with a proximal neck of  $>15$  mm combined with a  $\alpha \leq 60$  degrees and  $\beta = 60$  to 75 degrees or  $\alpha = 45$  to 60 degrees and  $\beta \leq 75$  degrees. CHA was defined as infrarenal necks that exceed at least one of the three defining factors.

RESULTS: Overall, 925 patients (75.9%) had REG anatomy, 189 patients (15.5%) had INT anatomy, and 104 patients (8.5%) had CHA anatomy. Patient demographics and risk factors were similar. There was a significant difference in AAA diameter between the REG and CHA groups (59.4 mm vs 65.2 mm;  $P < .001$ ). Technical success was similar among groups (REG 99.1% vs INT 99.5% vs CHA 97.1%). There were no differences in mortality or the need for secondary procedures within 30 days or at 1 year. A significantly higher rate of type I endoleaks within 30 days was seen in CHA compared with REG (adjusted odds ratio, 0.15; 95% confidence interval, 0.05-0.46) and INT (adjusted odds ratio, 0.08; 95% confidence interval, 0.01-0.70), but there was no difference at 1-year follow-up.

#### CONCLUSIONS:

This real-world, global experience shows promising results and indicates that endovascular AAA repair with the Endurant stent graft (Medtronic Vascular, Santa Rosa, Calif) is safe and effective in patients with challenging aortic neck anatomy. However, long-term follow-up of patients is required to confirm results.

*impactfactor:* 3.021

### Broos PP

#### Vascular complications and surgical interventions after world's largest Q fever outbreak

Broos PP\*, Hagenaaers JC, Kampschreur LM, Wever PC, Bleeker-Rovers CP, Koning OH, Teijink JA\*, Wegdam-Blans MC\*

J Vasc Surg. 2015 Nov;62(5):1273-80. Epub 2015 Sep 10

OBJECTIVE: Since chronic Q fever often develops insidiously, and symptoms are not always recognized at an early stage, complications are often present at the time of diagnosis. We describe complications associated with vascular chronic Q fever as found in the largest cohort of chronic Q fever patients so far.

METHODS: Patients with proven or probable chronic Q fever with a focus of infection in an aortic aneurysm or vascular graft were included in this study, using the Dutch national chronic Q fever database.

RESULTS: A total of 122 patients were diagnosed with vascular chronic Q fever between April 2008 and June 2012. The infection affected a vascular graft in 62 patients (50.8%) and an aneurysm in 53 patients (43.7%). Seven patients (5.7%) had a different vascular focus. Thirty-six patients (29.5%) presented with acute complications, and 35 of these patients (97.2%) underwent surgery. Following diagnosis and start of antibiotic treatment, 26 patients (21.3%) presented with a variety of complications requiring surgical treatment during a mean follow-up of  $14.1 \pm 9.1$  months. The overall mortality rate was 23.7%. Among these patients, mortality was associated with chronic Q fever in 18 patients (62.1%).

CONCLUSIONS: The management of vascular infections with *C. burnetii* tends to be complicated. Diagnosis is often difficult due to asymptomatic presentation. Patients undergo challenging surgical corrections and long-term antibiotic treatment. Complication rates and mortality are high in this patient cohort.

*impactfactor:* 3.021



## **Castelijns B**

### **Hiatal Hernia**

Castelijns B\*, Ponten JE\*, Van de Poll MC, Nienhuijs SW\*, Smulders JF\*, Hu ZW, Wu JM, Wang ZG, Idani H, Asami S, Nakano K, Miyake S, Harano M, Miyoshi H, Araki H, Ogawa T, Takahashi K, Shiozaki S, Ninomiya M, Prasad A, Todkar J, Asti E, Lovece A, Sironi A, Bonavina , Wright , Wurst H, Zhang C, Li HL, Ke LM, Loi K, Hua R, Yao QY, Chen H, Okinyi W, Odende K, Ndungu B, Ndonga A, Kiragu P, Kelimu A, Alimujiang M, Tian W, Bing M

Hernia. 2015 Apr;19 Suppl 1:S13-7

*Geen abstract beschikbaar*

*impactfactor:* 2.050

## **Cuypers PhW**

### **Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review**

Pouwels S\*, Willigendael EM, van Sambeek MR\*, Nienhuijs SW\*, Cuypers PW\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Jan;49(1):66-76

*Voor abstract zie:* Chirurgie - Pouwels S

*impactfactor:* 3.490

## **Cuypers Ph W**

### **Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair**

Broos PP\*, Stokmans RA\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*; ENGAGE Investigators

J Endovasc Ther. 2015 Oct;22(5):770-7

*Voor abstract zie:* Chirurgie - Broos PP

*impactfactor:* 2.826

## **Cuypers Ph W**

### **Endovascular Treatment of Ruptured Abdominal Aortic Aneurysms with Hostile Aortic Neck Anatomy**

Broos PP\*, 't Mannetje YW\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Sep;50(3):313-9. Epub 2015 May 28

*Voor abstract zie:* Chirurgie - Broos PP

*impactfactor:* 3.490

## **Cuypers Ph W**

### **Five-year results of a randomized clinical trial of conventional surgery, endovenous laser ablation and ultrasound-guided foam sclerotherapy in patients with great saphenous varicose veins**

van der Velden SK, Biemans AA, De Maeseneer MG Kockaert MA, Cuypers PW\*, Hollestein LM, Neumann HA, Nijsten T, van den Bos RR

Br J Surg. 2015 Sep;102(10):1184-94. Epub 2015 Jul 1

**BACKGROUND:** A variety of techniques exist for the treatment of patients with great saphenous vein (GSV) varicosities. Few data exist on the long-term outcomes of these interventions.

**METHODS:** Patients undergoing conventional surgery, endovenous laser ablation (EVLA) and ultrasound-guided foam sclerotherapy (UGFS) for GSV varicose veins were followed up for 5 years. Primary outcome was obliteration or absence of the treated GSV segment; secondary outcomes were absence of GSV reflux, and change in Chronic Venous Insufficiency quality-of-life Questionnaire (CIVIQ) and EuroQol - 5D (EQ-5D™) scores.

**RESULTS:** A total of 224 legs were included (69 conventional surgery, 78 EVLA, 77 UGFS), 193 (86.2 per cent) of which were evaluated at final follow-up. At 5 years, Kaplan-Meier estimates of obliteration or absence of the GSV were 85 (95 per cent c.i. 75 to 92), 77 (66 to 86) and 23 (14 to 33) per cent in the conventional surgery, EVLA and UGFS groups respectively. Absence of above-knee GSV reflux was found in 85 (73 to 92), 82 (72 to 90) and 41 (30 to 53) per cent respectively. CIVIQ scores deteriorated over time in patients in the UGFS group (0.98 increase per year, 95 per cent c.i. 0.16 to 1.79), and were significantly worse than those in the EVLA group (-0.44 decrease per year, 95 per cent c.i. -1.22 to 0.35) ( $P = 0.013$ ). CIVIQ scores for the conventional surgery group did not differ from those in the EVLA and UGFS groups (0.44 increase per year, 95 per cent c.i. -0.41 to 1.29). EQ-5D™ scores improved equally in all groups.

**CONCLUSION:** EVLA and conventional surgery were more effective than UGFS in obliterating the GSV 5 years after intervention. UGFS was associated with substantial rates of GSV reflux and inferior CIVIQ scores compared with EVLA and conventional surgery.

*impactfactor:* 5.542

## **Cuypers Ph W**

### **One-year efficacy of the RUDI technique for flow reduction in high-flow autologous brachial artery-based hemodialysis vascular access**

Vaes RH, van Loon M, Vaes SM, Cuypers P\*, Tordoir JH, Scheltinga MR

J Vasc Access. 2015;16 Suppl 9:S96-101

**PURPOSE:** Flow reduction is advised in hemodialysis (HD) patients with a high-flow ( $>2$  L/min) arteriovenous fistula (AVF). The revision using distal inflow (RUDI) technique is based on the premise that access flow is attenuated once inflow is provided by a smaller caliber forearm artery. Aim of the study was to evaluate the efficacy of RUDI during a 1-year follow-up. **METHODS:** All HD patients undergoing a RUDI operation using a greater saphenous vein (GSV) or a basilic vein (BaV) interposition for a high-flow access (HFA,  $>2$  L/min) during a 3.5-year time period were included. Serial access flow, percentage of freedom from recurrent high flow and complications were determined. **RESULTS:** A total of 19 HFA patients were studied (11 males, age  $55 \pm 3$  years). All AVFs were brachial artery based (brachiocephalic,  $n = 14$ ; brachio basilic,  $n = 5$ ). RUDI immediately reduced access flow by almost 2 L/min ( $3,080 \pm 200$  to  $1,170 \pm 160$  mL/min ( $p = 0.001$ )). Access flows at 1, 6 and 12 months were  $1,150 \pm 160$ ,  $1,460 \pm 200$  and  $1,580 \pm 260$  mL/min, respectively. Postoperative complications included insufficient flow reduction ( $n = 1$ , BaV) and occlusion requiring revision ( $n = 1$ , GSV). Recurrent HFA occurred three times ( $n = 2$  BaV,  $n = 1$  GSV). Access flows were significantly ( $p < 0.05$ ) higher in the BaV group compared to the GSV group. **CONCLUSIONS:** RUDI effectively reduces access flow in a brachial artery-based high-flow HD vascular access. A flow-reducing effect is sustained at 1-year follow-up in most patients. GSV is preferred as an interposition graft compared to a BaV.

*impactfactor:* 0.846

## **Cuypers Ph W**

### **Performance of the Endurant stent graft in challenging anatomy**

Broos PP\*, Stokmans RA\*, van Sterkenburg SM, Torsello G, Vermassen F, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

J Vasc Surg. 2015 Aug;62(2):312-8

Voor abstract zie: *Chirurgie - Broos PP*

impactfactor: 3.021

## **Dalen HC van**

### **Safety of supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Fokkenrood HJ\*, van Dalen HC\*, Scheltinga MR, Teijink JA\*, Peters RJ

J Vasc Surg. 2015 Feb;61(2):512-518.e2

Voor abstract zie: *Chirurgie - Gommans L*

impactfactor: 3.021

## **Dekkers M**

### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hilgsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

Voor abstract zie: *Chirurgie - Peters EG*

impactfactor: 1.731

## **Fokkenrood HJ**

### **Agreements and discrepancies between the estimated walking distance, nongraded and graded treadmill testing, and outside walking in patients with intermittent claudication**

Fokkenrood HJ\*, van den Houten MM\*, Houterman S\*, Breek JC, Scheltinga MR, Teijink JA\*

Ann Vasc Surg. 2015 Aug;29(6):1218-24

**BACKGROUND:** Disease severity in patients with intermittent claudication (IC) is often assessed using walking distances and treadmill tests. The aim of this study was to determine the agreement between walking distance as estimated by the patient, as measured during outside walking, and as determined using a nongraded treadmill protocol (NGTP), and an incremental graded (Gardner-Skinner) treadmill protocol (GSP).

**METHODS:** In this prospective observational study, 30 patients with IC estimated their maximal walking distance (MWD) and completed a "Walking Impairment Questionnaire" (WIQ). Outside walking was determined using a measuring wheel and a GSP controlled device. Primary outcomes were differences in MWD and variability (coefficient of variation, COV). Secondary outcomes were results of WIQ and differences in walking speed.

**RESULTS:** Estimated walking distance was significantly higher than MWD as objectively measured during outside walking (400 m vs. 309 m, respectively,  $P = 0.02$ ). A substantial variability (COV = 55%) was found between both parameters. A small 35-m MWD difference

between outside walking and GSP was found with a substantial scatter (COV = 42%). In contrast, a much larger 122-m MWD difference was present between outside walking and NGTP (COV = 89%). Patients walked significantly faster in the open air than on treadmills (median outside walking speed = 3.8 km/hr, GSP = 3.2 km/hr, NGTP = 2.8 km/hr;  $P < 0.001$ ).  
**CONCLUSIONS:** An incremental graded (Gardner-Skinner) treadmill protocol demonstrated the best agreement to outside walking. Discrepancies between treadmill tests and outside walking may be explained by a difference in walking speed. A single determination of a walking distance is a poor reflection of true walking capacity.

*impactfactor:* 1.170

## **Fokkenrood HJ**

### **Commentary on "Supervised versus unsupervised exercise for intermittent claudication: A systematic review and meta-analysis"**

Hageman D\*, Gommans LN\*, Fokkenrood HJ\*, Koelemay MJ, Teijink JA\*

Am Heart J. 2015 Aug;170(2):e1-3

*Geen abstract beschikbaar*

*impactfactor:* 4.463

## **Fokkenrood HJ**

### **Safety of supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Fokkenrood HJ\*, van Dalen HC\*, Scheltinga MR, Teijink JA\*, Peters RJ

J Vasc Surg. 2015 Feb;61(2):512-518.e2

*Voor abstract zie: Chirurgie - Gommans L*

*impactfactor:* 3.021

## **Fokkenrood HJ**

### **The effect of supervised exercise therapy on physical activity and ambulatory activities in patients with intermittent claudication**

Fokkenrood HJ\*, Lauret GJ, Verhofstad N\*, Bendermacher BL, Scheltinga MR, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Feb;49(2):184-91. Epub 2014 Dec 12

**OBJECTIVE/BACKGROUND:** Intermittent claudication (IC) is associated with a reduction in physical activity (PA) and a more rapid functional decline leading to a higher mortality rate compared with healthy individuals. Supervised exercise therapy (SET) is known to increase the walking capacity of patients with IC. However, it is unclear whether SET increases PA. The aim of this study was to investigate the effect of SET on PA levels and ambulatory activities in patients with IC.

**METHODS:** Patients newly diagnosed with IC were requested to wear an activity monitor 1 week prior to and 1 week immediately after 3 months of SET. The primary outcome was the percentage of patients meeting the minimum recommendations of PA (American College of Sports Medicine [ACSM]/American Heart Association [AHA] recommendation for public health of = 67 metabolic equivalents [METs]/min/day, in bouts of = 10 min) at baseline and after 3 months of SET. Additionally, daily PA level (METs/min), duration of ambulatory activities, daily number of steps, pain free walking distance (PFWD), maximal walking distance (MWD), and Short Form Health Survey (SF-36) health surveys were compared before and after SET.

**RESULTS:** Data from 41 participants were available for analysis. A higher number of participants met the ACSM minimum recommendation for PA at the 3 month follow up

(baseline: 43%; 3 months: 63%;  $p = .003$ ). Despite significant increases in PFWD (baseline: 210 m; 3 months: 390 m;  $p = .001$ ), MWD (baseline: 373 m; 3 months: 555 m;  $p = .002$ ) and physical functioning score (SF-36) following SET, no increase in the mean daily PA level was found ( $395 \pm 220$  vs.  $411 \pm 228$  METs/min;  $p = .43$ ). Furthermore, the total number of steps and time spent in ambulatory activities did not change following SET.

**CONCLUSION:** Three months of SET for IC leads to more patients meeting the ACSM/AHA public health minimum recommendations for PA. Assessment of PA could be incorporated as an outcome parameter in future research comparing different treatment modalities for peripheral arterial disease.

*impactfactor:* 3.490

## **Gommans L**

### **Attitudes to supervised exercise therapy**

Gommans L\*, Teijink JA\*

Br J Surg. 2015 Sep;102(10):1153-5. Epub 2015 Jul 23

*Geen abstract beschikbaar*

*impactfactor:* 5.542

## **Gommans L**

### **Commentary on "Supervised versus unsupervised exercise for intermittent claudication: A systematic review and meta-analysis"**

Hageman D\*, Gommans LN\*, Fokkenrood HJ\*, Koelemay MJ, Teijink JA\*

Am Heart J. 2015 Aug;170(2):e1-3

*Geen abstract beschikbaar*

*impactfactor:* 4.463

## **Gommans L**

### **Gender differences following supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Scheltinga MR, van Sambeek MR\*, Maas AH, Bendermacher BL, Teijink JA\* J Vasc Surg. 2015 Sep;62(3):681-8

**OBJECTIVE:** Prevalence of peripheral arterial disease is equal in men and women. However, women seem to suffer more from the burden of disease. Current studies on gender-related outcomes following supervised exercise therapy (SET) for intermittent claudication (IC) yield conflicting results.

**METHODS:** A follow-up analysis was performed on data from the 2010 Exercise Therapy in Peripheral Arterial Disease (EXITPAD) study, a multicenter randomized controlled trial including IC patients receiving SET or a walking advice. The SET program was supervised by physiotherapists and included interval-based treadmill walking approximating maximal pain combined with activities such as cycling and rowing. Patients usually started with three 30-minute sessions a week. Training frequency was adapted during the following year on the basis of individual needs. The primary outcome was gender differences regarding the change in absolute claudication distance (ACD) after SET. ACD was defined as the number of meters that a patient had covered just before he or she was forced to stop walking because of intolerable pain. Secondary outcomes were gender differences in change of functional walking distance, quality of life, and walking (dis)ability after SET. Walking distances were obtained by standardized treadmill testing according to the Gardner-Skinner protocol. Quality of life was measured by the 36-item Short Form Health Survey, and walking

(dis)ability was determined by the Walking Impairment Questionnaire (WIQ). Measurements were performed at baseline and after 3, 6, 9, and 12 months. Only patients who met the 12-month follow-up measure were included in the analysis.

**RESULTS:** A total of 113 men and 56 women were available for analysis. At baseline, groups were similar in terms of clinical characteristics and ACD walking distances (men, 250 meters; women, 270 meters;  $P = .45$ ). ACD improved for both sexes. However, ACD increase was significantly lower for women than for men during the first 3 months of SET (? 280 meters for men vs ? 220 meters for women;  $P = .04$ ). Moreover, absolute walking distance was significantly shorter for women compared with men after 1 year (565 meters vs 660 meters;  $P = .032$ ). Women also reported less on several WIQ subdomains, although total WIQ score was similar (0.69 for men vs 0.61 for women;  $P = .592$ ). No differences in quality of life after SET were observed.

**CONCLUSIONS:** Women with IC benefit less during the first 3 months of SET and have lower absolute walking distances after 12 months of follow-up compared with men. More research is needed to determine whether gender-based IC treatment strategies are required.

*impactfactor:* 3.021

## Gommans L

### [Infantile myofibroma: a neonate with a swelling on the arm] - Het infantiel myofibroom: een neonaat met een gezwel van de onderarm

Gommans LN<sup>∞</sup>, Spring In 't Veld LG, van der Putten ME, Wijnen MH

Ned Tijdschr Geneesk. 2015;159(0):A8685

**BACKGROUND:** An infantile myofibroma (IM) is a benign congenital soft-tissue tumour. IM is found in 1 per 150,000 live births, making it the most common fibrous tumour of infancy and early childhood.

**CASE DESCRIPTION:** We report on a full-term neonate presenting with an irregular tumour mass on the right lower-arm. The mass measured 5 cm in diameter, with surface ulceration. Magnetic resonance imaging (MRI) revealed characteristics that could be consistent with malignancy. On the basis of a biopsy and subsequent polymerase chain reaction we were able to make a diagnosis of 'benign infantile myofibroma'. We chose for conservative treatment in the expectation that the tumour would regress spontaneously.

**CONCLUSION:** Infantile myofibroma should be considered when a newborn presents with an atypical mass. It is difficult to make a diagnosis on the basis of the clinical characteristics alone due to the heterogenous presentation. A definitive diagnosis can only be made following histological investigation.

<sup>∞</sup> = Ten tijde van publicatie werkzaam bij: Radboudumc, Nijmegen. Afd Kindergeneeskunde, coassistent (thans: arts-onderzoeker Catharina Ziekenhuis Eindhoven)

*impactfactor:* --

## Gommans L

### Safety of supervised exercise therapy in patients with intermittent claudication

Gommans LN\*, Fokkenrood HJ\*, van Dalen HC\*, Scheltinga MR, Teijink JA\*, Peters RJ

J Vasc Surg. 2015 Feb;61(2):512-518.e2

**BACKGROUND:** Supervised exercise therapy (SET) is recommended as the primary treatment for patients with intermittent claudication (IC). However, there is concern regarding the safety of performing SET because IC patients are at risk for untoward cardiovascular events. The Dutch physical therapy guideline advocates cardiac exercise testing before SET, if indicated. Perceived uncertainties concerning safety may contribute to the underuse of SET

in daily practice. The objective of this review was to analyze the safety of supervised exercise training in patients with IC.

**METHODS:** Two authors independently studied clinical trials investigating SET. Data were obtained from MEDLINE, EMBASE, and The Cochrane Central Register of Controlled Trials. Complication rates were calculated and expressed as number of events per number of patient-hours. The usefulness of cardiac screening before SET was evaluated in a subanalysis.

**RESULTS:** Our search strategy revealed 2703 abstracts. We selected 121 articles, of which 74 met the inclusion criteria. Studies represent 82,725 hours of training in 2876 IC patients. Eight adverse events were reported, six of cardiac and two of noncardiac origin, resulting in an all-cause complication rate of one event per 10,340 patient-hours.

**CONCLUSIONS:** SET can safely be prescribed in patients with IC because an exceedingly low all-cause complication rate was found. Routine cardiac screening before commencing SET is not required. Our results may diminish perceived uncertainties regarding safety and will possibly increase the use of SET in daily practice.

*impactfactor:* 3.021

## **Hageman D**

### **Commentary on "Supervised versus unsupervised exercise for intermittent claudication: A systematic review and meta-analysis"**

Hageman D\*, Gommans LN\*, Fokkenrood HJ\*, Koelema MJ, Teijink JA\*

Am Heart J. 2015 Aug;170(2):e1-3

*Geen abstract beschikbaar*

*impactfactor:* 4.463

## **Heijkant AC van den**

### **Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery**

van den Heijkant TC\*, Costes LM, van der Lee DG\*, Aerts B, Osinga-de Jong M, Rutten HR\*, Hulsewé KW, de Jonge WJ, Buurman WA, Luyer MD\*

Br J Surg. 2015 Feb;102(3):202-11. Epub 2014 Dec 18

**BACKGROUND:** Postoperative ileus (POI) is a common complication following colorectal surgery that delays recovery and increases length of hospital stay. Gum chewing may reduce POI and therefore enhance recovery after surgery. The aim of the study was to evaluate the effect of gum chewing on POI, length of hospital stay and inflammatory parameters.

**METHODS:** Patients undergoing elective colorectal surgery in one of two centres were randomized to either chewing gum or a dermal patch (control). Chewing gum was started before surgery and stopped when oral intake was resumed. Primary endpoints were POI and length of stay. Secondary endpoints were systemic and local inflammation, and surgical complications. Gastric emptying was measured by ultrasonography. Soluble tumour necrosis factor receptor 1 (TNFRSF1A) and interleukin (IL) 8 levels were measured by enzyme-linked immunosorbent assay.

**RESULTS:** Between May 2009 and September 2012, 120 patients were randomized to chewing gum (58) or dermal patch (control group; 62). Mean(s.d.) length of hospital stay was shorter in the chewing gum group than in controls, but this difference was not significant: 9.5(4.9) versus 14.0(14.5) days respectively. Some 14 (27 per cent) of 52 analysed patients allocated to chewing gum developed POI compared with 29 (48 per cent) of 60 patients in the control group ( $P=0.020$ ). More patients in the chewing gum group first defaecated within 4 days of surgery (85 versus 57 per cent;  $P=0.006$ ) and passed first flatus within

48% (65 versus 50 per cent;  $P=0.044$ ). The decrease in antral area measured by ultrasonography following a standard meal was significantly greater among patients who chewed gum: median 25 (range -36 to 54) per cent compared with 10 (range -152 to 54) per cent in controls ( $P=0.004$ ). Levels of IL-8 (133 versus 288 pg/ml;  $P=0.045$ ) and TNFRSF1A (0.74 versus 0.92 ng/ml;  $P=0.043$ ) were lower among patients in the chewing gum group. Fewer patients in this group developed a grade IIIb complication (2 of 58 versus 10 of 62;  $P=0.031$ ).

**CONCLUSION:** Gum chewing is a safe and simple treatment to reduce POI, and is associated with a reduction in systemic inflammatory markers and complications.

*impactfactor:* 5.542

## Hingh IH de

### A Nationwide Comparison of Laparoscopic and Open Distal Pancreatectomy for Benign and Malignant Disease

de Rooij T, Jilesen AP, Boerma D, Bonsing BA, Bosscha K, van Dam RM, van Dieren S, Dijkgraaf MG, van Eijck CH, Gerhards MF, van Goor H, van der Harst E, de Hingh IH\*, Kazemier G, Klaase JM, Molenaar IQ, Nieveen van Dijkum EJ, Patijn GA, van Santvoort HC, Scheepers JJ, van der Schelling GP, Sieders E, Vogel JA, Busch OR, Besselink MG; Dutch Pancreatic Cancer Group

J Am Coll Surg. 2015 Mar;220(3):263-270.e1. Epub 2014 Nov 20

**BACKGROUND:** Cohort studies from expert centers suggest that laparoscopic distal pancreatectomy (LDP) is superior to open distal pancreatectomy (ODP) regarding postoperative morbidity and length of hospital stay. But the generalizability of these findings is unknown because nationwide data on LDP are lacking.

**STUDY DESIGN:** Adults who had undergone distal pancreatectomy in 17 centers between 2005 and 2013 were analyzed retrospectively. First, all LDPs were compared with all ODPs. Second, groups were matched using a propensity score. Third, the attitudes of pancreatic surgeons toward LDP were surveyed. The primary outcome was major complications (Clavien-Dindo grade  $\geq$  III).

**RESULTS:** Among 633 included patients, 64 patients (10%) had undergone LDP and 569 patients (90%) had undergone ODP. Baseline characteristics were comparable, except for previous abdominal surgery and mean tumor size. In the full cohort, LDP was associated with fewer major complications (16% vs 29%;  $p = 0.02$ ) and a shorter median [interquartile range, IQR] hospital stay (8 days [7-12 days] vs 10 days [8-14 days];  $p = 0.03$ ). Of all LDPs, 33% were converted to ODP. Matching succeeded for 63 LDP patients. After matching, the differences in major complications (9 patients [14%] vs 19 patients [30%];  $p = 0.06$ ) and median [IQR] length of hospital stay (8 days [7-12 days] vs 10 days [8-14 days];  $p = 0.48$ ) were not statistically significant. The survey demonstrated that 85% of surgeons welcomed LDP training.

**CONCLUSIONS:** Despite nationwide underuse and an impact of selection bias, outcomes of LDP seemed to be at least noninferior to ODP. Specific training is welcomed and could improve both the use and outcomes of LDP.

*impactfactor:* 5.122



**Hingh IH de**

**Adjuvant hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with colon cancer at high risk of peritoneal carcinomatosis; the COLOPEC randomized multicentre trial**

Klaver CE, Musters GD, Bemelman WA, Punt CJ, Verwaal VJ, Dijkgraaf MG, Aalbers AG, van der Bilt JD, Boerma D, Bremers AJ, Burger JW, Buskens CJ, Evers P, van Ginkel RJ, van Grevenstein WM, Hemmer PH, de Hingh IH\*, Lammers LA, van Leeuwen BL, Meijerink WJ, Nienhuijs SW, Pon J, Radema SA, van Ramshorst B, Snaebjornsson P, Tuynman JB, Te Velde E, Wiezer MJ, de Wilt JH, Tanis PJ

BMC Cancer. 2015 May 24;15:428

**BACKGROUND:** The peritoneum is the second most common site of recurrence in colorectal cancer. Early detection of peritoneal carcinomatosis (PC) by imaging is difficult. Patients eventually presenting with clinically apparent PC have a poor prognosis. Median survival is only about five months if untreated and the benefit of palliative systemic chemotherapy is limited. Only a quarter of patients are eligible for curative treatment, consisting of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CR/HIPEC). However, the effectiveness depends highly on the extent of disease and the treatment is associated with a considerable complication rate. These clinical problems underline the need for effective adjuvant therapy in high-risk patients to minimize the risk of outgrowth of peritoneal micro metastases. Adjuvant hyperthermic intraperitoneal chemotherapy (HIPEC) seems to be suitable for this purpose. Without the need for cytoreductive surgery, adjuvant HIPEC can be performed with a low complication rate and short hospital stay.

**METHODS/DESIGN:** The aim of this study is to determine the effectiveness of adjuvant HIPEC in preventing the development of PC in patients with colon cancer at high risk of peritoneal recurrence. This study will be performed in the nine Dutch HIPEC centres, starting in April 2015. Eligible for inclusion are patients who underwent curative resection for T4 or intra-abdominally perforated cM0 stage colon cancer. After resection of the primary tumour, 176 patients will be randomized to adjuvant HIPEC followed by routine adjuvant systemic chemotherapy in the experimental arm, or to systemic chemotherapy only in the control arm. Adjuvant HIPEC will be performed simultaneously or shortly after the primary resection. Oxaliplatin will be used as chemotherapeutic agent, for 30 min at 42-43 °C. Just before HIPEC, 5-fluorouracil and leucovorin will be administered intravenously. Primary endpoint is peritoneal disease-free survival at 18 months. Diagnostic laparoscopy will be performed routinely after 18 months postoperatively in both arms of the study in patients without evidence of disease based on routine follow-up using CT imaging and CEA.

**DISCUSSION:** Adjuvant HIPEC is assumed to reduce the expected 25 % absolute risk of PC in patients with T4 or perforated colon cancer to a risk of 10 %. This reduction is likely to translate into a prolonged overall survival.

*impactfactor:* 3.362

**Hingh IH de**

**Changes in gastrointestinal cancer resection rates**

Speelman AD, van Gestel YR, Rutten HJ\*, de Hingh IH\*, Lemmens VE  
Br J Surg. 2015 Aug;102(9):1114-22. Epub 2015 Jun 9

*Voor abstract zie:* Chirurgie - Rutten HJ

*impactfactor:* 5.542

**Hingh IH de**

**Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (CARTS study).**

Verseveld M, de Graaf EJ, Verhoef C, van Meerten E, Punt CJ, de Hingh IH\*, Nagtegaal ID, Nuyttens JJ, Marijnen CA, de Wilt JH; CARTS Study Group. Collaborator: Rutten HJ\*  
Br J Surg. 2015 Jun;102(7):853-60

BACKGROUND: This prospective multicentre study was performed to quantify the number of patients with minimal residual disease (ypT0-1) after neoadjuvant chemoradiotherapy and transanal endoscopic microsurgery (TEM) for rectal cancer.

METHODS: Patients with clinically staged T1-3?N0 distal rectal cancer were treated with long-course chemoradiotherapy. Clinical response was evaluated 6-8 weeks later and TEM performed. Total mesorectal excision was advocated in patients with residual disease (ypT2 or more).

RESULTS: The clinical stage was cT1?N0 in ten patients, cT2?N0 in 29 and cT3?N0 in 16 patients. Chemoradiotherapy-related complications of at least grade 3 occurred in 23 of 55 patients, with two deaths from toxicity, and two patients did not have TEM or major surgery. Among 47 patients who had TEM, ypT0-1 disease was found in 30, ypT0?N1 in one, ypT2 in 15 and ypT3 in one. Local recurrence developed in three of the nine patients with ypT2 tumours who declined further surgery. Postoperative complications grade I-IIIb occurred in 13 of 47 patients after TEM and in five of 12 after (completion) surgery. After a median follow-up of 17 months, four local recurrences had developed overall, three in patients with ypT2 and one with ypT1 disease.

CONCLUSION: TEM after chemoradiotherapy enabled organ preservation in one-half of the patients with rectal cancer.

*impactfactor: 5.542*

**Hingh IH de**

**Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease**

Orsini RG\*, Verhoeven RH, Lemmens VE, van Steenberg LN, de Hingh IH\*, Nieuwenhuijzen GA\*, Rutten HJ\*

Eur J Cancer. 2015 Sep;51(13):1675-82

*Voor abstract zie: Chirurgie - Orsini RG*

*impactfactor: 5.417*

**Hingh IH de**

**Diagnostic value of a pancreatic mass on computed tomography in patients undergoing pancreatoduodenectomy for presumed pancreatic cancer**

Gerritsen A, Bollen TL, Nio CY, Molenaar IQ, Dijkgraaf MG, van Santvoort HC, Offerhaus GJ, Brosens LA, Biermann K, Sieders E, de Jong KP, van Dam RM, van der Harst E, van Goor H, van Ramshorst B, Bonsing BA, de Hingh IH\*, Gerhards MF, van Eijck CH, Gouma DJ, Borel Rinkes IH, Busch OR, Besselink MG; Dutch Pancreatic Cancer Group Surgery. 2015 Jul;158(1):173-82

INTRODUCTION: Previous studies have shown that 5-14% of patients undergoing pancreatoduodenectomy for suspected malignancy ultimately are diagnosed with benign disease. A "pancreatic mass" on computed tomography (CT) is considered to be the strongest predictor of malignancy, but studies describing its diagnostic value are lacking. The aim of this study was to determine the diagnostic value of a pancreatic mass on CT in

patients with presumed pancreatic cancer, as well as the interobserver agreement among radiologists and the additional value of reassessment by expert-radiologists.

**METHODS:** Reassessment of preoperative CT scans was performed within a previously described multicenter retrospective cohort study in 344 patients undergoing pancreatoduodenectomy for suspected malignancy (2003-2010). Preoperative CT scans were reassessed by 2 experienced abdominal radiologists separately and subsequently in a consensus meeting, after defining a pancreatic mass as "a measurable space occupying soft tissue density, except for an enlarged papilla or focal steatosis".

**RESULTS:** CT scans of 86 patients with benign and 258 patients with (pre)malignant disease were reassessed. In 66% of patients a pancreatic mass was reported in the original CT report, versus 48% and 50% on reassessment by the 2 expert radiologists separately and 44% in consensus ( $P < .001$  vs original report). Interobserver agreement between the original CT report and expert consensus was fair ( $\kappa = 0.32$ , 95% confidence interval 0.23-0.42). Among both expert-radiologists agreement was moderate ( $\kappa = 0.47$ , 95% confidence interval 0.38-0.56), with disagreement on the presence of a pancreatic mass in 29% of cases. The specificity for malignancy of pancreatic masses identified in expert consensus was twice as high compared with the original CT report (87% vs 42%, respectively). Positive predictive value increased to 98% after expert consensus, but negative predictive value was low (12%).

**CONCLUSION:** Clinicians need to be aware of potential considerable disagreement among radiologists about the presence of a pancreatic mass. The specificity for malignancy doubled by expert radiologist reassessment when a uniform definition of "pancreatic mass" was used.

*impactfactor:* 3.380

### **Hingh IH de**

#### **Does extended surgery influence health-related quality of life in patients with rectal cancer?**

Orsini RG\*, Vermeer TA\*, Traa MJ, Nieuwenhuijzen GA\*, de Hingh IH\*, Rutten HJ\*

Dis Colon Rectum. 2015 Feb;58(2):179-85

*Voor abstract zie:* Chirurgie - Orsini RG

*impactfactor:* 2.615

### **Hingh IH de**

#### **Hospital of diagnosis and likelihood of surgical treatment for pancreatic cancer**

Bakens MJ\*, van Gestel YR, Bongers M, Besselink MG, Dejong CH, Molenaar IQ, Busch OR, Lemmens VE, de Hingh IH\*; Dutch Pancreatic Cancer Group

Br J Surg. 2015 Dec;102(13):1670-5. Epub 2015 Oct 5

*Voor abstract zie:* Chirurgie - Bakens MJ

*impactfactor:* 5.542

### **Hingh IH de**

#### **Hypertherme intraperitoneale chemotherapie voor het peritoneaal gemetastaseerd coloncarcinoom: stand van zaken in Nederland**

Hingh IH de

Oncotherapie Online

*impactfactor:* --

**Hingh IH de**

**Impact of centralization of pancreatoduodenectomy on reported radical resections rates in a nationwide pathology database**

Onete VG, Besselink MG, Salsbach CM, Van Eijck CH, Busch OR, Gouma DJ, de Hingh IH\*, Sieders E, Dejong CH, Offerhaus JG Molenaar IQ; Dutch Pancreatic Cancer Group HPB (Oxford). 2015 Aug;17(8):736-42

BACKGROUND: Centralization of a pancreatoduodenectomy (PD) leads to a lower post-operative mortality, but is unclear whether it also leads to improved radical (R0) or overall resection rates.

METHODS: Between 2004 and 2009, pathology reports of 1736 PDs for pancreatic and periampullary neoplasms from a nationwide pathology database were analysed. Pre-malignant lesions were excluded. High-volume hospitals were defined as performing  $\geq 20$  PDs annually. The relationship between R0 resections, PD-volume trends, quality of pathology reports and hospital volume was analysed.

RESULTS: During the study period, the number of hospitals performing PDs decreased from 39 to 23. High-volume hospitals reported more R0 resections in the pancreatic head and distal bile duct tumours than low-volume hospitals (60% versus 54%,  $P = 0.035$ ) although they operated on more advanced (T3/T4) tumours (72% versus 58%,  $P < 0.001$ ). The number of PDs increased from 258 in 2004 to 394 in 2009 which was partly explained by increased overall resection rates of pancreatic head and distal bile duct tumours (11.2% in 2004 versus 17.5% in 2009,  $P < 0.001$ ). The overall reported R0 resection rate of pancreatic head and distal bile duct tumours increased (6% in 2004 versus 11% in 2009,  $P < 0.001$ ). Pathology reports of low-volume hospitals lacked more data including tumour stage (25% versus 15%,  $P < 0.001$ ).

CONCLUSIONS: Centralization of PD was associated with both higher resection rates and more reported R0 resections. The impact of this finding on overall survival should be further assessed.

*impactfactor:* 2.675

**Hingh IH de**

**Implementation of a Standardized HIPEC Protocol Improves Outcome for Peritoneal Malignancy**

Kuijpers AM, Aalbers AG, Nienhuijs SW\*, de Hingh IH\*, Wiezer MJ, van Ramshorst B, van Ginkel RJ, Havenga K, Heemsbergen WD, Hauptmann M, Verwaal VJ  
World J Surg. 2015 Feb;39(2):453-60.

*Voor abstract zie: Chirurgie - Nienhuijs SW*

*impactfactor:* 2.642

**Hingh IH de**

**Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

*Voor abstract zie: Chirurgie - Oudheusden TR van*

*impactfactor:* 3.009

**Hingh IH de**

**Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial**

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruij PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22

Voor abstract zie: *Chirurgie - Nienhuijs SW*

impactfactor: 45.217

**Hingh IH de**

**Metal or plastic stents for preoperative biliary drainage in resectable pancreatic cancer**

Tol JA, van Hooft JE, Timmer R, Kubben FJ, van der Harst E, de Hingh IH\*, Vleggaar FP, Molenaar IQ, Keulemans YC, Boerma D, Bruno MJ, Schoon EJ\*, van der Gaag NA, Besselink MG, Fockens P, van Gulik TM, Rauws EA, Busch OR, Gouma DJ

Gut. 2015 Aug 25. pii: gutjnl-2014-308762

**INTRODUCTION:** In pancreatic cancer, preoperative biliary drainage (PBD) increases complications compared with surgery without PBD, demonstrated by a recent randomised controlled trial (RCT). This outcome might be related to the plastic endoprosthesis used. Metal stents may reduce the PBD-related complications risk. **METHODS:** A prospective multicentre cohort study was performed including patients with obstructive jaundice due to pancreatic cancer, scheduled to undergo PBD before surgery. This cohort was added to the earlier RCT (ISRCTN31939699). The RCT protocol was adhered to, except PBD was performed with a fully covered self-expandable metal stent (FCSEMS). This FCSEMS cohort was compared with the RCT's plastic stent cohort. PBD-related complications were the primary outcome. Three-group comparison of overall complications including early surgery patients was performed. **RESULTS:** 53 patients underwent PBD with FCSEMS compared with 102 patients treated with plastic stents. Patients' characteristics did not differ. PBD-related complication rates were 24% in the FCSEMS group vs 46% in the plastic stent group (relative risk of plastic stent use 1.9, 95% CI 1.1 to 3.2,  $p=0.011$ ). Stent-related complications (occlusion and exchange) were 6% vs 31%. Surgical complications did not differ, 40% vs 47%. Overall complication rates for the FCSEMS, plastic stent and early surgery groups were 51% vs 74% vs 39%. **CONCLUSIONS:** For PBD in pancreatic cancer, FCSEMS yield a better outcome compared with plastic stents. Although early surgery without PBD remains the treatment of choice, FCSEMS should be preferred over plastic stents whenever PBD is indicated.

impactfactor: 14.66

**Hingh IH de**

**Peritoneal Cancer Patients Not Suitable for Cytoreductive Surgery and HIPEC During Explorative Surgery: Risk Factors, Treatment Options, and Prognosis.**

van Oudheusden TR\*, Braam HJ, Luyer MD\*, Wiezer MJ, van Ramshorst B, Nienhuijs SW\*, de Hingh IH\*

Ann Surg Oncol. 2015 Apr;22(4):1236-42. Epub 2014 Oct 16

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.930

**Hingh IH de**

**Peritoneal metastases from small bowel cancer: Results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in The Netherlands**

van Oudheusden TR\*, Lemmens VE, Braam HJ, van Ramshorst B, Meijerink J, te Velde EA, Mehta AM, Verwaal VJ\*, de Hingh IH\*

Surgery. 2015 Jun;157(6):1023-7. Epub 2015 Mar 25

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.380

**Hingh IH de**

**[Peritonitis carcinomatosa from colorectal carcinoma: new treatment options] - Peritonitis carcinomatosa van colorectaal carcinoom : nieuwe behandel mogelijkheden**

Verwaal VJ\*, De Hingh IH\*, Boot H

Ned Tijdschr Geneeskd. 2015;159:A9319

Voor abstract zie: *Chirurgie - Verwaal VJ*

impactfactor: --

**Hingh IH de**

**Poor outcome after cytoreductive surgery and HIPEC for colorectal peritoneal carcinomatosis with signet ring cell histology**

van Oudheusden TR\*, Braam HJ, Nienhuijs SW\*, Wiezer MJ, van Ramshorst B, Luyer P\*, de Hingh IH\*

J Surg Oncol. 2015 Feb;111(2):237-42. Epub 2014 Sep 5

Voor abstract zie: *Oudheusden TR van - Chirurgie*

impactfactor: 2.644

**Hingh IH de**

**Postoperative care after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedures**

Rieff EA, Stolker RJ, Koning J, de Hingh IH\*, Buise MP\*

Anaesth Intensive Care. 2015 Jul;43(4):532-3

geen abstract beschikbaar

impactfactor: 1.296

**Hingh IH de**

**Respiratory distress due to malignant ascites palliated by hyperthermic intraperitoneal chemotherapy**

van den Houten MM\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, de Hingh IH\* World J Gastrointest Surg. 2015 Mar 27;7(3):39-42

Voor abstract zie: *Chirurgie - Houten MM van den*

impactfactor: 2.798

Hingh IH de

**Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial**

da Costa DW, Bouwense SA, Schepers NJ, Besselink MG, van Santvoort HC, van Brunschot S, Bakker OJ, Bollen TL, Dejong CH, van Goor H, Boermeester MA, Bruno MJ, van Eijck CH, Timmer R, Weusten BL, Consten EC, Brink MA, Spanier BW, Bilgen EJ, Nieuwenhuijs VB, Hofker HS, Rosman C, Voorburg AM, Bosscha K, van Duijvendijk P, Gerritsen JJ, Heisterkamp J, de Hingh IH\*, Witteman BJ, Kruijt PM, Scheepers JJ, Molenaar IQ, Schaapherder AF, Manusama ER, van der Waaij LA, van Unen J, Dijkgraaf MG, van Ramshorst B, Gooszen HG, Boerma D; Dutch Pancreatitis Study Group

Lancet. 2015 Sep 26;386(10000):1261-8

**BACKGROUND:** In patients with mild gallstone pancreatitis, cholecystectomy during the same hospital admission might reduce the risk of recurrent gallstone-related complications, compared with the more commonly used strategy of interval cholecystectomy. However, evidence to support same-admission cholecystectomy is poor, and concerns exist about an increased risk of cholecystectomy-related complications with this approach. In this study, we aimed to compare same-admission and interval cholecystectomy, with the hypothesis that same-admission cholecystectomy would reduce the risk of recurrent gallstone-related complications without increasing the difficulty of surgery.

**METHODS:** For this multicentre, parallel-group, assessor-masked, randomised controlled superiority trial, inpatients recovering from mild gallstone pancreatitis at 23 hospitals in the Netherlands (with hospital discharge foreseen within 48 h) were assessed for eligibility. Adult patients (aged ≥18 years) were eligible for randomisation if they had a serum C-reactive protein concentration less than 100 mg/L, no need for opioid analgesics, and could tolerate a normal oral diet. Patients with American Society of Anesthesiologists (ASA) class III physical status who were older than 75 years of age, all ASA class IV patients, those with chronic pancreatitis, and those with ongoing alcohol misuse were excluded. A central study coordinator randomly assigned eligible patients (1:1) by computer-based randomisation, with varying block sizes of two and four patients, to cholecystectomy within 3 days of randomisation (same-admission cholecystectomy) or to discharge and cholecystectomy 25-30 days after randomisation (interval cholecystectomy). Randomisation was stratified by centre and by whether or not endoscopic sphincterotomy had been done. Neither investigators nor participants were masked to group assignment. The primary endpoint was a composite of readmission for recurrent gallstone-related complications (pancreatitis, cholangitis, cholecystitis, choledocholithiasis needing endoscopic intervention, or gallstone colic) or mortality within 6 months after randomisation, analysed by intention to treat. The trial was designed to reduce the incidence of the primary endpoint from 8% in the interval group to 1% in the same-admission group. Safety endpoints included bile duct leakage and other complications necessitating re-intervention. This trial is registered with Current Controlled Trials, number ISRCTN72764151, and is complete.

**FINDINGS:** Between Dec 22, 2010, and Aug 19, 2013, 266 inpatients from 23 hospitals in the Netherlands were randomly assigned to interval cholecystectomy (n=137) or same-admission cholecystectomy (n=129). One patient from each group was excluded from the final analyses, because of an incorrect diagnosis of pancreatitis in one patient (in the interval group) and discontinued follow-up in the other (in the same-admission group). The primary endpoint occurred in 23 (17%) of 136 patients in the interval group and in six (5%) of 128 patients in the same-admission group (risk ratio 0.28, 95% CI 0.12-0.66; p=0.002). Safety endpoints occurred in four patients: one case of bile duct leakage and one case of

postoperative bleeding in each group. All of these were serious adverse events and were judged to be treatment related, but none led to death.

INTERPRETATION: Compared with interval cholecystectomy, same-admission cholecystectomy reduced the rate of recurrent gallstone-related complications in patients with mild gallstone pancreatitis, with a very low risk of cholecystectomy-related complications.

*Comment in: Cholecystectomy in mild gallstone pancreatitis: don't defer. [Lancet. 2015]*

*impactfactor: 45.217*

#### **Hingh IH de**

##### **Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

*Voor abstract zie: Chirurgie - Simkens GA*

*impactfactor: 3.930*

#### **Hingh IH de**

##### **Skeletal Muscle Depletion is Associated with Severe Postoperative Complications in Patients Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Colorectal Cancer**

van Vugt JL, Braam HJ, van Oudheusden TR\*, Vestering A, Bollen TL, Wiezer MJ, de Hingh IH\*, van Ramshorst B, Boerma D

Ann Surg Oncol. 2015 Oct;22(11):3625-31. Epub 2015 Feb 12

Erratum: Ann Surg Oncol. 2015 Dec;22 Suppl 3:1610

*Voor abstract zie: Chirurgie - Oudheusden TR van*

*impactfactor: 3.930*

#### **Hingh IH de**

##### **Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin**

van Oudheusden TR\*, Razenberg LG\*, van Gestel YR, Creemers GJ\*, Lemmens VE, de Hingh IH\*

Sci Rep. 2015 Dec 21;5:18632

*Voor abstract zie: Chirurgie - Oudheusden TR van*

*impactfactor: 5.578*

#### **Hingh IH de**

##### **Tailoring heated intraperitoneal mitomycin C for peritoneal metastases originating from colorectal carcinoma: a translational approach to improve survival**

Kwakman R, de Cuba EM, de Winter JP, de Hingh IH\*, Delis-van Diemen PM, Tijssen M, Rooimans MA, Krijgsman O, Carvalho B, Peters GJ, Bonjer HJ, Meijer GA, Te Velde EA

Br J Cancer. 2015 Mar 3;112(5):851-6

BACKGROUND: Patients with peritoneal metastases (PMs) originating from colorectal carcinoma (CRC) are curatively treated by cytoreductive surgery (CRS) and hyperthermic



intraperitoneal chemotherapy (HIPEC) with mitomycin C (MMC). We aim to improve patient selection for HIPEC by predicting MMC sensitivity.

**METHODS:** The MMC sensitivity was determined for 12 CRC cell lines and correlated to mRNA expression of 37 genes related to the Fanconi anaemia (FA)-BRCA pathway, ATM-ATR pathway and enzymatic activation of MMC. Functionality of the FA-BRCA pathway in cell lines was assessed using a chromosomal breakage assay and western blot for key protein FANCD2. Bloom syndrome protein (BLM) was further analysed by staining for the corresponding protein with immunohistochemistry (IHC) on both CRC cell lines (n=12) and patient material (n=20).

**RESULTS:** High sensitivity correlated with a low BLM ( $P=0.01$ ) and BRCA2 ( $P=0.02$ ) at mRNA expression level. However, FA-BRCA pathway functionality demonstrated no correlation to MMC sensitivity. In cell lines, weak intensity staining of BLM by IHC correlated to high sensitivity ( $P=0.04$ ) to MMC. Low BLM protein expression was significantly associated with an improved survival in patients after CRS and HIPEC ( $P=0.04$ ).

**CONCLUSIONS:** Low BLM levels are associated with high MMC sensitivity and an improved survival after HIPEC.

*impactfactor:* 4.836

#### **Hingh IH de**

##### **Targeting the Peritoneum with Novel Drug Delivery Systems in Peritoneal Carcinomatosis: A Review of the Literature**

Van Oudheusden TR\*, Grull H, Dankers PY, De Hingh IH\*

Anticancer Res. 2015 Feb;35(2):627-634

*Voor abstract zie:* Chirurgie - Oudheusden TR van

*impactfactor:* 1.826

#### **Hingh IH de**

##### **Ten weeks to live: A population-based study on treatment and survival of patients with metastatic pancreatic cancer in the south of the Netherlands**

Bernards N, Haj Mohammad N, Creemers GJ\*, de Hingh IH\*, van Laarhoven HW, Lemmens VE

Acta Oncol. 2015 Mar;54(3):403-10. Epub 2014 Sep 29

*Voor abstract zie:* Inwendige geneeskunde - Bernards N

*impactfactor:* 2.997

#### **Hingh IH de**

##### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hilgsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

*Voor abstract zie:* Chirurgie - Peters EG

*impactfactor:* 2.12

**Hingh IH de**

**The Prognostic Relevance of Histological Subtype in Patients With Peritoneal Metastases From Colorectal Cancer: A Nationwide Population-Based Study**

Razenberg LG\*, van Gestel YR, Lemmens VE, de Wilt JH, Creemers GJ\*, de Hingh IH\*

Clin Colorectal Cancer. 2015 Dec;14(4):e13-9. Epub 2015 Jun 6

Voor abstract zie: *Inwendige geneeskunde - Razenberg LG*

impactfactor: 2.813

**Hingh IH de**

**The relevance of pathological verification in suspected pancreatic cancer**

Bernards N\*, Creemers GJ\*, Huysentruyt CJ, de Hingh IH\*, van der Schelling GP, de Bruïne AP\*, Lemmens VE\*

Cancer Epidemiol. 2015 Apr;39(2):250-5

Voor abstract zie: *Inwendige geneeskunde - Bernards N*

impactfactor: 2.711

**Hingh IH de**

**Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

Voor abstract zie: *Inwendige geneeskunde - Bie AJ de*

impactfactor: 1.969

**Hingh IH de**

**Trends in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for the treatment of synchronous peritoneal carcinomatosis of colorectal origin in the Netherlands**

Razenberg LG\*, van Gestel YR, Creemers GJ\*, Verwaal VJ, Lemmens VE, de Hingh IH\*

Eur J Surg Oncol. 2015 Apr;41(4):466-71. Epub 2015 Jan 29

Voor abstract zie: *Inwendige geneeskunde - Razenberg LG*

impactfactor: 3.009

**Hingh IH de**

**Urological procedures in patients with peritoneal carcinomatosis of colorectal cancer treated with HIPEC: morbidity and survival analysis**

Braam HJ, van Oudheusden TR\*, de Hingh IH\*, Nienhuijs SW\*, Boerma D, Wiezer MJ, van Ramshorst B

Anticancer Res. 2015 Jan;35(1):295-300

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 1.826

**Houten MM van den**

**Agreements and discrepancies between the estimated walking distance, nongraded and graded treadmill testing, and outside walking in patients with intermittent claudication**

Fokkenrood HJ\*, van den Houten MM\*, Houterman S\*, Breek JC, Scheltinga MR, Teijink JA\*

Ann Vasc Surg. 2015 Aug;29(6):1218-24

Voor abstract zie: *Chirurgie - Fokkenrood HJ*

impactfactor: 1.170

**Houten MM van den**

**Respiratory distress due to malignant ascites palliated by hyperthermic intraperitoneal chemotherapy**

van den Houten MM\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, de Hingh IH\*

World J Gastrointest Surg. 2015 Mar 27;7(3):39-42

Malignant ascites is a common symptom in patients with peritoneal cancer. Current assumption is that an increased vascular permeability and obstruction of lymphatic channels lead to the accumulation of fluid in the abdominal cavity. This case report describes a severely symptomatic patient with malignant ascites. The previously healthy 73-year-old male was presented with abdominal distention causing respiratory distress. Computed tomography revealed large amounts of ascites, a recto-sigmoidal mass with locoregional lymphadenopathy and an omental cake. Biopsy taken during colonoscopy revealed an adenocarcinoma of the colon with signet cell differentiation. A widespread peritoneal carcinomatosis was found during a diagnostic laparoscopy. The extent of peritoneal disease rendered the patient not suitable for cytoreductive surgery with curative intent. The ascites proved to be refractory to ultrasound-guided paracentesis; thus, a decision was made to perform palliative hyperthermic intraperitoneal chemotherapy without cytoreductive surgery. Consequently, ascites production stopped, and the respiratory distress was relieved thereafter. The postoperative recovery was uneventful. Ascites recurred eight months later, and a second hyperthermic intraperitoneal chemotherapy procedure was performed. The patient was still alive at the time of writing, 16 mo after the initial diagnosis.

impactfactor: 2.798

**Jakimowicz JJ**

**Gastric Wall Thickness in Sleeve Gastrectomy Patients: Thickness Variation of the Gastric Wall**

van Rutte PW\*, Naagen BJ, Spek M, Jakimowicz JJ\*, Nienhuijs SW\*

Surg Technol Int. 2015 Nov;27:123-8

Voor abstract zie: *Chirurgie - van Rutte PW*

impactfactor: --

**Klaver YL**

**[A woman with lumps in her breast] / Een vrouw met knobbeltjes in de borst**

Klaver YL\*, Keymeulen KB, Lobbjes MB.

Ned Tijdschr Geneesk. 2015;159:A9299

A 61-year-old woman was examined for multiple lumps and an ulcer in her breast, 23 years after breast-conserving therapy for breast cancer, including surgery, chemotherapy and

radiation therapy. Clinical examination and imaging showed extensive calcifications as a late effect of irradiation, which was confirmed by the pathologist after surgery.

impactfactor: --

#### **Koëter M**

##### **Determinants in decision making for curative treatment and survival in patients with resectable oesophageal cancer in the Netherlands: a population-based study**

Koëter M\*, van Steenberghe LN, Lemmens VE, Rutten HJ\*, Roukema JA, Nieuwenhuijzen GA\*

Cancer Epidemiol. 2015 Dec;39(6):863-9

**BACKGROUND:** Preferred treatment for resectable oesophageal cancer is surgery with or without neoadjuvant treatment. However, oesophageal surgery has high morbidity and in vulnerable patients with co-morbidity other treatment modalities can be proposed. We examined determinants in decision making for surgery and factors affecting survival in patients with resectable oesophageal cancer in southern Netherlands.

**METHODS:** All patients with resectable (T1-3, N0-1, M0-1A) oesophageal cancer (n=849) diagnosed between 2003 and 2010 were selected from the population-based data of the Eindhoven Cancer Registry. Logistic regression analysis and multivariable Cox survival analysis were conducted to examine determinants of surgery and survival.

**RESULTS:** Forty-five percent of the patients underwent surgery. In multivariable survival analysis only surgery, chemoradiation alone and tumour stage influenced overall survival (OS). Patients aged  $\geq 70$  yrs, a low socioeconomic status (SES), one or more co-morbidities, cT1-tumours, cN1-tumours, a squamous-cell carcinoma, and those with a proximal tumour were significantly less often offered surgical resection. Older patients and patients with cT1 tumours were less likely to receive chemoradiation alone. Patients with clinically positive lymph nodes or a proximal tumour were more likely to receive chemoradiation alone.

**CONCLUSION:** Treatment modalities including surgery and chemoradiation alone as well as stage of disease were independent predictors of a better OS in patients with potentially resectable oesophageal cancer. Therefore, the decision to perform potentially curative treatment is of crucial importance to improve OS for patients with potentially resectable oesophageal cancer. Although age and SES had no significant influence on overall survival, a higher age and low SES negatively influenced the probability to propose potentially curative treatment.

impactfactor: 2.711

#### **Koëter M**

##### **Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59

**BACKGROUND:** Neoadjuvant chemoradiation might increase anastomotic leakage and stenosis in patients with esophageal cancer treated with neoadjuvant chemoradiation and esophagectomy. The aim of this study was to determine the influence of radiation dose on the incidence of leakage and stenosis.

**METHODS:** Fifty-three patients with esophageal cancer received neoadjuvant chemoradiation (23 Gy  $\times$  1.8 Gy) (combined with Paclitaxel and Carboplatin) followed by a

transhiatal esophagectomy between 2009 and 2011. On planning CT, the future anastomotic region was determined and the mean radiation dose, V20, V25, V30, V35 and V40 were calculated. Logistic regression analysis was conducted to examine determinants of anastomotic leakage and stenosis.

**RESULTS:** Anastomotic leaks occurred in 13 of 53 patients (25.5%) and anastomotic stenosis occurred in 24 of 53 patients (45.3%). Median follow-up was 20 months. Logistic regression analysis showed that mean dose, V20-V40, age, co-morbidity, method of anastomosis, operating time and interval between last radiotherapy treatment and surgery were not predictors of anastomotic leakage and stenosis.

**CONCLUSIONS:** A radiation dose of 23-24.8 Gy on the future anastomotic region has no influence on the occurrence of anastomotic leakage and stenosis in patients with esophageal cancer treated with neoadjuvant chemoradiation followed by transhiatal esophagectomy.

*impactfactor:* 2.546

### **Kools-Aarts M**

#### **Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*

Springerplus. 2015 Jul 7;4:322

*Voor abstract zie:* Chirurgie - Pouwels S

*impactfactor:* --

### **Kusters M**

#### **Survival after pelvic exenteration for T4 rectal cancer**

Kusters M\*, Austin KK, Solomon MJ, Lee PJ, Nieuwenhuijzen GA\*, Rutten HJ\*

Br J Surg. 2015 Jan;102(1):125-31

**BACKGROUND:** The purpose of this study was to analyse retrospectively the pooled results after pelvic exenteration for locally advanced T4 rectal cancer. Historically, patients with T4 rectal cancers requiring pelvic exenteration have been offered only palliative surgery or no operation.

**METHODS:** The basic treatment principle was preoperative (chemo)radiotherapy, radical surgery and, in some patients, adjuvant chemotherapy. Risk factors for local recurrence, distant metastases and overall survival were studied in univariable and multivariable analyses.

**RESULTS:** Ninety-five patients with T4 rectal cancer who underwent pelvic exenteration in two tertiary referral centres up to 2013 were studied. Clear margins (R0) were achieved in 87% per cent of patients. Adjuvant chemotherapy was administered in 33% per cent, independent of the resection margin, lymph node status and postoperative T category. The 5-year local recurrence rate was 17% per cent, with a distant metastasis rate of 16% per cent and overall survival rate of 62% per cent. In multivariable analysis the only factor associated with death was omission of adjuvant chemotherapy ( $P=0.016$ ). The effect of adjuvant chemotherapy was more pronounced in the elderly: patients aged over 70 years who had chemotherapy had a 5-year overall survival rate of 80% per cent, compared with 39% per cent of elderly patients who did not receive chemotherapy ( $P=0.019$ ).

**CONCLUSION:** Pelvic exenteration led to an R0 resection rate of 87% per cent for T4 rectal cancer, giving good local control and overall survival comparable to population-based colorectal cancer survival rates. Adjuvant chemotherapy may improve overall survival further, even in the elderly.

*impactfactor:* 5.542

**Lee D van der**

**Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery**

van den Heijkant TC\*, Costes LM, van der Lee DG\*, Aerts B, Osinga-de Jong M, Rutten HR\*, Hulsewé KW, de Jonge WJ, Buurman WA, Luyer MD.

Br J Surg. 2015 Feb;102(3):202-11. Epub 2014 Dec 18

Voor abstract zie: *Chirurgie - Heijkant TC van den*

*impactfactor: 5.542*

**Luyer MD**

**Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy**

Berkelmans GH\*, Kouwenhoven EA, Smeets BJ\*, Weijs TJ\*, Silva Corten LC, van Det MJ, Nieuwenhuijzen GA\*, Luyer MD\*

World J Gastroenterol. 2015 Aug 14;21(30):9118-25

AIM: To investigate the value of elevated drain amylase concentrations for detecting anastomotic leakage (AL) after minimally invasive Ivor-Lewis esophagectomy (MI-ILE).

METHODS: This was a retrospective analysis of prospectively collected data in two hospitals in the Netherlands. Consecutive patients undergoing MI-ILE were included. A Jackson-Pratt drain next to the dorsal side of the anastomosis and bilateral chest drains were placed at the end of the thorascopic procedure. Amylase levels in drain fluid were determined in all patients during at least the first four postoperative days. Contrast computed tomography scans and/or endoscopic imaging were performed in cases of a clinically suspected AL. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis on endoscopy, re-operation, radiographic investigations, post mortal examination or when gastro-intestinal contents were found in drain fluid. Receiver operator characteristic curves were used to determine the cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value, risk ratio and overall test accuracy were calculated for elevated drain amylase concentrations.

RESULTS: A total of 89 patients were included between March 2013 and August 2014. No differences in group characteristics were observed between patients with and without AL, except for age. Patients with AL were older than were patients without AL ( $P = 0.01$ ). One patient (1.1%) without AL died within 30 d after surgery due to pneumonia and acute respiratory distress syndrome. Anastomotic leakage that required any intervention occurred in 15 patients (16.9%). Patients with proven anastomotic leakage had higher drain amylase levels than patients without anastomotic leakage [median 384 IU/L (IQR 34-6263) vs median 37 IU/L (IQR 26-66),  $P = 0.003$ ]. Optimal cut-off values on postoperative days 1, 2, and 3 were 350 IU/L, 200 IU/L and 160 IU/L, respectively. An elevated amylase level was found in 9 of the 15 patients with AL. Five of these 9 patients had early elevations of their amylase levels, with a median of 2 d (IQR 2-5) before signs and symptoms occurred.

CONCLUSION: Measurement of drain amylase levels is an inexpensive and easy tool that may be used to screen for anastomotic leakage soon after MI-ILE. However, clinical validation of this marker is necessary.

*impactfactor: 2.369*

## **Luyer MD**

### **Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.009

## **Luyer MD**

### **Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial**

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruyt PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22

Voor abstract zie: *Chirurgie - Nienhuijs SW*

impactfactor: 45.217

## **Luyer MD**

### **Laparoscopic versus open gastrectomy for gastric cancer, a multicenter prospectively randomized controlled trial (LOGICA-trial)**

Haverkamp L, Brenkman HJ, Seesing MF, Gisbertz SS, van Berge Henegouwen MI, Luyer MD, Nieuwenhuijzen GA, Wijnhoven BP, van Lanschot JJ, de Steur WO, Hartgrink HH, Stoot JH, Hulsewé KW, Spillenaar Bilgen EJ, Rütter JE, Kouwenhoven EA, van Det MJ, van der Peet DL, Daams F, Draaisma WA, Broeders IA, van Stel HF, Lacle MM, Ruurda JP, van Hillegersberg R; LOGICA study group

BMC Cancer. 2015 Jul 29;15(1):556

**BACKGROUND:** For gastric cancer patients, surgical resection with en-bloc lymphadenectomy is the cornerstone of curative treatment. Open gastrectomy has long been the preferred surgical approach worldwide. However, this procedure is associated with considerable morbidity. Several meta-analyses have shown an advantage in short-term outcomes of laparoscopic gastrectomy compared to open procedures, with similar oncologic outcomes. However, it remains unclear whether the results of these Asian studies can be extrapolated to the Western population. In this trial from the Netherlands, patients with resectable gastric cancer will be randomized to laparoscopic or open gastrectomy. **METHODS:** The study is a non-blinded, multicenter, prospectively randomized controlled superiority trial. Patients (=18 years) with histologically proven, surgically resectable (cT1-4a, N0-3b, M0) gastric adenocarcinoma and European Clinical Oncology Group performance status 0, 1 or 2 are eligible to participate in the study after obtaining informed consent. Patients (n=?210) will be included in one of the ten participating Dutch centers and are randomized to either laparoscopic or open gastrectomy. The primary outcome is postoperative hospital stay (days). Secondary outcome parameters include postoperative morbidity and mortality, oncologic outcomes, readmissions, quality of life and cost-effectiveness. **DISCUSSION:** In this

randomized controlled trial laparoscopic and open gastrectomy are compared in patients with resectable gastric cancer. It is expected that laparoscopic gastrectomy will result in a faster recovery of the patient and a shorter hospital stay. Secondly, it is expected that laparoscopic gastrectomy will be associated with a lower postoperative morbidity, less readmissions, higher cost-effectiveness, better postoperative quality of life, but with similar mortality and oncologic outcomes, compared to open gastrectomy. The study started on 1 December 2014. Inclusion and follow-up will take 3 and 5 years respectively. Short-term results will be analyzed and published after discharge of the last randomized patient.

*impactfactor:* 3.362

## **Luyer MD**

### **Leaving a Mobilized Thoracic Esophagus In Situ When Incurable Cancer Is Discovered Intraoperatively**

Weijts TJ\*, Toxopeus EL, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, Schraepen MC, Sosef MN, Wijnhoven BP, Schets IR, Bleys RL, van Hillegersberg R

Ann Thorac Surg. 2015 Feb;99(2):490-4. Epub 2014 Dec 10

*Voor abstract zie:* Chirurgie - Wijs TJ

*impactfactor:* 3.849

## **Luyer MD**

### **Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*.

Obes Surg. 2015 Aug;25(8):1425-30

*Voor abstract zie:* Chirurgie - Wezenbeek MR van

*impactfactor:* 3.747

## **Luyer MD**

### **Neural reflex pathways in intestinal inflammation: hypotheses to viable therapy**

Willemze RA, Luyer MD\*, Buurman WA, de Jonge WJ

Nat Rev Gastroenterol Hepatol. 2015 Jun;12(6):353-62

Studies in neuroscience and immunology have clarified much of the anatomical and cellular basis for bidirectional interactions between the nervous and immune systems. As with other organs, intestinal immune responses and the development of immunity seems to be modulated by neural reflexes. Sympathetic immune modulation and reflexes are well described, and in the past decade the parasympathetic efferent vagus nerve has been added to this immune-regulation network. This system, designated 'the inflammatory reflex', comprises an afferent arm that senses inflammation and an efferent arm that inhibits innate immune responses. Intervention in this system as an innovative principle is currently being tested in pioneering trials of vagus nerve stimulation using implantable devices to treat IBD. Patients benefit from this treatment, but some of the working mechanisms remain to be established, for instance, treatment is effective despite the vagus nerve not always directly innervating the inflamed tissue. In this Review, we will focus on the direct neuronal regulatory mechanisms of immunity in the intestine, taking into account current advances regarding the innervation of the spleen and lymphoid organs, with a focus on the potential for treatment in IBD and other gastrointestinal pathologies.

*impactfactor:* 12.610



**Luyer MD****Peritoneal Cancer Patients Not Suitable for Cytoreductive Surgery and HIPEC During Explorative Surgery: Risk Factors, Treatment Options, and Prognosis**

van Oudheusden TR\*, Braam HJ, Luyer MD\*, Wiezer MJ, van Ramshorst B, Nienhuijs SW\*, de Hingh IH\*

Ann Surg Oncol. 2015 Apr;22(4):1236-42. Epub 2014 Oct 16

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.930

**Luyer MD****Poor outcome after cytoreductive surgery and HIPEC for colorectal peritoneal carcinomatosis with signet ring cell histology**

van Oudheusden TR\*, Braam HJ, Nienhuijs SW\*, Wiezer MJ, van Ramshorst B, Luyer P\*, de Hingh IH\*

J Surg Oncol. 2015 Feb;111(2):237-42. Epub 2014 Sep 5

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 2.644

**Luyer MD****Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59

Voor abstract zie: *Chirurgie - Koëter M*

impactfactor: 2.546

**Luyer MD****Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery**

van den Heijkant TC\*, Costes LM, van der Lee DG\*, Aerts B, Osinga-de Jong M, Rutten HR\*, Hulsewé KW, de Jonge WJ, Buurman WA, Luyer MD\*

Br J Surg. 2015 Feb;102(3):202-11. Epub 2014 Dec 18

Voor abstract zie: *Chirurgie - Heijkant TC van den*

impactfactor: 5.542

**Luyer MD****Respiratory distress due to malignant ascites palliated by hyperthermic intraperitoneal chemotherapy**

van den Houten MM\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, de Hingh IH\*

World J Gastrointest Surg. 2015 Mar 27;7(3):39-42

Voor abstract zie: *Chirurgie - Houten MM van den*

impactfactor: 2.798

#### **Luyer MD**

##### **Routes for early enteral nutrition after esophagectomy. A systematic review**

Weijs TJ\*, Berkelmans GH\*, Nieuwenhuijzen GA\*, Ruurda JP, Hillegersberg RV, Soeters PB, Luyer MD\*

Clin Nutr. 2015 Feb;34(1):1-6. Epub 2014 Aug 1

Voor abstract zie: *Chirurgie - Weijs TJ*

impactfactor: 4.476

#### **Luyer MD**

##### **Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

Voor abstract zie: *Chirurgie - Simkens GA*

impactfactor: 3.930

#### **Luyer MD**

##### **The contribution of mast cells to postoperative ileus in experimental and clinical studies**

Peters EG\*, De Jonge WJ, Smeets BJ\*, Luyer MD\*

Neurogastroenterol Motil. 2015 Jun;27(6):743-9

Voor abstract zie: *Chirurgie - Peters EG*

impactfactor: --

#### **Luyer MD**

##### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reijlingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hilgsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

Voor abstract zie: *Chirurgie - Peters EG*

impactfactor: 1.731

#### **Luyer MD**

##### **Topic: Rare and Special Cases, The Real "Strange Cases".**

Zarrinkhoo E, Miller J, Walker A, Weisman M, Towfigh S, Tushev R, Petkov I, Tsutsumi G, Leija C, Castillo E, Moncada F, Mendoza M, Morua AG, Bravo R, Azcarate A, Zavala H, Coman IS, Radu EV, David OI, Stoian AR, Strambu VE, Iancu C, Gheorghiu LI, Grigorean VT, Sinescu DR, Plesa E, Lupascu C, Straja DN, Iacobini MA, Ponten J\*, Luyer M\*, Nienhuijs S\*, Permekerlis A, Petousis S, Miroforidis A, Miliadis K, Kouridakis P, Park J, Kim D, Nakata R, Chihara N, Suzuki H, Watanabe M, Uchida E, Nakanaga H, Irie S, Endo Y, Sonoda H, Minamimura K, Kobayashi T, Hirata T, Mafune K, Milosevic P, Babovic M,

Sorat D, Light D, Aawsaj Y, Horgan L, Latham L, Ceriani I, Livraghi L, Berselli M, Gambitta B, Galvanin J, Cotronea C, Pagano G, Farassino L, Ambrosoli A, Crespi A, Coccozza E, Kulic V, Matkovic M, Percevic G, Katayama T, Kumata Y, Ogawa E, Horikawa M, Yaguchi Y, Inaba T, Fukushima R, Jaroszewski D, Johnson K, Harold K, Mori M, Kumata M, Guarnieri F, Smaldone W, Gaspard M, Bomben F, Ceranto S, Gamarra MF, Soria MP, Olivero CF, Martinez MJ, Contin MP, Gómez JC, Jiménez-Valladolid D, Torres García A, Descloux A, Pohle S, Schramm B, Schneider U, Nocito A, Navarrete MC, Solis A, Ortega N, Bergamini S, Semeraro C, Armengol M, Cano ML, Torrecilla NO, Cavallaro G, Iorio O, Avallone M, Ruscio S, Rizzello M, Silecchia G, Butron T, Rubio E, Passas J, Sopeña R, Lagaron E, Silan F, Garcia V, Bernal J, Ortiz M, Guadarrama J, Shirai K, Lomas M, Shah BB, Degloorkar SS.

Hernia. 2015 Apr;19 Suppl 1:S317-27

*geen abstract beschikbaar*

*impactfactor:* 2.050

### **Luyer MD**

#### **Topography and extent of pulmonary vagus nerve supply with respect to transthoracic oesophagectomy.**

Weijs TJ\*, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, van Hillegersberg R, Bleys RL  
J Anat. 2015 Oct;227(4):431-9

*Voor abstract zie:* Chirurgie – Weijs TJ

*impactfactor:* --

### **Maaskant-Braat AJ**

#### **Contralateral lymph node recurrence in breast cancer: Regional event rather than distant metastatic disease. A systematic review of the literature**

Moosdorff M, Vugts G\*, Maaskant-Braat AJ\*, Strobbe LJ, Voogd AC, Smidt ML, Nieuwenhuijzen GA\*

Eur J Surg Oncol. 2015 Sep;41(9):1128-36

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.009

### **Maaskant-Braat AJ**

#### **Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.930

**Maaskant-Braat AJ****Repeat sentinel node biopsy should be considered in patients with locally recurrent breast cancer.**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Luiten EJ, Rutgers EJ, Rutten HJ\*, Roumen RM, Nieuwenhuijzen GA\*

Breast Cancer Res Treat. 2015 Oct;153(3):549-56

Voor abstract zie: *Chirurgie - Vugts G*

impactfactor: 3.940

**Mannetje Y 't****Endovascular Treatment of Ruptured Abdominal Aortic Aneurysms with Hostile Aortic Neck Anatomy**

Broos PP\*, 't Mannetje YW\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Sep;50(3):313-9. Epub 2015 May 28

Voor abstract zie: *Chirurgie - Broos PP*

impactfactor: 3.490

**Montfort G van****Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial**

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruijt PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22

Voor abstract zie: *Chirurgie - Nienhuijs SW*

impactfactor: 45.217

**Montfort G van****Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*

Obes Surg. 2015 Aug;25(8):1425-30

Voor abstract zie: *Chirurgie - Wezenbeek MR van*

impactfactor: 3.747

**Nienhuijs SW****A consecutive series of 235 epigastric hernias**

Ponten JE\*, Leenders BJ, Charbon JA, Nienhuijs SW\*

Hernia. 2015 Oct;19(5):821-5. Epub 2014 Feb 12

Voor abstract zie: *Cardiologie - Ponten JE*

impactfactor: 2.050

### **Nienhuijs SW**

#### **A Rare Cause of Haematemesis; a Primary Aorto-Esophageal Fistula: Case Report and Review of Literature**

Denise Strijbos\*, Johanna W M Holtkamp, Marc R H M Van Sambeek\*, Simon W Nienhuijs\*, Arnold Stronkhorst\* and Lennard P L Gilissen\*

Gastro Open Access, 2015; 3(1): 118

Impactfactor --

### **Nienhuijs SW**

#### **Aspects of Exercise before or after Bariatric Surgery: A Systematic Review**

Pouwels S\*, Wit M\*, Teijink JA\*, Nienhuijs SW\*

Obes Facts. 2015;8(2):132-46

Voor abstract zie: Chirurgie - Pouwels S

impactfactor: 2.245

### **Nienhuijs SW**

#### **Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review**

Pouwels S\*, Willigendael EM, van Sambeek MR\*, Nienhuijs SW\*, Cuypers PW\*, Teijink JA\*

Eur J Vasc Endovasc Surg.2015;49 (1): 66–76 Epub 2014 Nov 14

Voor abstract zie: Chirurgie - Pouwels S

impactfactor: 3.490

### **Nienhuijs SW**

#### **Complex Ventral Situation**

Mommers E, Wegdam J, Nienhuijs S, van der Wolk S, de Vries Reilingh T  
Hernia. 2015 Apr;19 Suppl 1:S33

Geen abstract beschikbaar

impactfactor: 2.050

### **Nienhuijs SW**

#### **Complexe buikwandbreuk verdient aandacht : excelleren in de buikwandoperaties die anderen links laten liggen**

Wegdam J, de Vries-Reilingh T, Nienhuijs S\*

Medisch Contact 2015; 14: 680-2

Geen abstract beschikbaar

impactfactor: --

### **Nienhuijs SW**

#### **Costs of Leaks and Bleeding After Sleeve Gastrectomies**

Bransen J\*, Gilissen LP\*, van Rutte PW, Nienhuijs SW\*

Obes Surg. 2015 Oct;25(10):1767-71

Voor abstract zie: Chirurgie - Bransen J

impactfactor: 3.747

## **Nienhuijs SW**

### **Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*

Springerplus. 2015 Jul 7;4:322

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: --

## **Nienhuijs SW**

### **Gastric Wall Thickness in Sleeve Gastrectomy Patients: Thickness Variation of the Gastric Wall**

van Rutte PW\*, Naagen BJ, Spek M, Jakimowicz JJ\*, Nienhuijs SW\*

Surg Technol Int. 2015 Nov;27:123-8

Voor abstract zie: *Chirurgie - Jakimowicz JJ*

impactfactor: --

## **Nienhuijs SW**

### **Hiatal Hernia**

Castelijns B\*, Ponten JE\*, Van de Poll MC, Nienhuijs SW\*, Smulders JF\*, Hu ZW, Wu JM, Wang ZG, Idani H, Asami S, Nakano K, Miyake S, Harano M, Miyoshi H, Araki H, Ogawa T, Takahashi K, Shiozaki S, Ninomiya M, Prasad A, Todkar J, Asti E, Lovece A, Sironi A, Bonavina , Wright , Wurst H, Zhang C, Li HL, Ke LM, Loi K12, Hua R, Yao QY, Chen H, Okinyi W, Odende K, Ndungu B, Ndonga A, Kiragu P, Kelimu A, Alimujiang M, Tian W, Bing M

Hernia. 2015 Apr;19 Suppl 1:S13-7

Geen abstract beschikbaar

impactfactor: 2.050

## **Nienhuijs SW**

### **Implementation of a Standardized HIPEC Protocol Improves Outcome for Peritoneal Malignancy**

Kuijpers AM, Aalbers AG, Nienhuijs SW\*, de Hingh IH\*, Wiezer MJ, van Ramshorst B, van Ginkel RJ, Havenga K, Heemsbergen WD, Hauptmann M, Verwaal VJ

World J Surg. 2015 Feb;39(2):453-60

**BACKGROUND:** Experience with Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in a pioneer hospital resulted in a treatment protocol that has become the standard in the Netherlands. Outcome of CRS and HIPEC was reviewed to assure differences between the pioneer phase and the period wherein the Dutch HIPEC protocol was clinically implemented

**METHODS:** The first consecutive 100 CRS and HIPEC procedures performed in the Netherlands were included as pioneer cohort (1995-1999). Two-hundred and seventy-two procedures that were performed in three participating HIPEC centres after the implementation of the Dutch HIPEC protocol were included as the implementation cohort (2005-2012). Another 100 recent patients of the first centre were included as a control group (2009-2011). Indications for the CRS and HIPEC treatment were peritoneal carcinomatosis (PC) from colorectal carcinoma and pseudomyxoma peritonei (PMP).

**RESULTS:** Of the 472 included procedures, 327 (69 %) procedures were performed for PC from colorectal carcinoma and 145 for PMP (31 %). Compared with the implementation

phase, the pioneer phase was characterized by more affected abdominal regions (mean 4.3 vs. 3.5,  $p < 0.001$ ), more resections (mean 3.8 vs. 3.4,  $p < 0.001$ ), less macroscopic radical cytoreductions (66 vs. 86 %,  $p < 0.001$ ) and more patients with major morbidity (grade III-V) (64 vs. 32 %,  $p < 0.001$ ). Other determinants of morbidity were high tumour load and multiple organ resections. Outcome of the implementation phase was similar to the control group.

**CONCLUSIONS:** This study determined that outcome had improved ever since the Dutch HIPEC protocol has been implemented based on completeness of cytoreduction and decreasing morbidity.

*impactfactor:* 2.642

## **Nienhuijs SW**

### **Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

*Voor abstract zie:* Chirurgie - Oudheusden TR van

*impactfactor:* 3.009

## **Nienhuijs SW**

### **Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial**

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruyt PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22

**BACKGROUND:** Case series suggest that laparoscopic peritoneal lavage might be a promising alternative to sigmoidectomy in patients with perforated diverticulitis. We aimed to assess the superiority of laparoscopic lavage compared with sigmoidectomy in patients with purulent perforated diverticulitis, with respect to overall long-term morbidity and mortality.

**METHODS:** We did a multicentre, parallel-group, randomised, open-label trial in 34 teaching hospitals and eight academic hospitals in Belgium, Italy, and the Netherlands (the Ladies trial). The Ladies trial is split into two groups: the LOLA group comparing laparoscopic lavage with sigmoidectomy and the DIVA group comparing Hartmann's procedure with sigmoidectomy plus primary anastomosis. The DIVA section of this trial is still underway but here we report the results of the LOLA section. Patients with purulent perforated diverticulitis were enrolled for LOLA, excluding patients with faecal peritonitis, aged older than 85 years, with high-dose steroid use ( $\geq 20$  mg daily), and haemodynamic instability. Patients were randomly assigned (2:1:1; stratified by age [ $< 60$  years vs  $\geq 60$  years]) using secure online computer randomisation to laparoscopic lavage, Hartmann's procedure, or primary anastomosis in a parallel design after diagnostic laparoscopy. Patients were analysed according to a modified intention-to-treat principle and were followed up after the index operation at least once in the outpatient setting and after sigmoidoscopy and stoma reversal, according to local protocols. The primary endpoint was a composite endpoint of

major morbidity and mortality within 12 months. This trial is registered with ClinicalTrials.gov, number NCT01317485.

**FINDINGS:** Between July 1, 2010, and Feb 22, 2013, 90 patients were randomly assigned in the LOLA section of the Ladies trial when the study was terminated by the data and safety monitoring board because of an increased event rate in the lavage group. Two patients were excluded for protocol violations. The primary endpoint occurred in 30 (67%) of 45 patients in the lavage group and 25 (60%) of 42 patients in the sigmoidectomy group (odds ratio 1.28, 95% CI 0.54-3.03,  $p=0.58$ ). By 12 months, four patients had died after lavage and six patients had died after sigmoidectomy ( $p=0.43$ ).

*impactfactor:* 45.217

## **Nienhuijs SW**

### **Long-term outcome after randomizing prolene hernia system, mesh plug repair and lichtenstein for inguinal hernia repair**

Nienhuijs SW\*, Rosman C

Hernia. 2015 Feb;19(1):77-81

**PURPOSE:** To assess long-term superiority in terms of chronic pain between prolene hernia system (PHS), mesh plug repair (MPR) and Lichtenstein (L) technique for inguinal hernia repair. **METHODS:** Eight years after randomizing three commonly used techniques for primary inguinal hernia repair, the outcome was evaluated with a questionnaire measuring pain on verbal descriptor and visual analogue scales, including limitations on daily life activities, sensory disturbances and recurrences. From previous results patients characteristics, operative details and short- and mid-term pain outcome were extracted.

**RESULTS:** 270 out of 308 eligible patients (88 %) completed the follow-up after median 7.6 years (range 6.9-9.2) after the inguinal hernia operation. No significant differences between the repair techniques were found for pain, sensory disturbances or recurrences. Overall, the hernia recurrence rate was 6.3 %. In total 63 patients (23 %) reported long-term pain of which one-fourth graded this moderate to severe. Pain was experienced at least weekly by 26 patients (10 %) and limiting daily activities for 36 patients (13 %). With regard to the previously reported pain at 3 and 15 months follow-up, 106 patients (39 %) experience no pain at all. For 101 patients (37 %), initial pain disappeared. 41 patients (15 %) suffered persisting pain at all three measure moments. 22 patients (8 %) reported pain at 8 years follow-up after an initial pain-free period. **CONCLUSIONS:** Long-term outcome after randomizing PHS, MPR and L showed no clinically relevant differences in chronic pain and its consequences. Although chronic pain is diminishing over time it remains a serious complication and has sometimes an onset long after the inguinal repair.

*impactfactor:* 2.050

## **Nienhuijs SW**

### **Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*

Obes Surg. 2015 Aug;25(8):1425-30

*Voor abstract zie:* Chirurgie - Wezenbeek MR van

*impactfactor:* 3.747



**Nienhuijs SW**

**Peritoneal Cancer Patients Not Suitable for Cytoreductive Surgery and HIPEC During Explorative Surgery: Risk Factors, Treatment Options, and Prognosis**

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Ann Surg Oncol. 2015 Apr;22(4):1236-42. Epub 2014 Oct 16

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.930

**Nienhuijs SW**

**Poor outcome after cytoreductive surgery and HIPEC for colorectal peritoneal carcinomatosis with signet ring cell histology**

van Oudheusden TR\*, Braam HJ, Nienhuijs SW\*, Wiezer MJ, van Ramshorst B, Luyer P\*, de Hingh IH\*

J Surg Oncol. 2015 Feb;111(2):237-42. Epub 2014 Sep 5

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 2.644

**Nienhuijs SW**

**Respiratory distress due to malignant ascites palliated by hyperthermic intraperitoneal chemotherapy**

van den Houten MM\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, de Hingh IH\*

World J Gastrointest Surg. 2015 Mar 27;7(3):39-42

Voor abstract zie: *Chirurgie - Houten MM van den*

impactfactor: 2.798

**Nienhuijs SW**

**Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

Voor abstract zie: *Chirurgie - Simkens GA*

impactfactor: 3.930

**Nienhuijs SW**

**Technology-based interventions in the treatment of overweight and obesity: A systematic review**

Raaijmakers LC\*, Pouwels S\*, Berghuis KA\*, Nienhuijs SW\*

Appetite. 2015 Jul 10;95:138-151

Voor abstract zie: *Chirurgie - Raaijmakers LC*

impactfactor: 2.691

## Nienhuijs SW

### Topic: Rare and Special Cases, The Real "Strange Cases"

Zarrinkhoo E, Miller J, Walker A, Weisman M, Towfigh S, Tushev R, Petkov I, Tsutsumi G, Leija C, Castillo E, Moncada F, Mendoza M, Morua AG, Bravo R, Azcarate A, Zavala H, Coman IS, Radu EV, David OI, Stoian AR, Strambu VE, Iancu C, Gheorghiu LI, Grigorean VT, Sinescu DR, Plesa E, Lupascu C, Straja DN, Iacobini MA, Ponten J, Luyer M, Nienhuijs S, Permekerlis A, Petousis S, Miroforidis A, Milias K, Kouridakis P, Park J, Kim D, Nakata R, Chihara N, Suzuki H, Watanabe M, Uchida E, Nakanaga H, Irie S, Endo Y, Sonoda H, Minamimura K, Kobayashi T, Hirata T, Mafune K, Milosevic P, Babovic M, Sorat D, Light D, Aawsaj Y, Horgan L, Latham L, Ceriani I, Livraghi L, Berselli M, Gambitta B, Galvanin J, Cotronea C, Pagano G, Farassino L, Ambrosoli A, Crespi A, Coccozza E, Kulic V, Matkovic M, Percevic G, Katayama T, Kumata Y, Ogawa E, Horikawa M, Yaguchi Y, Inaba T, Fukushima R, Jaroszewski D, Johnson K, Harold K, Mori M, Kumata M, Guarnieri F, Smaldone W, Gaspard M, Bomben F, Ceranto S, Gamarra MF, Soria MP, Olivero CF, Martinez MJ, Contin MP, Gómez JC, Jiménez-Valladolid D, Torres García A, Descloux A, Pohle S, Schramm B, Schneider U, Nocito A, Navarrete MC, Solis A, Ortega N, Bergamini S, Semeraro C, Armengol M, Cano ML, Torrecilla NO, Cavallaro G, Iorio O, Avallone M, Ruscio S, Rizzello M, Silecchia G, Butron T, Rubio E, Passas J, Sopeña R, Lagaron E, Silan F, Garcia V, Bernal J, Ortiz M, Guadarrama J, Shirai K, Lomas M, Shah BB, Degloorkar SS.

Hernia. 2015 Apr;19 Suppl 1:S317-27

*Geen abstract beschikbaar*

*impactfactor: 2.050*

## Nienhuijs SW

### Topic: Recent Innovations in Hernia Surgery

Vestberg R, Guerin M, Radlovic A, Lefranc O, Ladet S, Takahashi M, Matsuya H, Nishinari N, Matsui Y, Tosya T, Minagawa Y, Shimooki O, Abe T, Pietrantoni S, Pietrantoni C, Nguyen D, Szomstein S, Dip F, Rajan M, Lo Menzo E, Rosenthal R, Musil J, Kohoutek L, Plechacova P, Gryga A, Marek D, Bures T, Mora M, Kowalski R, Desilets D, Romanelli J, Earle D, Mommers E, Wegdam J, Nienhuijs S\*, de Vries Reilingh T, Giordano P, Majumder A, Hope W, Novitsky YN, Köhler G, Emmanuel K, Schrittwieser R, Kuniyoshi N, Nishihara M, Miyahira T, Hanashiro N, Okushima N, Takushi Y, Aka H, Nakagawa H, Takehara H, Kudsi O, Piscoya J, Naranjo-Fernandez JR, Curado-Soriano A, Martin-Orta E, Infantes-Ormad M, Valera-Sanchez Z, Piñan-Diez J, Dominguez-Amodeo A, Ruiz-Zafra A, Navarrete-Carcen E, Oliva-Mompean F, Padillo-Ruiz J, Holihan J, Alawadi ZM, Kao LS, Liang MK, Henriksen NA, Meisner S, Jorgensen LN, Morales-Conde S, Gómez-Menchero J, Del Agua IA, Ramirez MS, Macías MS, Moreno AB, Luque JA, Grau JM, Eckhart K 3rd, Costanzi A, Miranda A, Pessi F, Galfrascoli E, Crippa J, Mari G, Maggioni D, Augenstein V, Colavita P, Wormer B, Walters A, Bradley J, Dacey K, Lincourt A, Horton J, Kercher K, Heniford T, Tian ML, Wang MG, Chen J, Xiu DR, Nie YS, Zhao XF, Liu J, Yao HW, Jiang B, Zhang LF, Wang HY, Gerhart C, Dheri A, Harth R, Marr D, Mensch D, Thoma MR.

Hernia. 2015 Apr;19 Suppl 1:S328-37

*Geen abstract beschikbaar*

*impactfactor: 2.050*

## **Nienhuijs SW**

### **Trial & Guidelines**

Roumen R, Boelens O, Van Assen T, Scheltinga M, Wijerathne S, Agarwal N, Ramzi A, Liem D, Lomanto D, Simon T, Buechler MW, Koeckerling F, Siawash M, de Jager-Kieviet JW, Roumen RM, Scheltinga MR, Lincourt A, Augenstein V, Kercher K, Heniford B, Andresen K, Burcharth J, Hupfeld L, Fonnes S, Rothman JP, Winther D, Deigaard SL, Sørensen F, Bjerg J, Therkildsen R, Errebo M, Hauge D, Rosenberg J, Fischer J, Fox J, Basta M, Kovach S, East B, Krejci T, Hoch J, Jorgensen LN, Kullman E, Tollens T, Nienhuijs S\*, Doerhoff C, Muzi MG, Hopson S, Velanovich V, Muysoms F, Leblanc K, Schwartz M, Berrevoet F, Holihan J, Nguyen DH, Flores-Gonzalez JR, Alawadi ZM, Nguyen MT, Kao LS, Liang MK, Hassan S, Raslan C28, Henley N28, Van Veenendaal N, Poelman MM, Van den Heuvel B, Schreurs H, Dwars B, Bonjer HJ, Kaufmann R, Halm JA, Nieuwenhuizen J, Klitsie P, Eker HH, van Geldere D, Simons MP, Van't Riet M, Jeekel J, Lange JF, Pathania B

Hernia. 2015 Apr;19 Suppl 1:S43-9

*Geen abstract beschikbaar*

*impactfactor:* 2.050

## **Nienhuijs SW**

### **Urological procedures in patients with peritoneal carcinomatosis of colorectal cancer treated with HIPEC: morbidity and survival analysis**

Braam HJ, van Oudheusden TR\*, de Hingh IH\*, Nienhuijs SW\*, Boerma D, Wiezer MJ, van Ramshorst B

Anticancer Res. 2015 Jan;35(1):295-300

*Voor abstract zie: Chirurgie - Oudheusden TR van*

*impactfactor:* 1.826

## **Nieuwenhuijzen GA**

### **Accuracy of Detecting Residual Disease After Cross Neoadjuvant Chemoradiotherapy for Esophageal Cancer (preSANO Trial): Rationale and Protocol**

Noordman BJ, Shapiro J, Spaander MC, Krishnadath KK, van Laarhoven HW, van Berge Henegouwen MI, Nieuwenhuijzen GA\*, van Hillegersberg R, Sosef MN, Steyerberg EW, Wijnhoven BP, van Lanschot JJ; SANO study group

JMIR Res Protoc. 2015 Jun 29;4(2):e79

**BACKGROUND:** Results from the recent CROSS trial showed that neoadjuvant chemoradiotherapy (nCRT) significantly increased survival as compared to surgery alone in patients with potentially curable esophageal cancer. Furthermore, in the nCRT arm 49% of patients with a squamous cell carcinoma (SCC) and 23% of patients with an adenocarcinoma (AC) had a pathologically complete response in the resection specimen. These results provide a rationale to reconsider and study the timing and necessity of esophagectomy in (all) patients after application of the CROSS regimen.

**OBJECTIVE:** We propose a "surgery as needed" approach after completion of nCRT. In this approach, patients will undergo active surveillance after completion of nCRT. Surgical resection would be offered only to those patients in whom residual disease or a locoregional recurrence is highly suspected or proven. However, before a surgery as needed approach in oesophageal cancer patients (SANO) can be tested in a randomized controlled trial, we aim

to determine the accuracy of detecting the presence or absence of residual disease after nCRT (preSANO trial).

**METHODS:** This study is set up as a prospective, single arm, multicenter, diagnostic trial. Operable patients with potentially curable SCC or AC of the esophagus or esophagogastric junction will be included. Approximately 4-6 weeks after completion of nCRT all included patients will undergo a first clinical response evaluation (CRE-I) including endoscopy with (random) conventional mucosal biopsies of the primary tumor site and of any other suspected lesions in the esophagus and radial endo-ultrasonography (EUS) for measurement of tumor thickness and area. Patients in whom no locoregional or disseminated disease can be proven by cytohistology will be offered a postponed surgical resection 6-8 weeks after CRE-I (ie, approximately 12-14 weeks after completion of nCRT). In the week preceding the postponed surgical resection, a second clinical response evaluation (CRE-II) will be planned that will include a whole body PET-CT, followed again by endoscopy with (random) conventional mucosal biopsies of the primary tumor site and any other suspected lesions in the esophagus, radial EUS for measurement of tumor thickness and area, and linear EUS plus fine needle aspiration of PET-positive lesions and/or suspected lymph nodes. The main study parameter is the correlation between the clinical response assessment during CRE-I and CRE-II and the final pathological response in the resection specimen.

**RESULTS:** The first patient was enrolled on July 23, 2013, and results are expected in January 2016.

**CONCLUSIONS:** If this preSANO trial shows that the presence or absence of residual tumor can be predicted reliably 6 or 12 weeks after completion of nCRT, a randomized trial comparing nCRT plus standard surgery versus chemoradiotherapy plus "surgery as needed" will be conducted (SANO trial).

*impactfactor:* --

## **Nieuwenhuijzen GA**

### **Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease**

Orsini RG\*, Verhoeven RH, Lemmens VE, van Steenberghe LN, de Hingh IH\*, Nieuwenhuijzen GA\*, Rutten HJ\*

Eur J Cancer. 2015 Sep;51(13):1675-82

*Voor abstract zie:* Chirurgie - Orsini RG

*impactfactor:* 5.417

## **Nieuwenhuijzen GA**

### **Contralateral lymph node recurrence in breast cancer: Regional event rather than distant metastatic disease. A systematic review of the literature**

Moosdorff M, Vugts G\*, Maaskant-Braat AJ\*, Strobbe LJ, Voogd AC, Smidt ML, Nieuwenhuijzen GA\*

Eur J Surg Oncol. 2015 Sep;41(9):1128-36

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.009

## **Nieuwenhuijzen GA**

### **Determinants in decision making for curative treatment and survival in patients with resectable oesophageal cancer in the Netherlands: a population-based study**

Koëter M\*, van Steenberghe LN, Lemmens VE, Rutten HJ\*, Roukema JA, Nieuwenhuijzen GA\*

Cancer Epidemiol. 2015 Dec;39(6):863-9

Voor abstract zie: *Chirurgie - Koëter M*

impactfactor: 2.711

## **Nieuwenhuijzen GA**

### **Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy**

Berkelmans GH\*, Kouwenhoven EA, Smeets BJ\*, Weijs TJ\*, Silva Corten LC, van Det MJ, Nieuwenhuijzen GA\*, Luyer MD\*

World J Gastroenterol. 2015 Aug 14;21(30):9118-25

AIM: To investigate the value of elevated drain amylase concentrations for detecting anastomotic leakage (AL) after minimally invasive Ivor-Lewis esophagectomy (MI-ILE).

METHODS: This was a retrospective analysis of prospectively collected data in two hospitals in the Netherlands. Consecutive patients undergoing MI-ILE were included. A Jackson-Pratt drain next to the dorsal side of the anastomosis and bilateral chest drains were placed at the end of the thorascopic procedure. Amylase levels in drain fluid were determined in all patients during at least the first four postoperative days. Contrast computed tomography scans and/or endoscopic imaging were performed in cases of a clinically suspected AL. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis on endoscopy, re-operation, radiographic investigations, post mortal examination or when gastro-intestinal contents were found in drain fluid. Receiver operator characteristic curves were used to determine the cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value, risk ratio and overall test accuracy were calculated for elevated drain amylase concentrations.

RESULTS: A total of 89 patients were included between March 2013 and August 2014. No differences in group characteristics were observed between patients with and without AL, except for age. Patients with AL were older than were patients without AL ( $P = 0.01$ ). One patient (1.1%) without AL died within 30 d after surgery due to pneumonia and acute respiratory distress syndrome. Anastomotic leakage that required any intervention occurred in 15 patients (16.9%). Patients with proven anastomotic leakage had higher drain amylase levels than patients without anastomotic leakage [median 384 IU/L (IQR 34-6263) vs median 37 IU/L (IQR 26-66),  $P = 0.003$ ]. Optimal cut-off values on postoperative days 1, 2, and 3 were 350 IU/L, 200 IU/L and 160 IU/L, respectively. An elevated amylase level was found in 9 of the 15 patients with AL. Five of these 9 patients had early elevations of their amylase levels, with a median of 2 d (IQR 2-5) before signs and symptoms occurred.

CONCLUSION: Measurement of drain amylase levels is an inexpensive and easy tool that may be used to screen for anastomotic leakage soon after MI-ILE. However, clinical validation of this marker is necessary.

impactfactor: 2.369

#### **Nieuwenhuijzen GA**

##### **Does extended surgery influence health-related quality of life in patients with rectal cancer?**

Orsini RG\*, Vermeer TA\*, Traa MJ, Nieuwenhuijzen GA\*, de Hingh IH\*, Rutten HJ\*

Dis Colon Rectum. 2015 Feb;58(2):179-85

Voor abstract zie: Orsini RG - Chirurgie

impactfactor: 2.615

#### **Nieuwenhuijzen GA**

##### **Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

Voor abstract zie: Chirurgie - Vugts G

impactfactor: 3.930

#### **Nieuwenhuijzen GA**

##### **Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

Voor abstract zie: Chirurgie - Oudheusden TR van

impactfactor: 3.009

#### **Nieuwenhuijzen GA**

##### **Intensified follow-up in colorectal cancer patients using frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging: Results of the randomized "CEAwatch" trial**

Verberne CJ, Zhan Z, van den Heuvel E, Grossmann I, Doornbos PM, Havenga K, Manusama E, Klaase J, van der Mijle HC, Lamme B, Bosscha K1, Baas P12, van Ooijen B13, Nieuwenhuijzen G\*, Marinelli A, van der Zaag E, Wasowicz D, de Bock GH, Wiggers T

Eur J Surg Oncol. 2015 Sep;41(9):1188-96. Epub 2015 Jun 30

AIM: The value of frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging for detecting recurrent disease in colorectal cancer (CRC) patients was investigated in search for an evidence-based follow-up protocol.

METHODS: This is a randomized-controlled multicenter prospective study using a stepped-wedge cluster design. From October 2010 to October 2012, surgically treated non-metastasized CRC patients in follow-up were followed in eleven hospitals. Clusters of hospitals sequentially changed their usual follow-up care into an intensified follow-up schedule consisting of CEA measurements every two months, with imaging in case of two CEA rises. The primary outcome measures were the proportion of recurrences that could be treated with curative intent, recurrences with definitive curative treatment outcome, and the time to detection of recurrent disease.

RESULTS: 3223 patients were included; 243 recurrences were detected (7.5%). A higher proportion of recurrences was detected in the intervention protocol compared to the control protocol (OR = 1.80; 95%-CI: 1.33-2.50; p = 0.0004). The proportion of recurrences that could be treated with curative intent was higher in the intervention protocol (OR = 2.84; 95%-CI: 1.38-5.86; p = 0.0048) and the proportion of recurrences with definitive curative treatment outcome was also higher (OR = 3.12, 95%-CI: 1.25-6.02, p-value: 0.0145). The time to detection of recurrent disease was significantly shorter in the intensified follow-up protocol (HR = 1.45; 95%-CI: 1.08-1.95; p = 0.013).

CONCLUSION: The CEAwatch protocol detects recurrent disease after colorectal cancer earlier, in a phase that a significantly higher proportion of recurrences can be treated with curative intent.

impactfactor: 3.009

### **Nieuwenhuijzen GA**

#### **Laparoscopic versus open gastrectomy for gastric cancer, a multicenter prospectively randomized controlled trial (LOGICA-trial)**

Haverkamp L, Brenkman HJ, Seesing MF, Gisbertz SS, van Berge Henegouwen MI, Luyer MD, Nieuwenhuijzen GA, Wijnhoven BP, van Lanschot JJ, de Steur WO, Hartgrink HH, Stoot JH, Hulsewé KW, Spillenaar Bilgen EJ, Rütter JE, Kouwenhoven EA, van Det MJ, van der Peet DL, Daams F, Draaisma WA, Broeders IA, van Stel HF, Lacle MM, Ruurda JP, van Hillegersberg R; LOGICA study group

BMC Cancer. 2015 Jul 29;15(1):556

Voor abstract zie: Chirurgie - Luyer MD

impactfactor: 3.362

### **Nieuwenhuijzen GA**

#### **Leaving a Mobilized Thoracic Esophagus In Situ When Incurable Cancer Is Discovered Intraoperatively**

Weijs TJ\*, Toxopeus EL, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, Schraepen MC, Sosef MN, Wijnhoven BP, Schets IR, Bleys RL, van Hillegersberg R

Ann Thorac Surg. 2015 Feb;99(2):490-4. Epub 2014 Dec 10

Voor abstract zie: Chirurgie - Weijs TJ

impactfactor: 3.849

### **Nieuwenhuijzen GA**

#### **Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial**

Shapiro J, van Lanschot JJ, Hulshof MC, van Hagen P, van Berge Henegouwen MI, Wijnhoven BP, van Laarhoven HW, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Ten Kate FJ, Creemers GM\*, Punt CJ, Plukker JT, Verheul HM, Bilgen EJ, van Dekken H, van der Sangen MJ\*, Rozema T, Biermann K, Beukema JC, Piet AH, van Rij CM, Reinders JG, Tilanus HW, Steyerberg EW, van der Gaast A; CROSS study group

Lancet Oncol. 2015 Sep;16(9):1090-8. Epub 2015 Aug 5

BACKGROUND: Initial results of the ChemoRadiotherapy for Oesophageal cancer followed by Surgery Study (CROSS) comparing neoadjuvant chemoradiotherapy plus surgery versus surgery alone in patients with squamous cell carcinoma and adenocarcinoma of the

oesophagus or oesophagogastric junction showed a significant increase in 5-year overall survival in favour of the neoadjuvant chemoradiotherapy plus surgery group after a median of 45 months' follow-up. In this Article, we report the long-term results after a minimum follow-up of 5 years.

**METHODS:** Patients with clinically resectable, locally advanced cancer of the oesophagus or oesophagogastric junction (clinical stage T1N1M0 or T2-3N0-1M0, according to the TNM cancer staging system, sixth edition) were randomly assigned in a 1:1 ratio with permuted blocks of four or six to receive either weekly administration of five cycles of neoadjuvant chemoradiotherapy (intravenous carboplatin [AUC 2 mg/mL per min] and intravenous paclitaxel [50 mg/m<sup>2</sup> of body-surface area] for 23 days) with concurrent radiotherapy (41.4 Gy, given in 23 fractions of 1.8 Gy on 5 days per week) followed by surgery, or surgery alone. The primary endpoint was overall survival, analysed by intention-to-treat. No adverse event data were collected beyond those noted in the initial report of the trial. This trial is registered with the Netherlands Trial Register, number NTR487, and has been completed.

**FINDINGS:** Between March 30, 2004, and Dec 2, 2008, 368 patients from eight participating centres (five academic centres and three large non-academic teaching hospitals) in the Netherlands were enrolled into this study and randomly assigned to the two treatment groups: 180 to surgery plus neoadjuvant chemoradiotherapy and 188 to surgery alone. Two patients in the neoadjuvant chemoradiotherapy group withdrew consent, so a total of 366 patients were analysed (178 in the neoadjuvant chemoradiotherapy plus surgery group and 188 in the surgery alone group). Of 171 patients who received any neoadjuvant chemoradiotherapy in this group, 162 (95%) were able to complete the entire neoadjuvant chemoradiotherapy regimen. After a median follow-up for surviving patients of 84.1 months (range 61.1-116.8, IQR 70.7-96.6), median overall survival was 48.6 months (95% CI 32.1-65.1) in the neoadjuvant chemoradiotherapy plus surgery group and 24.0 months (14.2-33.7) in the surgery alone group (HR 0.68 [95% CI 0.53-0.88]; log-rank  $p=0.003$ ). Median overall survival for patients with squamous cell carcinomas was 81.6 months (95% CI 47.2-116.0) in the neoadjuvant chemoradiotherapy plus surgery group and 21.1 months (15.4-26.7) in the surgery alone group (HR 0.48 [95% CI 0.28-0.83]; log-rank  $p=0.008$ ); for patients with adenocarcinomas, it was 43.2 months (24.9-61.4) in the neoadjuvant chemoradiotherapy plus surgery group and 27.1 months (13.0-41.2) in the surgery alone group (HR 0.73 [95% CI 0.55-0.98]; log-rank  $p=0.038$ ).

**INTERPRETATION:** Long-term follow-up confirms the overall survival benefits for neoadjuvant chemoradiotherapy when added to surgery in patients with resectable oesophageal or oesophagogastric junctional cancer. This improvement is clinically relevant for both squamous cell carcinoma and adenocarcinoma subtypes. Therefore, neoadjuvant chemoradiotherapy according to the CROSS trial followed by surgical resection should be regarded as a standard of care for patients with resectable locally advanced oesophageal or oesophagogastric junctional cancer.

*impactfactor:* 24.690



#### **Nieuwenhuijzen GA**

##### **Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59

Voor abstract zie: *Chirurgie - Koëter M*

impactfactor: 2.546

#### **Nieuwenhuijzen GA**

##### **Repeat sentinel node biopsy should be considered in patients with locally recurrent breast cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Luiten EJ, Rutgers EJ, Rutten HJ\*, Roumen RM, Nieuwenhuijzen GA\*

Breast Cancer Res Treat. 2015 Oct;153(3):549-56

Voor abstract zie: *Chirurgie - Vugts G*

impactfactor: 3.940

#### **Nieuwenhuijzen GA**

##### **Routes for early enteral nutrition after esophagectomy. A systematic review**

Weijs TJ\*, Berkelmans GH\*, Nieuwenhuijzen GA\*, Ruurda JP, Hillegersberg RV, Soeters PB, Luyer MD\*

Clin Nutr. 2015 Feb;34(1):1-6. Epub 2014 Aug 1

Voor abstract zie: *Chirurgie - Weijs TJ*

impactfactor: 4.476

#### **Nieuwenhuijzen GA**

##### **Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

Voor abstract zie: *Chirurgie - Simkens GA*

impactfactor: 3.930

#### **Nieuwenhuijzen GA**

##### **Survival after pelvic exenteration for T4 rectal cancer**

Kusters M\*, Austin KK, Solomon MJ, Lee PJ, Nieuwenhuijzen GA\*, Rutten HJ\*

Br J Surg. 2015 Jan;102(1):125-31

Voor abstract zie: *Chirurgie - Kusters M*

impactfactor: 5.542

## **Nieuwenhuijzen GA**

### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hiligsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

Voor abstract zie: *Chirurgie - Peters EG*

impactfactor: 1.731

## **Nieuwenhuijzen GA**

### **Topography and extent of pulmonary vagus nerve supply with respect to transthoracic oesophagectomy**

Weijs TJ\*, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, van Hillegersberg R, Bleys RL

J Anat. 2015 Oct;227(4):431-9

Voor abstract zie: *Chirurgie - Luyer MD*

impactfactor: 2.097

## **Orsini RG**

### **Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease**

Orsini RG\*, Verhoeven RH, Lemmens VE, van Steenberg LN, de Hingh IH\*, Nieuwenhuijzen GA\*, Rutten HJ\*

Eur J Cancer. 2015 Sep;51(13):1675-82

**BACKGROUND:** Young patients with rectal cancer tend to present with more advanced-stage disease and unfavourable tumour morphology. The effects of these tumour characteristics on survival in this particular patient group are unclear.

**METHODS:** Population-based data from the Netherlands Cancer Registry (NCR) were used. Data from patients diagnosed with rectal cancer between 1989 and 2010 were selected. Younger patients (?40years) were compared with middle-aged patients (41-70years) with respect to disease stage, tumour characteristics, treatment and outcomes. Patients aged older than 70years were excluded. Relative excess risk (RER) models were used to perform uni- and multivariate survival analyses.

**FINDINGS:** A total of 37.056 patients were included (?40years n=1.102). Compared with middle-aged patients, young patients were more likely to have stage III (33.8% versus 27.8%) and stage IV (24.3% versus 19.6%) disease ( $p<0.001$ ). Young patients also presented more frequently with mucinous tumours (10.8% versus 9.0%), signet cell carcinomas (2.6% versus 0.6%) and poorly differentiated tumours (16.6% versus 12.3%) ( $p=0.001$ ). The treatment of stage I-III patients did not differ between the two groups, except regarding adjuvant chemotherapy, which was more often given to young patients (24.3% versus 14.4%,  $p<0.001$ ). Young age was a prognostic factor for better survival in stage I-III patients (RER 0.82 CI 0.71-0.94). Adjuvant chemotherapy was associated with improved survival in stage I-III patients (RER 0.76, 95%CI 0.70-0.83). In an exploratory analysis, adjuvant chemotherapy in young stage III and pN1 patients was associated with improved survival.

**CONCLUDING STATEMENT:** Young patients present with more advanced disease and have more unfavourable tumour characteristics compared with middle-aged patients. Despite

these characteristics, survival rates are equal, and young age is a prognostic factor for better survival. Although the use of adjuvant chemotherapy is controversial, a positive correlation with survival was found in this study.

*impactfactor:* 5.417

## **Orsini RG**

### **Does extended surgery influence health-related quality of life in patients with rectal cancer?**

Orsini RG\*, Vermeer TA\*, Traa MJ, Nieuwenhuijzen GA\*, de Hingh IH\*, Rutten HJ\*

Dis Colon Rectum. 2015 Feb;58(2):179-85

**BACKGROUND:** In locally advanced rectal cancer, an extended resection peripheral to the mesorectal fascia is needed to achieve a radical resection. The influence of extended resections on health-related quality of life is unclear.

**OBJECTIVE:** Differences in health-related quality of life and sexuality between patients receiving standard surgery and patients receiving extended surgery were examined, with a focus on age.

**DESIGN:** Patients operated on for rectal cancer between 2000 and 2010 were selected from a database and invited to complete the European Organization for Research and Treatment of Cancer quality-of-life questionnaires (C30 and ColoRectal 38).

**SETTINGS:** All patients were treated at the Catharina Hospital, Eindhoven, the Netherlands.

**PATIENTS:** All patients received total mesorectal excision surgery or extended surgery for rectal cancer.

**MAIN OUTCOME MEASURES:** Health-related quality of life and sexual activity was compared between patients treated with total mesorectal excision surgery and extended surgery and further stratified by age at the time of surgery (<70 and =70).

**RESULTS:** Two hundred twenty-nine (64.1%) patients with standard surgery and 128 (35.9%) patients treated with extended resections responded. Extended surgery in patients <70 years resulted in lower body image compared with patients <70 years receiving standard surgery. Patients =70 years had lower sexual function and more male sexual dysfunction than patients <70 years undergoing standard surgery. In all groups, sexual activity dropped significantly after treatment.

**LIMITATIONS:** No information was available of the patients' health-related quality of life before treatment except for the retrospective question about sexual activity.

**CONCLUSIONS:** This study showed no major differences between patients undergoing total mesorectal excision surgery and those receiving extended surgery, with the exception of body image, which was significantly lower in patients <70 years undergoing extended surgery. In all patient groups, treatment for rectal cancer influenced sexual activity dramatically. Awareness of the impact of surgery on health-related quality of life and sexuality is needed.

*impactfactor:* 2.615

## **Orsini RG**

### **Evaluating quality of life and response shift from a couple-based perspective: a study among patients with colorectal cancer and their partners**

Traa MJ, Braeken J, De Vries J, Roukema JA, Orsini RG\*, Den Oudsten BL. Qual Life Res. 2015 Jun;24(6):1431-41. Epub 2014 Nov 28

**OBJECTIVES:** To examine (1) measurement invariance of quality of life (QoL) domains over time for patients with colorectal cancer and partners (i.e., response shift-recalibration, reprioritization, and reconceptualization), (2) between dyad-member measurement

invariance and (3) QoL trajectories. **METHODS:** Participants completed the WHOQOL-Bref preoperative (Time-0) and 3 (Time-1) and 6 months (Time-2) postoperative. A stepwise procedure, using nested factor models, examined the viability of restricting specific model parameters to be equal across measurements and between dyad members. **FINDINGS:** No reconceptualization and reprioritization was detected, but indications for recalibration were present. Therefore, comparisons were restricted to group-level statistics at factor level. For patients, a decrease in the Physical Health domain occurred at Time-1 ( $p < 0.001$ ), with partial recovery to baseline at Time-2 ( $p = 0.055$ ). For partners, factor means in this domain remained constant ( $p's > 0.05$ ) and were at each time point higher than patients' factor means ( $p's < 0.05$ ). Patients' and partners' Psychological Health decreased at Time-1 ( $p's < 0.05$ ), with stabilization at Time-2 ( $p's > 0.05$ ). Patients and partners' factor means were comparable ( $p's > 0.05$ ). Patients and partners' Social Relationship factor means decreased at Time-1 ( $p's < 0.05$ ), which decreased further for patients ( $p = 0.011$ ) but stabilized for partners ( $p = 0.214$ ). Partners' factor means were only lower than patients' factor means at Time-1. A similar decrease in the Environmental domain factor means occurred for both patients and partners at Time-1 ( $p's < 0.05$ ), with stabilization at Time-2 ( $p's > 0.05$ ). **CONCLUSION:** Since both patients and partners are affected by the patients' disease and treatment, we recommend that attention is paid to the couple instead of solely the patient.

*impactfactor:* 2.412

## **Oudheusden TR van**

### **Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

**INTRODUCTION:** The optimal treatment for peritoneal carcinomatosis (PC) of colorectal origin is a combination of cytoreductive surgery and intraperitoneal chemotherapy (CRS + IPC). Although 5-year survival rates of up to 40% have been reported, recurrent disease remains common and is estimated to be a strong negative prognostic factor for survival. This systematic review elaborates on the incidence of recurrent disease and the possibilities to prevent and treat recurrence.

**METHODS:** Two searches were performed. To identify the magnitude of recurrent the disease, a search was performed in Pubmed and EMBASE until September 2014. A second search was performed in Pubmed to identify treatment of recurrent disease with secondary CRS + IPC.

**RESULTS:** The first search resulted in 139 and 94 articles in Pubmed and EMBASE respectively. Among those, 28 were included. Overall recurrence rates ranged from 22.5 to 82%. Local, systemic and combined local-systemic recurrence ranged from 6 to 42.5%, 10.4-43% and 5.8-21.5%. Median time to recurrence varied from 9 to 23 months, three-year disease free survival ranged from 14 to 41.5%. The second search resulted in 140 articles among which 17 met the inclusion criteria. A total of 190 patients underwent secondary CRS. Median survival after the second procedure ranged from 18 to 55.7 months. One, two and three-year survival ranged between 66 and 94, 44-50 and 0-66%.

**CONCLUSION:** Recurrence is very common after cytoreductive surgery and intraperitoneal chemotherapy for PC of colorectal origin. Repeat cytoreductive surgery suggests a potential

survival benefit for a highly selected group. Therefore, strategies to prevent recurrence are of the utmost importance.

*impactfactor: 3.009*

#### **Oudheusden TR van**

#### **Peritoneal Cancer Patients Not Suitable for Cytoreductive Surgery and HIPEC During Explorative Surgery: Risk Factors, Treatment Options, and Prognosis**

van Oudheusden TR\*, Braam HJ, Luyer MD\*, Wiezer MJ, van Ramshorst B, Nienhuijs SW\*, de Hingh IH\*

Ann Surg Oncol. 2015 Apr;22(4):1236-42. Epub 2014 Oct 16

**BACKGROUND:** Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is currently the only curative option for patients with peritoneal carcinomatosis of colorectal origin. Despite meticulous preoperative assessment, CRS and HIPEC appear to be impossible in a subset of patients at the time of surgery. This study investigated which clinical factors may identify these patients before surgery and reported on factors influencing survival.

**METHODS:** All patients with PC of colorectal origin between April 2005 and November 2013 who underwent exploratory surgery to determine whether cytoreduction and HIPEC was feasible were included in this study. Details concerning preoperative patient characteristics, perioperative outcomes, treatment and survival were compared.

**RESULTS:** In total, 350 patients with PC were referred to evaluate the possibility of CRS + HIPEC of which 268 (76.6 %) underwent CRS and HIPEC and 82 (23.4 %) had an open-close procedure. The main reason for discontinuing surgery was widespread peritoneal disease (50 %). A preoperative ostomy and an ASA score of 3 were associated with an increased risk for "open and close" (O&C). Median survival was 11.2 months in patients treated with palliative chemotherapy (75 %) compared with 2.7 months with palliative care only.

**CONCLUSIONS:** CRS and HIPEC were deemed unsuitable in almost a quarter of all patients undergoing surgery. No strong clinical predictors for O&C were found, stressing the need for better preoperative imaging modalities. Survival in these patients is limited, but the majority could be treated with palliative chemotherapy resulting in survival of almost 1 year.

*impactfactor: 3.930*

#### **Oudheusden TR van**

#### **Peritoneal metastases from small bowel cancer: Results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in The Netherlands**

van Oudheusden TR\*, Lemmens VE, Braam HJ, van Ramshorst B, Meijerink J, te Velde EA, Mehta AM, Verwaal VJ, de Hingh IH\*

Surgery. 2015 Jun;157(6):1023-7. Epub 2015 Mar 25

**INTRODUCTION:** Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) is currently considered the standard of care for pseudomyxoma peritonei, mesothelioma and peritoneal metastases (PM) from colorectal cancer. CRS + HIPEC has also been suggested as a potential treatment option in PM of the much rarer small bowel cancer. Therefore, the current study was undertaken to investigate the results of CRS + HIPEC in all HIPEC centers in The Netherlands.

**METHODS:** From the 4 tertiary referral centers for peritoneal surface malignancies in The Netherlands, data from all patients with peritoneally metastasized small bowel carcinoma intended to undergo CRS and HIPEC were collected between January 2005 and July 2014. Primary tumor characteristics, operative details, and survival outcomes were collected.

RESULTS: Sixteen of 19 patients (84.2%) who underwent explorative laparotomy underwent CRS + HIPEC. Of these patients, 81.3% were female, and primary tumors were mainly located in the ileum (50%). A complete macroscopic resection was achieved in 93.8%. Serious adverse events requiring re-intervention occurred in 25%, and no in-hospital mortality was observed. Recurrent disease was observed in 50% of patients and median survival after CRS and HIPEC was 31 months.

CONCLUSION: In a select group of patients in whom a complete macroscopic resection can be achieved, survival rates comparable with those in colorectal PM are attainable with acceptable morbidity. The role of adjuvant chemotherapy needs further research.

*impactfactor:* 3.380

### **Oudheusden TR van**

#### **Poor outcome after cytoreductive surgery and HIPEC for colorectal peritoneal carcinomatosis with signet ring cell histology**

van Oudheusden TR\*, Braam HJ, Nienhuijs SW\*, Wiezer MJ, van Ramshorst B, Luyer P\*, de Hingh IH\*

J Surg Oncol. 2015 Feb;111(2):237-42. Epub 2014 Sep 5

BACKGROUND: Signet ring cell cancer (SRCC) patients have a poor oncologic outcome. The aim of this study was to determine whether the potential drawbacks of hyperthermic intraperitoneal chemotherapy (HIPEC) outweigh the benefits in patients with peritoneally metastasized SRCC.

METHODS: Patients with peritoneal carcinomatosis (PC) of colorectal origin referred to two tertiary centers between April 2005 and December 2013 were identified and retrospectively analyzed. Data were compared between SRCC histology and other differentiations.

RESULTS: Three-hundred-fifty-one patients were referred for CRS+HIPEC among which 20 (5.7%) patients were identified with SRCC histology. CRS+HIPEC was performed in 16 of these 20 (80%) and 252 out of the 331 remaining patients (76.1%). A higher proportion of patients in the SRCC-group were diagnosed with N2 stage (62.5% vs. 36.1%,  $P=0.04$ ). A macroscopic complete resection was achieved in 87.5% and 97.2% respectively ( $P=0.04$ ). Median survival was 14.1 months compared to 35.1 months ( $P<0.01$ ). Recurrence occurred in 68.8% of the SRCC patients and in 43.7% of the other histology patients ( $P=0.05$ ).

CONCLUSION: Patients with SRCC and PC treated with CRS+HIPEC have a poor median survival only slightly reaching over 1 year. In the presence of other relative contraindications, SRCC histology should refrain a surgeon from performing CRS and HIPEC.

*impactfactor:* 2.644

### **Oudheusden TR van**

#### **Respiratory distress due to malignant ascites palliated by hyperthermic intraperitoneal chemotherapy**

van den Houten MM\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, de Hingh IH\*

World J Gastrointest Surg. 2015 Mar 27;7(3):39-42

Voor abstract zie: Chirurgie - Houten MM van den

*impactfactor:* 2.798

**Oudheusden TR van**

**30 After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosi**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

Voor abstract zie: *Chirurgie - Simkens GA*

impactfactor: 3.943

**Oudheusden TR van**

**Skeletal Muscle Depletion is Associated with Severe Postoperative Complications in Patients Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Colorectal Cancer**

van Vugt JL, Braam HJ, van Oudheusden TR\*, Vestering A, Bollen TL, Wiezer MJ, de Hingh IH\*, van Ramshorst B, Boerma D

Ann Surg Oncol. 2015 Oct;22(11):3625-31. Epub 2015 Feb 12

Erratum to: Skeletal Muscle Depletion is Associated with Severe Postoperative Complications in Patients Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Colorectal Cancer

Ann Surg Oncol. 2015 Dec;22 Suppl 3:1610

**BACKGROUND:** In patients undergoing colorectal cancer surgery, skeletal muscle depletion (sarcopenia) is associated with impaired postoperative recovery and decreased survival. This study aimed to determine whether skeletal muscle depletion can predict postoperative complications for patients undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) for peritoneal carcinomatosis of colorectal cancer.

**METHODS:** All consecutive patients with an available preoperative computed tomography (CT) scan who underwent CRS-HIPEC for peritoneal carcinomatosis of colorectal cancer in two centers were analyzed. Skeletal muscle mass was determined using the L3 muscle index on the preoperative CT scan. The cutoff values defined by Prado et al. were used to classify the patients as sarcopenic or nonsarcopenic.

**RESULTS:** Of the study's 206 patients, 90 (43.7 %) were classified as sarcopenic. The sarcopenic patients underwent significantly more reoperations than the nonsarcopenic patients (25.6 vs. 12.1 %;  $p = 0.012$ ). The mean L3 muscle index was significantly lower for the patients who experienced severe postoperative complications than for the patients without severe postoperative complications (85.6 vs. 110.2 cm<sup>2</sup>/m<sup>2</sup>;  $p = 0.008$ ). In a multivariable logistic regression model, L3 muscle index was the only parameter independently associated with the risk of severe postoperative complications (odds ratio 0.93; 95 % confidence interval 0.87-0.99;  $p = 0.018$ ).

**CONCLUSION:** Skeletal muscle mass depletion, assessed using CT-based muscle mass measurements, is associated with an increased risk of severe postoperative complications in patients undergoing CRS-HIPEC for colorectal peritoneal carcinomatosis and could therefore be used in preoperative risk assessment.

impactfactor: 3.930

**Oudheusden TR van**

**Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin**

van Oudheusden TR\*, Razenberg LG\*, van Gestel YR, Creemers GJ\*, Lemmens VE, de Hingh IH\*

Sci Rep. 2015 Dec 21;5:18632

Combining chemotherapy and targeted therapies has resulted in an enhanced survival in metastatic colorectal cancer (mCRC) patients. However, the result of this palliative treatment in patients with metachronous peritoneal carcinomatosis (PC) remains unknown. The current population-based study aims to investigate the use and effect of palliative systemic treatment in patients with metachronous PC of colorectal origin. Data on metachronous PC were collected between 2010 and 2011 for all patients who were diagnosed with M0 colorectal cancer between 2003 and 2008 in the Dutch Eindhoven Cancer Registry. Patient demographics and detailed data on chemotherapeutic treatment were collected and compared. Ninety-two patients with metachronous PC received chemotherapy in a palliative setting compared to 94 patients without treatment. In 36 patients, Bevacizumab was added to the treatment (39%). Overall survival was 3.4, 13, and 20.3 months in the no treatment, systemic treatment and systemic treatment+Bevacizumab respectively ( $P < 0.001$ ). Male gender was a positive predictor and right sided primary tumor location a negative predictor of receiving bevacizumab. Approximately 40% of patients with metachronous PC received bevacizumab in addition to chemotherapy. Treatment with systemic chemotherapy in combination with bevacizumab may increase survival in a patients with metachronous colorectal PC.

*impactfactor:* 5.578

**Oudheusden TR van**

**Targeting the Peritoneum with Novel Drug Delivery Systems in Peritoneal Carcinomatosis: A Review of the Literature**

Van Oudheusden TR\*, Grull H, Dankers PY, De Hingh IH\*

Anticancer Res. 2015 Feb;35(2):627-634

The Peritoneal cavity is a well-known metastatic site for several intra-abdominal malignancies, such as stomach, colon, pancreas and rectal cancer. For long, it was thought that treatment with curative intent was impossible but that was challenged by the introduction of cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC). Although their effectiveness has been proven both experimentally and clinically, there is need for improvement. Firstly, a significant proportion of patients develop recurrent disease. Secondly, HIPEC demands presence of dedicated perfusion devices not readily available in most hospitals. Since intraperitoneal administration of chemotherapy is thought to play a crucial role, new modalities to deliver effective chemotherapeutics to the peritoneum are developed. The current review aims to present an overview of the experimental data on new drug delivery systems (DDS) in peritoneal cancer.

*impactfactor:* 1.826



**Oudheusden TR van**

**Urological procedures in patients with peritoneal carcinomatosis of colorectal cancer treated with HIPEC: morbidity and survival analysis**

Braam HJ, van Oudheusden TR\*, de Hingh IH\*, Nienhuijs SW\*, Boerma D, Wiezer MJ, van Ramshorst B

Anticancer Res. 2015 Jan;35(1):295-300

AIM: To investigate whether cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) is a feasible and effective option for patients with urological involvement of peritoneal carcinomatosis from colorectal cancer (CRC-PC).

PATIENTS AND METHODS: The characteristics of patients with CRC-PC treated with CRS+HIPEC, with or without a urological procedure, between April 2005 and June 2013 in two tertiary Centres were analyzed.

RESULTS: Thirty-eight patients (14%) out of 267 CRC-PC patients treated with CRS+HIPEC had a urological procedure during cytoreduction. The median survival was not significantly different between patients with or without a urological procedure (26.9 versus 32.1 months,  $p=0.29$ ). Severe complications occurred more in patients with a urological procedure (47% versus 20%,  $p<0.001$ ). In patients with a urological procedure, the most frequent complications were gastrointestinal leakage ( $n=9$ ) and intra-abdominal abscess formation ( $n=5$ ).

CONCLUSION: Urological resections as a part of CRS+HIPEC in patients with peritoneal carcinomatosis of colorectal origin are feasible and effective. Severe complications are prevalent in these patients but survival is comparable to patients without involvement of the urinary system.

*impactfactor:* 1.826

**Peters EG**

**The contribution of mast cells to postoperative ileus in experimental and clinical studies**

Peters EG\*, De Jonge WJ, Smeets BJ\*, Luyer MD\*

Neurogastroenterol Motil. 2015 Jun;27(6):743-9

The persistent phase of postoperative ileus (POI) is mediated by inflammatory activation of the resident myeloid immune cell population in the gut wall, likely elicited by neurogenic activation. Mast cells are thought to play a critical role in this inflammatory response and involvement of mast cells in POI has been investigated and described thoroughly in experimental studies. Intestinal manipulation (IM) leads to degranulation of mast cells, resulting in an increase in mast cell proteases in peritoneal fluid and gut tissue. The inflammatory infiltrate formed in the intestinal wall thereby impairs gastrointestinal motility. In the clinical study by Berdun et al., the experimentally known association between mast cell degranulation and delayed motility is shown in a clinical setting. These findings are important and open up therapeutic opportunities to reduce or prevent POI. In this mini-review, the role of mast cells in POI is discussed. Furthermore, an update is given on the involvement of the inflammatory response in POI and potential therapeutic strategies.

*impactfactor:* --

**Peters EG**

**The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hiligsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

Background: Postoperative ileus and anastomotic leakage are important complications following colorectal surgery associated with short-term morbidity and mortality. Previous experimental and preclinical studies have shown that a short intervention with enriched enteral nutrition dampens inflammation via stimulation of the autonomic nervous system and thereby reduces postoperative ileus. Furthermore, early administration of enteral nutrition reduced anastomotic leakage. This study will investigate the effect of nutritional stimulation of the autonomic nervous system just before, during and early after colorectal surgery on inflammation, postoperative ileus and anastomotic leakage.

Methods/Design: This multicenter, prospective, double-blind, randomized controlled trial will include 280 patients undergoing colorectal surgery. All patients will receive a selfmigrating nasojejunal tube that will be connected to a specially designed blinded tubing system. Patients will be allocated either to the intervention group, receiving perioperative nutrition, or to the control group, receiving no nutrition. The primary endpoint is postoperative ileus. Secondary endpoints include anastomotic leakage, local and systemic inflammation, (aspiration) pneumonia, surgical complications classified according to Clavien-Dindo, quality of life, gut barrier integrity and time until functional recovery. Furthermore, a cost-effectiveness analysis will be performed.

Discussion: Activation of the autonomic nervous system via perioperative enteral feeding is expected to dampen the local and systemic inflammatory response. Consequently, postoperative ileus will be reduced as well as anastomotic leakage. The present study is the first to investigate the effects of enriched nutrition given shortly before, during and after surgery in a clinical setting.

*impactfactor:* 1.731

**Pouwels S**

**Aspects of Exercise before or after Bariatric Surgery: A Systematic Review**

Pouwels S\*, Wit M\*, Teijink JA\*, Nienhuijs SW\*

Obes Facts. 2015;8(2):132-46

BACKGROUND: Bariatric surgery has a considerable effect on weight loss. A positive relation of exercise and weight loss has been described before. However, the mode of exercise and its timing pre- or postoperatively or a combination remains unclear.

METHODS: A multi-database search was conducted. Identified articles were reviewed on description of exercise, timing around a bariatric intervention, and outcome. Methodological quality of the included studies was rated using the Physiotherapy Evidence Database scale. A Cohen's kappa score assessed the level of agreement. Outcome measurements were improvement of anthropometric and physical fitness variables, operation related complications, weight regain, and quality of life.

RESULTS: A total of 8 prospective studies were included. Four focused on training before and 4 on training after a bariatric procedure. Details of exercises varied from 45 min treadmill up

to full descriptive programs. Supervision was frequently included. Significant improvement was encountered for biometric results physical fitness variables.

**CONCLUSION:** In the majority of reports on exercising in a (future) bariatric population, positive effects on anthropometrics, cardiovascular risk factors and physical fitness were described. However, the results were not unanimous, with a wide range of exercise programs and perioperative timing, therefore hampering adequate practical guidance.

*impactfactor:* 2.245

## **Pouwels S**

### **Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review**

Pouwels S\*, Willigendael EM, van Sambeek MR\*, Nienhuijs SW\*, Cuypers PW\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Jan;49(1):66-76

**OBJECTIVE/BACKGROUND:** The impact of post-operative complications in abdominal aortic aneurysm (AAA) surgery is substantial, and increases with age and concomitant co-morbidities. This systematic review focuses on the possible effects of pre-operative exercise therapy (PET) in patients with AAA on post-operative complications, aerobic capacity, physical fitness, and recovery.

**METHODS:** A systematic search on PET prior to AAA surgery was conducted. The methodological quality of the included studies was rated using the Physiotherapy Evidence Database scale. The agreement between the reviewers was assessed with Cohen's kappa.

**RESULTS:** Five studies were included, with a methodological quality ranging from moderate to good. Cohen's kappa was 0.79. Three studies focused on patients with an AAA (without indication for surgical repair) with physical fitness as the outcome measure. One study focused on PET in patients awaiting AAA surgery and one study focused on the effects of PET on post-operative complications, length of stay, and recovery.

**CONCLUSION:** PET has beneficial effects on various physical fitness variables of patients with an AAA. Whether this leads to less complications or faster recovery remains unclear. In view of the large impact of post-operative complications, it is valuable to explore the possible benefits of a PET program in AAA surgery.

*impactfactor:* 3.490

## **Pouwels S**

### **Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*

Springerplus. 2015 Jul 7;4:322

**BACKGROUND:** The respiratory function is affected by obesity due to an increased deposition of fat on the chest wall. The objective of this study was to investigate the strength of the inspiratory respiratory muscles of obese individuals and the possible influence of bariatric surgery on it by measuring the maximum inspiratory pressure (MIP).

**METHODS:** Patients referred to a bariatric centre between the 3rd of October 2011 and the 3rd of May 2012 were screened preoperatively by a multidisciplinary team. Their MIP was measured at screening and 3, 6 and 9 months postoperative. In case of a preoperative MIP lower than 70% of predicted pressure training was provided supervised by a physiotherapist.

**RESULTS:** The mean age of 124 included patients was  $42.9 \pm 11.0$  years and mean BMI was  $43.1 \pm 5.2$  kg/m<sup>2</sup>. The mean predicted MIP preoperatively was  $127 \pm 31$  in cm H<sub>2</sub>O and the mean measured MIP was  $102 \pm 24$  in cm H<sub>2</sub>O. Three patients (2.4%) received training. Three

months after surgery the MIP was  $76 \pm 26$  cm H<sub>2</sub>O, after 6 months  $82 \pm 28$  cm H<sub>2</sub>O and after 9 months  $86 \pm 28$  cm H<sub>2</sub>O. All postoperative measurements were significantly lower than preoperatively ( $P < 0.05$ ). The only influencing factor for the preoperative MIP was age ( $p = 0.014$ ).

**CONCLUSION:** The preoperative MIP values were significantly lower than the predicted MIP values, probably due to altered respiratory mechanics.

*impactfactor:* --

## **Pouwels S**

### **Preoperative exercise therapy in lung surgery patients: A systematic review**

Pouwels S\*, Fiddelaers J, Teijink JA\*, Woorst JF\*, Siebenga J, Smeenk FW\*

Respir Med. 2015 Dec;109(12):1495-504. Epub 2015 Aug 15

**OBJECTIVES:** The impact of postoperative complications after lung surgery for cancer is substantial, with the increasing age of patients and the presence of comorbidities. This systematic review summarises the effects of Preoperative Exercise Therapy (PET) in patients scheduled for lung surgery on aerobic capacity, physical fitness, postoperative complications, length of hospital stay, quality of life and recovery. **METHODS:** A systematic search on PET prior to lung surgery was conducted. The methodological quality of the included studies was rated using the Physiotherapy Evidence Database (PEDro) scale. The agreement between the reviewers was assessed with Cohen's kappa. **RESULTS:** A total of eleven studies were included with a methodological quality ranging from poor to good. The agreement between the reviewers, assessed with the Cohen's kappa, was 0.79. Due to substantial heterogeneity in the interventions across the included studies, it was impossible to conduct a meta-analysis. The most important finding of this systematic review was that PET based on moderate to intense exercise in patients scheduled for lung surgery has beneficial effects on aerobic capacity, physical fitness and quality of life. Also PET may reduce postoperative complications and length of hospital stay. **CONCLUSION:** PET may have beneficial effects on various physical fitness variables and postoperative complications in patients with lung cancer scheduled for surgery. Future research must focus on developing patient tailored exercise programs and investigate the influence of co-existing comorbidities on the outcome measures. Definitions of PET, including timing, (acceptable) duration, intensity and exercise training methods should be determined and compared.

*impactfactor:* 3.086

## **Pouwels S**

### **Technology-based interventions in the treatment of overweight and obesity: A systematic review**

Raaijmakers LC\*, Pouwels S\*, Berghuis KA\*, Nienhuijs SW\*

Appetite. 2015 Jul 10;95:138-151

Voor abstract zie: Chirurgie - Raaijmakers LC

*impactfactor:* 2.691

## **Raaijmakers LC**

### **Technology-based interventions in the treatment of overweight and obesity: A systematic review**

Raaijmakers LC\*, Pouwels S\*, Berghuis KA\*, Nienhuijs SW\*

Appetite. 2015 Jul 10;95:138-151

The prevalence of obesity increases worldwide. The use of technology-based interventions can be beneficial in weight loss interventions. This review aims to provide insight in the effectiveness of technology-based interventions on weight loss and quality of life for patients suffering overweight or obesity compared to standard care. Pubmed, PsycInfo, Web of Science, ScienceDirect, CINAHL and Embase were searched from the earliest date (of each database) up to February 2015. Interventions needed to be aimed at reducing or maintaining weight loss in persons with a body mass index (BMI) = 25 kg/m<sup>2</sup> and have a technology aspect. Cochrane Collaboration's tool for assessing risk of bias was used for rating the methodological quality. Twenty-seven trials met inclusion criteria. Thirteen studies showed significant effects on weight loss compared to controls. Most interventions used a web-based approach (42%). Interventions were screened for five technical key components: self-monitoring, counsellor feedback and communication, group support, use of a structured program and use of an individually tailored program. All interventions that used a combination of all five or four components showed significant decreases in weight compared to controls. No significant results for quality of life were found. Outcomes on program adherence were reported in six studies. No significant results were found between weight loss and program adherence. Evidence is lacking about the optimal use of technology in weight loss interventions. However, when the optimal combination of technological components is found, technology-based interventions may be a valid tool for weight loss. Furthermore, more outcomes on quality of life and information about the effect of technology-based intervention after bariatric surgery are needed.

*impactfactor:* 2.691

#### **Riet EA van**

#### **[Breast-conserving surgery and radiotherapy as a one-day procedure] - Borstsparende ingreep en bestraling in dagbehandeling**

Koper PC, Marinelli AW, van den Berg HA\*, van Riet YE\*, van der Sijp JR, Struikmans H  
Ned Tijdschr Geneesk. 2015;159:A8195

*Voor abstract zie:* Radiotherapie - van den Berg HA

*impactfactor:* --

#### **Riet EA van**

#### **Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.930

#### **Riet EA van**

#### **Repeat sentinel node biopsy should be considered in patients with locally recurrent breast cancer.**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Luiten EJ, Rutgers EJ, Rutten HJ\*, Roumen RM, Nieuwenhuijzen GA\*

Breast Cancer Res Treat. 2015 Oct;153(3):549-56

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.940

**Rutte PW van**

### **Association Between Postprandial Symptoms and Gastric Emptying After Sleeve Gastrectomy**

Burgerhart JS, van Rutte PW\*, Edelbroek MA\*, Wyndaele DN\*, Smulders JF\*, van de Meeberg PC, Siersema PD, Smout AJ

Obes Surg. 2015 Feb;25(2):209-14

**BACKGROUND:** Laparoscopic sleeve gastrectomy (LSG) is an effective bariatric procedure. However, postprandial symptoms can compromise its beneficial effect. It is not known if a changed gastric emptying and these symptoms are related. This study aimed to assess the association between postprandial symptoms and the gastric emptying pattern after LSG.

**METHODS:** A gastric emptying study with a solid and liquid meal component was performed in the second year after LSG. Before the test, symptoms were assessed using a standardized questionnaire, and during the test, symptoms were scored on a visual analog scale (VAS). Gastric emptying results were expressed as lag phase, half time of gastric emptying ( $T_{1/2}$ ), and caloric emptying rate/minute.

**RESULTS:** Twenty patients (14 F/6 M; age  $45.6 \pm 7.7$  years, weight  $93.4 \pm 28.2$  kg, BMI  $31.6 \pm 8.1$  kg/m<sup>2</sup>) participated in this study; 13 had a low symptom score (=9, group I), 7 a high symptom score (=18, group II). VAS scores for epigastric pain, nausea, and belching were significantly higher in group II. Lag phase (solid) was  $6.4 \pm 4.5$  min in group I,  $7.3 \pm 6.3$  in group II ( $p = 0.94$ );  $T_{1/2}$  (solid) was  $40.6 \pm 10.0$  min in group I,  $34.4 \pm 9.3$  in group II ( $p = 0.27$ ); caloric emptying rate was  $3.9 \pm 0.6$  kcal/min in group I,  $3.9 \pm 1.0$  kcal/min in group II ( $p = 0.32$ ).

**CONCLUSIONS:** Patients with postprandial symptoms after LSG reported more symptoms during the gastric emptying study than patients without symptoms. However, there was no difference between gastric emptying characteristics between both groups, suggesting that abnormal gastric emptying is not a major determinant of postprandial symptoms after LSG.

*impactfactor:* 3.747

**Rutte PW van**

### **Gastric Wall Thickness in Sleeve Gastrectomy Patients: Thickness Variation of the Gastric Wall**

van Rutte PW\*, Naagen BJ, Spek M, Jakimowicz JJ\*, Nienhuijs SW\*

Surg Technol Int. 2015 Nov;27:123-8

The sleeve gastrectomy has been accepted as a primary bariatric procedure. One of the most feared complications is staple line leakage. It is important to use the right staple sizes to minimize the risk of leak. Knowledge of gastric thickness is important. The goal of this study was to measure the thickness of the gastric wall after elimination of the gastric folds in the mucosa. An electronic thickness gauge was developed that measured the anterior and posterior wall of the fresh stomach specimen together at 5 points at a pressure based on the finger pressure necessary to flatten the gastric folds. Thirty-three fresh specimens were measured. The mean compression pressure was 714 grams, and no difference was found between the 5 measure points. There was a significant difference in stomach wall thickness. The gastric antrum was more than 1 mm thicker than the fundus. No difference was found between BMI groups < 40Kg/m<sup>2</sup>, 40-50Kg/m<sup>2</sup>, or >50Kg/m<sup>2</sup>. No bleeding occurred, leakage occurred in 1 case. There is a significant difference in thickness of the stomach wall between the gastric fundus and the antrum. A pressure 2.5 times lower than applied in prior studies was necessary to achieve full tissue compression. Choosing thinner staple sizes for the

gastric fundus might be the optimal technique for compression. However, there are several additional factors that influence the risk of staple line leaks.

*impactfactor:* --

#### **Rutten HJ**

##### **Adjuvant chemotherapy for rectal cancer patients treated with preoperative (chemo)radiotherapy and total mesorectal excision: a Dutch Colorectal Cancer Group (DCCG) randomized phase III trial†**

Breugom AJ, van Gijn W, Muller EW, Berglund Å, van den Broek CB, Fokstuen T, Gelderblom H, Kapiteijn E, Leer JW, Marijnen CA, Martijn H\*, Meershoek-Klein Kranenbarg E, Nagtegaal ID, Pålman L, Punt CJ, Putter H, Roodvoets AG, Rutten HJ\*, Steup WH, Glimelius B, van de Velde CJ; Cooperative Investigators of the Dutch Colorectal Cancer Group and the Nordic Gastrointestinal Tumour Adjuvant Therapy Group.

Ann Oncol. 2015 Apr;26(4):696-701

*Voor abstract zie:* Radiotherapie - Martijn H

*impactfactor:* 7.040

#### **Rutten HJ**

##### **Axillary reverse mapping (ARM) in clinically node positive breast cancer patients**

Beek MA, Gobardhan PD, Klompenhouwer EG\*, Rutten HJ\*, Voogd AC, Luiten EJ

Eur J Surg Oncol. 2015 Jan;41(1):59-63

*Voor abstract zie:* Radiologie - Klompenhouwer E

*impactfactor:* 3.009

#### **Rutten HJ**

##### **Biopsychosocial predictors of sexual function and quality of sexual life: a study among patients with colorectal cancer**

Traa MJ, Roukema JA, De Vries J, Rutten HJ\*, Langenhoff B, Jansen W, Den Oudsten BL  
Transl Androl Urol. 2015 Apr;4(2):206-17

**OBJECTIVE:** A low sexual function (SF) has been reported in patients with colorectal cancer. However, research often focusses on clinical predictors of SF, hereby omitting patients' subjective evaluation of SF [i.e., the quality of sexual life (QoSL)] and psychosocial predictors of SF and QoSL. In addition, research incorporating a biopsychosocial approach to SF and QoSL is scarce. Therefore, this study aimed to evaluate (I) relatedness between SF and the QoSL, (II) the course of SF and QoSL, and (III) biopsychosocial predictors of SF and QoSL.

**METHODS:** Patients completed questionnaires assessing sociodemographic factors (i.e., age, sex) and personality characteristics (i.e., neuroticism, trait anxiety) before surgery. Questionnaires assessing psychological (i.e., anxious and depressive symptoms, body image, fatigue) and social (i.e., sexual activity, SF, non-sensuality, avoidance of sexual activity, non-communication, relationship function) aspects were measured preoperative and 3, 6, and 12 months after surgery. Clinical characteristics were obtained from the Eindhoven Cancer Registry (ECR). Bivariate correlations evaluated relatedness between SF and QoSL. Linear mixed-effects models examined biopsychosocial predictors of SF and QoSL.

**RESULTS:** SF and QoSL are related constructs ( $r=0.206$  to  $0.642$ ). Compared to preoperative scores, SF did not change over time ( $P>0.05$ ). Overall, patients' QoSL decreased postoperatively ( $P=0.001$ ). A higher age ( $\beta=-0.02$ ,  $P=0.006$ ), fatigue ( $\beta=-0.02$ ,  $P=0.034$ ), not being sexually active ( $\beta=-0.081$ ,  $P<0.001$ ), and having a stoma ( $\beta=0.37$ ,  $P=0.035$ ) contributed

to a lower SF. Having rectal cancer ( $\beta=-1.64$ ,  $P=0.003$ ), depressive symptoms ( $\beta=-0.09$ ,  $P=0.001$ ), lower SF ( $\beta=1.05$ ,  $P<0.001$ ), and more relationship maladjustment ( $\beta=-0.05$ ,  $P=0.027$ ) contributed to a lower QoSL ( $P<0.05$ ). In addition, partners' SF ( $\beta=0.24$ ,  $P<0.001$ ) and QoSL ( $\beta=0.30$ ,  $P<0.001$ ) were predictive for patients' SF and QoSL, respectively. A significant interaction between time and gender was reported for both outcomes ( $P$ 's=0.002).

**CONCLUSIONS:** SF and QoSL are related but distinctive constructs. The course of SF and QoSL differed. Different biopsychosocial predictors were found for SF and QoSL. The contribution of partner-related variables to patients' outcomes suggests interdependence between patients and partners. Men and women showed different SF and QoSL trajectories. We recommend that health care professionals, when discussing sexuality, realize that SF and QoSL are no interchangeable terms and should, therefore, be discussed as two separate entities. In addition, it is favored that clinicians focus not only on biological predictors of SF and QoSL, but obtain a broader perspective in which they also pay attention to psychosocial factors that may impair SF and QoSL. More in depth research on interdependence between patients and partners, biopsychosocial predictors of partners' SF and QoSL, and gender effects is needed.

*impactfactor:* --

## **Rutten HJ**

### **Changes in gastrointestinal cancer resection rates**

Speelman AD, van Gestel YR, Rutten HJ\*, de Hingh IH\*, Lemmens VE

Br J Surg. 2015 Aug;102(9):1114-22. Epub 2015 Jun 9

**BACKGROUND:** Many developments in medicine are likely to have influenced the treatment of gastrointestinal cancer, including rates of resection. This study sought to investigate changes in surgical resection rates over time among patients with gastrointestinal cancer.

**METHODS:** Patients diagnosed between 1995 and 2012 in the Eindhoven Cancer Registry area were included. Multivariable logistic regression analysis was used to determine the independent influence of interval of diagnosis on the likelihood of having a resection.

**RESULTS:** Among 43 370 patients, crude resection rates decreased between 1995 and 2012 for gastric, colonic and rectal cancer, most notably for patients aged at least 85 years with gastric cancer (from 37.3 to 13.3 per cent), and patients aged 75-84 years and 85 years or more with rectal cancer (from 80.5 to 64.4 per cent, and from 58.9 to 36.0 per cent respectively). After adjustment for patient and tumour characteristics, patients diagnosed between 2008 and 2012 with gastric (odds ratio (OR) 0.71, 95 per cent c.i. 0.55 to 0.92), colonic (OR 0.52, 0.44 to 0.62), rectal (OR 0.39, 0.33 to 0.48) and periampullary (OR 0.42, 0.27 to 0.66) cancers were less likely to undergo resection than those diagnosed between 1995 and 1998. Patients diagnosed with pancreatic cancer were more likely to undergo resection in recent periods (OR 4.13, 2.57 to 6.64).

**CONCLUSION:** Resection rates have fallen over time for several gastrointestinal cancers. This might reflect increased availability of other treatments, better selection of patients as a result of improved diagnostic accuracy, risk-avoiding behaviour and transparency related to surgical outcomes at hospital and surgeon level.

*impactfactor:* 5.542



**Rutten HJ**

**Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease**

Orsini RG\*, Verhoeven RH, Lemmens VE, van Steenberg LN, de Hingh IH\*, Nieuwenhuijzen GA\*, Rutten HJ\*

Eur J Cancer. 2015 Sep;51(13):1675-82

Voor abstract zie: *Chirurgie - Orsini RG*

impactfactor: 5.417

**Rutten HJ**

**COMPRES: A prospective post-marketing evaluation of the compression anastomosis ring CAR 27™ /Colonring™**

D'Hoore A, Albert MR, Cohen SM, Herbst F, Matter I, Speeten KV, Dominguez J, Rutten H\*, Muldoon JP, Bardakcioglu O, Senagore AJ, Ruppert R, Mills S, Stamos MJ, Pahlman L, Choman E, Wexner SD; The COMPRES collaborative study group

Colorectal Dis. 2015 Jun;17(6):522-9

AIM: Preclinical studies have suggested that the Nitinol-based compression anastomosis might be a viable solution. A prospective multicentre open label study was designed to evaluate the performance of the ColonRing™ in (low) colorectal anastomosis. METHOD: The primary outcome measure was anastomotic leakage. Patients were recruited at 13 different colorectal surgical units in Europe, the United States and Israel. Institutional review board (IRB) approval was obtained. RESULTS: Between March 21 2010 and August 3 2011, 266 patients completed the study protocol. The overall anastomotic leakage rate was 5.3% for all anastomoses, including a rate of 3.1% for low anastomoses. Overall septic anastomotic complications occurred in 8.3% and 8.2%. CONCLUSION: The Nitinol compression anastomosis is safe, effective, and easy to use and may offer an advantage for low colorectal anastomosis. A prospective randomized trial comparing ColonRing™ with conventional stapling is needed.

impactfactor: 2.351

**Rutten HJ**

**Determinants in decision making for curative treatment and survival in patients with resectable oesophageal cancer in the Netherlands: a population-based study**

Koëter M\*, van Steenberg LN, Lemmens VE, Rutten HJ\*, Roukema JA, Nieuwenhuijzen GA\* Cancer Epidemiol. 2015 Dec;39(6):863-9

Voor abstract zie: *Chirurgie - Koëter M*

impactfactor: 2.711

**Rutten HJ**

**Does extended surgery influence health-related quality of life in patients with rectal cancer?**

Orsini RG\*, Vermeer TA\*, Traa MJ, Nieuwenhuijzen GA\*, de Hingh IH\*, Rutten HJ\*

Dis Colon Rectum. 2015 Feb;58(2):179-85

Voor abstract zie: *Chirurgie - Orsini RG*

impactfactor: 2.615

**Rutten HJ**

**Effect of adjuvant chemotherapy on recurrence-free survival varies by neo-adjuvant treatment in patients with stage III rectal cancer**

van Erning FN, Rutten HJ\*, van den Berg HA\*, Lemmens VE, van Halteren HK

Eur J Surg Oncol. 2015 Dec;41(12):1630-5

**INTRODUCTION:** Adjuvant chemotherapy still is a controversial therapy for rectal cancer patients. The aim of this study was to analyze the effect of adjuvant chemotherapy on recurrence-free survival (RFS) for patients with stage III rectal cancer treated in clinical practice, taking into account which neo-adjuvant treatment patients received.

**METHODS:** Patients from regions in the Netherlands diagnosed between 1996 and 2013 with pathological stage III rectal cancer who received short-course radiotherapy, chemoradiation or no neo-adjuvant treatment and who underwent surgery were included. After stratification by neo-adjuvant treatment, 5-year RFS according to adjuvant chemotherapy receipt was calculated using Kaplan-Meier curves. Cox regression was used to discriminate the independent effect of adjuvant chemotherapy on the risk of recurrence/death.

**RESULTS:** The study population consisted of 829 patients, of whom 537 (65%) patients received short-course radiotherapy, 128 (15%) patients received chemoradiation and 164 (20%) patients received no neo-adjuvant treatment. Adjuvant chemotherapy was administered to 152 (18%) patients. Adjuvant chemotherapy was associated with improved 5-year RFS for patients who received short-course radiotherapy (61% vs. 46%,  $p = 0.005$ ) and for patients who did not receive any neo-adjuvant treatment (70% vs. 28%,  $p < 0.0001$ ). In multivariable analyses, adjuvant chemotherapy was associated with a reduced risk of recurrence/death for patients treated with short-course radiotherapy (HR 0.65, 95% CI 0.46-0.93) and for patients without neo-adjuvant treatment (HR 0.35, 95% CI 0.18-0.71), but not for patients treated with chemoradiation (HR 1.11, 95% CI 0.51-2.41).

**CONCLUSION:** Among patients with stage III rectal cancer, the effect of adjuvant chemotherapy on RFS seems to vary by neo-adjuvant treatment.

*impactfactor:* 3.009

**Rutten HJ**

**Effect of preoperative treatment strategies on the outcome of patients with clinical T3, non-metastasized rectal cancer: A comparison between Dutch and Canadian expert centers**

Brugom AJ, Vermeer TA\*, van den Broek CB, Vuong T, Bastiaannet E, Azoulay L, Dekkers OM, Niazi T, van den Berg HA\*, Rutten HJ\*, van de Velde CJ

Eur J Surg Oncol. 2015 Aug;41(8):1039-44

*Voor abstract zie:* Chirurgie - Vermeer TA

*impactfactor:* 3.009

**Rutten HJ**

**Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.930

**Rutten HJ**

**Incidence and treatment of recurrent disease after cytoreductive surgery and intraperitoneal chemotherapy for peritoneally metastasized colorectal cancer: A systematic review**

van Oudheusden TR\*, Nienhuijs SW\*, Luyer MD\*, Nieuwenhuijzen GA\*, Lemmens VE, Rutten HJ\*, de Hingh IH\*

Eur J Surg Oncol. 2015 Oct;41(10):1269-77. Epub 2015 Jul 3

Voor abstract zie: *Chirurgie - Oudheusden TR van*

impactfactor: 3.009

**Rutten HJ**

**Modern Treatment of Rectal Cancer Closes the Gap Between Common Adenocarcinoma and Mucinous Carcinoma**

Hugen N, van de Velde CJ, Bosch SL, Fütterer JJ, Elferink MA, Marijnen CA, Rutten HJ\*, de Wilt JH, Nagtegaal ID

Ann Surg Oncol. 2015 Aug;22(8):2669-76. Epub 2015 Jan 7

BACKGROUND: Mucinous carcinoma (MC) is a distinct form of rectal cancer (RC) comprising 10 % of all cases and has been associated with an impaired prognosis compared with non-mucinous adenocarcinoma (AC). The benefit of today's modern treatment for MC patients is unknown but a prospective randomized trial to answer this does not seem feasible. This study provides an analysis of the modern treatment of rectal MC and efficacy of preoperative therapies for MC patients. METHODS: Data from three large (trial) cohorts were used. Data from the Netherlands Cancer Registry (NCR) were used to analyze the prognosis of RC patients over time (N = 38,035). To study the benefit of preoperative short-term radiotherapy, patients from the total mesorectal excision (TME) trial (N = 1,530) were selected, and the benefit from preoperative chemoradiotherapy was analyzed with data on 540 locally advanced RC (LARC) patients from two hospitals.

RESULTS: Data from the NCR confirmed that 5-year overall survival for MC was significantly worse from 1989 to 1998, but no longer different from AC from 1999 onwards. MC patients had a higher rate of positive circumferential resection margin than AC patients (TME trial 27.2 vs. 16.5 %,  $p = 0.006$ ; LARC cohort 34.5 vs. 9.8 %,  $p < 0.0001$ ), but there was no difference in outcome between MC and AC patients after preoperative short-term radiotherapy or chemoradiotherapy. CONCLUSIONS: Modern treatment of RC has benefited MC patients, leading to equal survival for MC and AC patients. Enhancements in the fields of imaging and quality of surgery have improved outcome and preoperative therapies should be recommended for both histological subtypes.

impactfactor: 3.930

**Rutten HJ**

**No Increased Risk of Second Cancer After Radiotherapy in Patients Treated for Rectal or Endometrial Cancer in the Randomized TME, PORTEC-1, and PORTEC-2 Trials**

Wiltink LM, Nout RA1, Fiocco M, Meershoek-Klein Kranenburg E, Jürgenliemk-Schulz IM, Jobsen JJ, Nagtegaal ID, Rutten HJ\*, van de Velde CJ, Creutzberg CL, Marijnen CA

J Clin Oncol. 2015 May 20;33(15):1640-6. Epub 2014 Dec 22

PURPOSE: This study investigated the long-term probability of developing a second cancer in a large pooled cohort of patients treated with surgery with or without radiotherapy (RT).

PATIENTS AND METHODS: All second cancers diagnosed in patients included in the TME, PORTEC-1, and PORTEC-2 trials were analyzed. In the TME trial, patients with rectal cancer (n

= 1,530) were randomly allocated to preoperative external-beam RT (EBRT; 25 Gy in five fractions) or no RT. In the PORTEC trials, patients with endometrial cancer were randomly assigned to postoperative EBRT (46 Gy in 2-Gy fractions) versus no RT (PORTEC-1; n = 714) or EBRT versus vaginal brachytherapy (VBT; PORTEC-2; n = 427). RESULTS: A total of 2,554 patients were analyzed (median follow-up, 13.0 years; range 1.8 to 21.2 years). No differences were found in second cancer probability between patients who were treated without RT (10- and 15-year rates, 15.8% and 26.5%, respectively) and those treated with EBRT (10- and 15-year rates, 15.4% and 25.6%, respectively) or VBT (10-year rate, 14.9%). In the individual trials, no significant differences were found between treatment arms. All cancer survivors had a higher risk of developing a second cancer compared with an age- and sex-matched general population. The standardized incidence ratio for any second cancer was 2.98 (95% CI, 2.82 to 3.14). CONCLUSION: In this pooled trial cohort of > 2,500 patients with pelvic cancers, those who underwent EBRT or VBT had no higher probability of developing a second cancer than patients who were treated with surgery alone. However, patients with rectal or endometrial cancer had an increased probability of developing a second cancer compared with the general population.

*impactfactor:* 18.428

#### **Rutten HJ**

##### **Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59.

*Voor abstract zie:* Chirurgie - Koëter M

*impactfactor:* 2.546

#### **Rutten HJ**

##### **Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery**

van den Heijkant TC\*, Costes LM, van der Lee DG\*, Aerts B, Osinga-de Jong M, Rutten HR\*, Hulsewé KW, de Jonge WJ, Buurman WA, Luyer MD\*.

Br J Surg. 2015 Feb;102(3):202-11. Epub 2014 Dec 18

*Voor abstract zie:* Chirurgie - Heijkant TC van den

*impactfactor:* 5.542

#### **Rutten HJ**

##### **Reliability of the Inverse Water Volumetry Method to Measure the Volume of the Upper Limb**

Beek MA, te Slaa A, van der Laan L, Mulder PG, Rutten HJ\*, Voogd AC, Luiten EJ, Gobardhan PD

Lymphat Res Biol. 2015 Jun;13(2):126-30

BACKGROUND: Lymphedema of the upper extremity is a common side effect of lymph node dissection or irradiation of the axilla. Several techniques are being applied in order to examine the presence and severity of lymphedema. Measurement of circumference of the upper extremity is most frequently performed. An alternative is the water-displacement method. The aim of this study was to determine the reliability and the reproducibility of the

"Inverse Water Volumetry apparatus" (IWV-apparatus) for the measurement of arm volumes.

**PATIENTS AND METHODS:** The IWV-apparatus is based on the water-displacement method. Measurements were performed by three breast cancer nurse practitioners on ten healthy volunteers in three weekly sessions.

**RESULTS:** The intra-class correlation coefficient, defined as the ratio of the subject component to the total variance, equaled 0.99. The reliability index is calculated as 0.14?kg. This indicates that only changes in a patient's arm volume measurement of more than 0.14?kg would represent a true change in arm volume, which is about 6% of the mean arm volume of 2.3?kg.

**CONCLUSION:** the IWV-apparatus proved to be a reliable and reproducible method to measure arm volume.

*impactfactor:* 1.709

## **Rutten HJ**

### **Repeat sentinel node biopsy should be considered in patients with locally recurrent breast cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Luiten EJ, Rutgers EJ, Rutten HJ\*, Roumen RM, Nieuwenhuijzen GA\*

Breast Cancer Res Treat. 2015 Oct;153(3):549-56

*Voor abstract zie:* Chirurgie - Vugts G

*impactfactor:* 3.940

## **Rutten HJ**

### **Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

*Voor abstract zie:* Chirurgie - Simkens GA

*impactfactor:* 3.930

## **Rutten HJ**

### **Survival after pelvic exenteration for T4 rectal cancer**

Kusters M\*, Austin KK, Solomon MJ, Lee PJ, Nieuwenhuijzen GA\*, Rutten HJ\*

Br J Surg. 2015 Jan;102(1):125-31

*Voor abstract zie:* Chirurgie - Kusters M

*impactfactor:* 5.542

## **Rutten HJ**

### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Wegdam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hiligsmann M, Buurman WA, Luyer M\*

*Trials.* 2015 Jan 27;16(1):20

*Voor abstract zie: Chirurgie - Peters EG*

*impactfactor: 1.731*

## **Rutten HJ**

### **Treatment of colorectal cancer in older patients. International Society of Geriatric Oncology (SIOG) consensus recommendations 2013**

Papamichael D, Audisio RA, Glimelius B, de Gramont A, Glynne-Jones R, Haller D, Köhne CH, Rostoft S, Lemmens V, Mitry E, Rutten H\*, Sargent D, Sastre J, Seymour M, Starling N, Van Cutsem E, Aapro M

*Ann Oncol.* 2015 Mar;26(3):463-76. Epub 2014 Jul 11

Colorectal cancer (CRC) is one of the most commonly diagnosed cancers both in Europe and worldwide, with the peak incidence in patients >70 years of age. However, as the treatment algorithms for the treatment of patients with CRC become ever more complex, it is clear that a significant percentage of older CRC patients (>70 years) are being less than optimally treated. This document provides a summary of an International Society of Geriatric Oncology (SIOG) task force meeting convened in Paris in 2013 to update the existing expert recommendations for the treatment of older (geriatric) CRC patients published in 2009 and includes overviews of the recent data on epidemiology, geriatric assessment as it relates to surgery and oncology, and the ability of older CRC patients to tolerate surgery, adjuvant chemotherapy, treatment of their metastatic disease including palliative chemotherapy with and without the use of the biologics, and finally the use of adjuvant and palliative radiotherapy in the treatment of older rectal cancer patients. An overview of each area was presented by one of the task force experts and comments invited from other task force members.

*impactfactor: 7.040*

## **Rutten HJ**

### **Two decades of axillary management in breast cancer**

Beek MA, Verheuve NC, Luiten EJ, Klompenhouwer EG\*, Rutten HJ\*, Roumen RM, Gobardhan PD, Voogd AC

*Br J Surg.* 2015 Dec;102(13):1658-64

*Voor abstract zie: Radiologie - Klompenhouwer EG*

*impactfactor: 5.542*

**Rutten HJ**

**Understanding the surgical pitfalls in total mesorectal excision: Investigating the histology of the perirectal fascia and the pelvic autonomic nerves**

Kraima AC, West NP, Treanor D, Magee DR, Bleys RL, Rutten HJ\*, van de Velde CJ, Quirke P, DeRuiter MC

Eur J Surg Oncol. 2015 Dec;41(12):1621-9. Epub 2015 Sep 16

AIM: Excellent understanding of fasciae and nerves surrounding the rectum is necessary for total mesorectal excision (TME). However, fasciae anterolateral to the rectum and surrounding the low rectum are still poorly understood. We studied the perirectal fascia enfolding the extraperitoneally located part of the rectum in en-bloc cadaveric specimens and the University Medical Center Utrecht (UMCU) pelvic dataset, and describe implications for TME.

METHODS: Four donated human adult cadaveric specimens (two males, two females) were obtained through the Leeds GIFT Research Tissue Programme. Paraffin-embedded blocks were produced and serially sectioned at 50 and 250 µm intervals. Whole mount sections were stained with haematoxylin & eosin, Masson's trichrome and Millers' elastin. Additionally, the UMCU pelvic dataset including digitalised cryosections of a female pelvis in three axes was studied.

RESULTS: The mid and lower rectum were surrounded by a multi-layered perirectal fascia, of which the mesorectal fascia (MRF) and parietal fascia bordered the 'holy plane'. There was no extra constant fascia forming a potential surgical plane. Nerves ran laterally to the MRF. More caudally, the mesorectal fat strongly reduced and the MRF approached the rectal muscularis propria. The MRF had a variable appearance in terms of thickness and completeness, most prominently at the anterolateral lower rectum.

CONCLUSION: Dissection onto the MRF allows nerve preservation in TME. Rectal surgeons are challenged in doing so as the MRF varies in thickness and shows gaps, most prominently at the anterolateral lower rectum. At this site, the risk of entering the mesorectum is great and may result in an incomplete specimen.

*impactfactor:* 3.009

**Rutten HJ**

**Variation in circumferential resection margin: Reporting and involvement in the South-Netherlands**

Homan J, Bökkérink GM, Aarts MJ, Lemmens VE, van Lijnschoten G\*, Rutten HJ\*, Wijsman JH, Nagtegaal ID, de Wilt JH

Eur J Surg Oncol. 2015 Nov;41(11):1485-92

BACKGROUND: Since the introduction of total mesorectal surgery the outcome of rectal cancer patients has improved significantly. Involvement of the circumferential resection margin (CRM) is an important predictor of increased local recurrence, distant metastases and decreased overall survival. Abdomino perineal excision (APE) is associated with increased risk of CRM involvement. Aim of this study was to analyze reporting of CRM and to identify predictive factors for CRM involvement.

METHODS: A population-based dataset was used selecting 2153 patients diagnosed between 2008 and 2013 with primary rectal cancer undergoing surgery. Variation in CRM reporting was assessed and predictive factors for CRM involvement were calculated and used in multivariate analyses.

RESULTS: Large variation in CRM reporting was found between pathology departments, with missing cases varying from 6% to 30%. CRM reporting increased from 77% in 2008 to 90% in

2012 ( $p < 0.001$ ). CRM involvement significantly decreased from 12% to 6% over the years ( $p < 0.001$ ). In multivariate analysis type of operation, low anterior resection or APE, did not influence the risk of CRM involvement. Clinical T4-stage [odds ratio (OR) = 3.51; 95% confidence interval (CI) = 1.85-6.65] was associated with increased risk of CRM involvement, whereas neoadjuvant treatment ( $5 \times 5$  gray radiotherapy [OR 0.39; CI 0.25-0.62] or chemoradiation therapy [OR 0.30; CI 0.17-0.53]) were associated with significant decreased risk of CRM involvement.

**CONCLUSION:** Although significant improvements are made during the last years there still is variation in reporting of CRM involvement in the Southern Netherlands. In multivariate analysis APE was no longer associated with increased risk of CRM involvement.

*impactfactor:* 3.009

## **Rutten HJ**

### **Whole mount microscopic sections reveal that Denonvilliers' fascia is one entity and adherent to the mesorectal fascia; implications for the anterior plane in total mesorectal excision?**

Kraima AC, West NP, Treanor D, Magee DR, Rutten HJ, Quirke P, DeRuiter MC, van de Velde CJ

Eur J Surg Oncol. 2015 Jun;41(6):738-45

**BACKGROUND:** Excellent anatomical knowledge of the rectum and surrounding structures is essential for total mesorectal excision (TME). Denonvilliers' fascia (DVF) has been frequently studied, though the optimal anterior plane in TME is still disputed. The relationship of the lateral edges of DVF to the autonomic nerves and mesorectal fascia is unclear. We studied whole mount microscopic sections of en-bloc cadaveric pelvic exenteration and describe implications for TME.

**METHODS:** Four donated human adult cadaveric specimens (two males, two females) were obtained from the Leeds GIFT Research Tissue Programme. Paraffin-embedded mega blocks were produced and serially sectioned at 50 and 250  $\mu$ m intervals. Sections were stained with haematoxylin & eosin, Masson's trichrome and Millers' elastin. Additionally, a series of eleven human fetal specimens (embryonic age of 9-20 weeks) were studied.

**RESULTS:** DVF consisted of multiple fascial condensations of collagen and smooth muscle fibres and was indistinguishable from the anterior mesorectal fascia and the prostatic fascia or posterior vaginal wall. The lateral edges of DVF appeared fan-shaped and the most posterior part was continuous with the mesorectal fascia. Fasciae were not identified in fetal specimens.

**CONCLUSION:** DVF is adherent to and continuous with the mesorectal fascia. Optimal surgical dissection during TME should be carried out anterior to DVF to ensure radical removal, particularly for anterior tumours. Autonomic nerves are at risk, but can be preserved by closely following the mesorectal fascia along the anterolateral mesorectum. The lack of evident fasciae in fetal specimens suggested that these might be formed in later developmental stages.

*impactfactor:* 3.009

## **Said M**

### **Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*

Springerplus. 2015 Jul 7;4:322

*Voor abstract zie:* Chirurgie - Pouwels S

*impactfactor:* --



**Sambeek MR van**

**A Rare Cause of Haematemesis; a Primary Aorto-Esophageal Fistula: Case Report and Review of Literature**

Denise Strijbos\*, Johanna W M Holtkamp, Marc R H M Van Sambeek\*, Simon W Nienhuijs\*, Arnold Stronkhorst\* and Lennard P L Gilissen\*

Gastro Open Access, 2015;3(1):118

Aorto-Esophageal fistula is a rare condition, causes excessive bleeding from the upper gastrointestinal tract and is associated with a high mortality. This case report demonstrates the presentation of a 63-year old female with a primary aorto-esophageal fistula, due to a ruptured thoracic aneurysm. She first presented with a sentinel haemorrhage, followed by a new bleeding several hours later. An earlier performed upper gastrointestinal endoscopy elsewhere, because of dysphasia, already mentioned an impression from a non pulsing compressive swelling. No further analysis was performed. At current presentation, she was hemodynamically instable, with mild haematemesis. After stabilising she was admitted to the Intensive Care unit; however, haematemesis worsened. An immediate Computed Tomography (CT) scan showed an Aorto-Esophageal Fistula (AEF), due to a ruptured thoracic aortic aneurysm. Emergent surgical treatment consisted of endovascular stent-graft of the thoracic aorta and a total thoracic esophagectomy combined with immediate esophago-gastrostomy. Unfortunately, the subsequent multi-organ failure was fatal. A critical view to the surgical approach is given, combined with a review of diagnostic and therapeutic options in aorto-esophageal fistulae.

Voor abstract zie: *Maag-darm-leverziekten - Strijbos D*

impactfactor: --

**Sambeek MR van**

**Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review**

Pouwels S\*, Willigendael EM, van Sambeek MR\*, Nienhuijs SW\*, Cuypers PW\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Jan;49(1):66-76

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: 3.490

**Sambeek MR van**

**Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair**

Broos PP\*, Stokmans RA\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*; ENGAGE Investigators

J Endovasc Ther. 2015 Oct;22(5):770-7

Voor abstract zie: *Chirurgie - Broos PP*

impactfactor: 2.826

**Sambeek MR van**

**Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial**

Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JA\*, Hoffmann WH, Smits TM, van Brussel JP, Stultiens GN, Derom A, den Hoed PT, Ho GH, van Dijk LC, Verhofstad N\*, Orsini M, van Petersen A, Woltman K, Hulst , van Sambeek MR\*, Rizopoulos D, Rouwet EV, Hunink MG

JAMA. 2015 Nov 10;314(18):1936-44

*Voor abstract zie: Chirurgie - Teijink JA*

*impactfactor: 35.289*

**Sambeek MR van**

**Endovascular Treatment of Ruptured Abdominal Aortic Aneurysms with Hostile Aortic Neck Anatomy**

Broos PP\*, 't Mannetje YW\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Sep;50(3):313-9. Epub 2015 May 28

*Voor abstract zie: Chirurgie - Broos PP*

*impactfactor: 3.490*

**Sambeek MR van**

**Gender differences following supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Scheltinga MR, van Sambeek MR\*, Maas AH, Bendermacher BL, Teijink JA\*

J Vasc Surg. 2015 Sep;62(3):681-8

*Voor abstract zie: Chirurgie - Gommans L*

*impactfactor: 3.021*

**Sambeek MR van**

**Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk**

Gensicke H, van der Worp HB, Nederkoorn PJ, Macdonald S, Gaines PA, van der Lugt A, Mali WP, Lyrer PA, Peters N, Featherstone RL, de Borst GJ, Engelter ST, Brown MM, Bonati LH; ICSS-MRI Substudy Investigators; Collaborator: Sambeek MR van\*

J Am Coll Cardiol. 2015 Feb 17;65(6):521-9

**BACKGROUND:** Brain lesions on diffusion-weighted imaging (DWI) are frequently found after carotid artery stenting (CAS), but their clinical relevance remains unclear.

**OBJECTIVES:** This study sought to investigate whether periprocedural ischemic DWI lesions after CAS or carotid endarterectomy (CEA) are associated with an increased risk of recurrent cerebrovascular events.

**METHODS:** In the magnetic resonance imaging (MRI) substudy of ICSS (International Carotid Stenting Study), 231 patients with symptomatic carotid stenosis were randomized to undergo CAS (n=124) or CEA (n=107). MRIs were performed 1 to 7 days before and 1 to 3 days after treatment. The primary outcome event was stroke or transient ischemic attack in any territory occurring between the post-treatment MRI and the end of follow-up. Time to occurrence of the primary outcome event was compared between patients with (DWI+) and

without (DWI-) new DWI lesions on the post-treatment scan in the CAS and CEA groups separately.

**RESULTS:** Median time of follow-up was 4.1 years (interquartile range: 3.0 to 5.2). In the CAS group, recurrent stroke or transient ischemic attack occurred more often among DWI+ patients (12 of 62) than among DWI- patients (6 of 62), with a cumulative 5-year incidence of 22.8% (standard error [SE]: 7.1%) and 8.8% (SE: 3.8%), respectively (unadjusted hazard ratio: 2.85; 95% confidence interval: 1.05 to 7.72;  $p=0.04$ ). In DWI+ and DWI- patients, 8 and 2 events, respectively, occurred within 6 months after treatment. In the CEA group, there was no difference in recurrent cerebrovascular events between DWI+ and DWI- patients.

**CONCLUSIONS:** Ischemic brain lesions discovered on DWI after CAS seem to be a marker of increased risk for recurrent cerebrovascular events. Patients with periprocedural DWI lesions might benefit from more aggressive and prolonged antiplatelet therapy after CAS. (A Randomised Comparison of the Risks, Benefits and Cost Effectiveness of Primary Carotid Stenting With Carotid Endarterectomy: International Carotid Stenting Study; ISRCTN25337470).

*impactfactor:* 16.503

### **Sambeek MR van**

#### **Local anisotropic mechanical properties of human carotid atherosclerotic plaques - Characterisation by micro-indentation and inverse finite element analysis**

Chai CK, Akyildiz AC, Speelman L, Gijsen FJ, Oomens CW, van Sambeek MR\*, Lugt AV, Baaijens FP

J Mech Behav Biomed Mater. 2015 Mar;43:59-68. Epub 2014 Dec 22

Biomechanical models have the potential to predict failure of atherosclerotic plaques and to improve the risk assessment of plaque rupture. The applicability of these models depends strongly on the used material models. Current biomechanical models employ isotropic material models, although it is generally accepted that plaque tissue behaves highly anisotropic. The aim of the present study is to determine the local anisotropic mechanical properties of human atherosclerotic plaque tissue by means of micro-indentation tests. The indentation was performed on top of an inverted confocal microscope allowing the visualisation and quantification of the collagen fibre deformations perpendicular to the indentation direction of the plaque. Based on this, the anisotropic properties of plaque tissue perpendicular to the indentation direction (middle of the fibrous cap, shoulder of the cap, remaining intima tissue) were derived. There were no significant differences between the different indentation locations for the fibre stiffness (total median 80.6kPa, 25th-75th percentile 17.7-157.0kPa), and fibre dispersion.

*impactfactor:* 3.417

### **Sambeek MR van**

#### **Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial**

Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, Mali WP, Beard JD, Cleveland T, Engelter ST, Lyrer PA, Ford GA, Dormann PJ, Brown MM; International Carotid Stenting Study investigators; Collaborator: Sambeek MR van\* Lancet. 2015 Feb 7;385(9967):529-38

**BACKGROUND:** Stenting is an alternative to endarterectomy for treatment of carotid artery stenosis, but long-term efficacy is uncertain. We report long-term data from the randomised International Carotid Stenting Study comparison of these treatments.

**METHODS:** Patients with symptomatic carotid stenosis were randomly assigned 1:1 to open treatment with stenting or endarterectomy at 50 centres worldwide. Randomisation was computer generated centrally and allocated by telephone call or fax. Major outcomes were assessed by an independent endpoint committee unaware of treatment assignment. The primary endpoint was fatal or disabling stroke in any territory after randomisation to the end of follow-up. Analysis was by intention to treat ([ITT] all patients) and per protocol from 31 days after treatment (all patients in whom assigned treatment was completed). Functional ability was rated with the modified Rankin scale. This study is registered, number ISRCTN25337470.

**FINDINGS:** 1713 patients were assigned to stenting (n=855) or endarterectomy (n=858) and followed up for a median of 4.2 years (IQR 3.0-5.2, maximum 10.0). Three patients withdrew immediately and, therefore, the ITT population comprised 1710 patients. The number of fatal or disabling strokes (52 vs 49) and cumulative 5-year risk did not differ significantly between the stenting and endarterectomy groups (6.4% vs 6.5%; hazard ratio [HR] 1.06, 95% CI 0.72-1.57, p=0.77). Any stroke was more frequent in the stenting group than in the endarterectomy group (119 vs 72 events; ITT population, 5-year cumulative risk 15.2% vs 9.4%, HR 1.71, 95% CI 1.28-2.30, p<0.001; per-protocol population, 5-year cumulative risk 8.9% vs 5.8%, 1.53, 1.02-2.31, p=0.04), but were mainly non-disabling strokes. The distribution of modified Rankin scale scores at 1 year, 5 years, or final follow-up did not differ significantly between treatment groups.

**INTERPRETATION:** Long-term functional outcome and risk of fatal or disabling stroke are similar for stenting and endarterectomy for symptomatic carotid stenosis.

*impactfactor:* 45.217

### **Sambeek MR van**

#### **Performance of the Endurant stent graft in challenging anatomy**

Broos PP\*, Stokmans RA\*, van Sterkenburg SM, Torsello G, Vermassen F, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

J Vasc Surg. 2015 Aug;62(2):312-8

*Voor abstract zie:* Chirurgie - Broos PP

*impactfactor:* 3.021

### **Sambeek MR van**

#### **Significante dosisreductie door gebruik van strooistraling werend afdek materiaal bij EVAR procedures**

Carla Kloeze, Elisabeth G. Klompenhouwer, Peter Brands, Marc R.H.M. van Sambeek, Philippe W.M. Cuypers, Joep A.W. Teijink

Gamma Professional, 2015; 65(3): 3-7

*Voor abstract zie:* Geen abstract beschikbaar

*impactfactor:* --

**Sambeek MR van**

**The year in cardiology 2014: peripheral circulation**

Aboyans V, Brodmann M, De Carlo M, Clement D, Mazzolai L, van Bortel L, van Sambeek MR, Vlachopoulos C; On Behalf the ESC Working Group of Peripheral Circulation

Eur Heart J. 2015 Mar 7;36(10):591-7

In 2014, the debate on the indication of revascularization in case of asymptomatic carotid disease continued, while another one regarding the use of surgery vs. stenting addressed some new issues regarding the long-term cardiac risk of these patients. Renal arteries interventions trials were disappointing, as neither renal denervation nor renal artery stenting was found associated with better blood pressure management or outcome. In contrast, in lower-extremities artery disease, the endovascular techniques represent in 2014 major alternatives to surgery, even in distal arteries, with new insights regarding the interest of drug-eluting balloons. Regarding the aorta, the ESC published its first guidelines document on the entire vessel, emphasizing on the role of every cardiologist for screening abdominal aorta aneurysm during echocardiography. Among vascular wall biomarkers, the aorta stiffness is of increasing interest with new data and meta-analysis confirming its ability to stratify risk, whereas carotid intima-media thickness showed poor performances in terms of reclassifying patients into risk categories beyond risk scores. Regarding the veins, new data suggest the interest of D-dimers and residual venous thrombosis to help the decision of anti-coagulation prolongation or discontinuation after the initial period of treatment for deep vein thrombosis.

*impactfactor:* 15.203

**Schipper RJ**

**Diagnostic Performance of Dedicated Axillary T2- and Diffusion-weighted MR Imaging for Nodal Staging in Breast Cancer**

Schipper RJ\*, Paiman ML, Beets-Tan RG, Nelemans PJ, de Vries B, Heuts EM, van de Vijver KK, Keymeulen KB, Brans B, Smidt ML, Lobbes MB

Radiology. 2015 May;275(2):345-55

**PURPOSE:** To evaluate the diagnostic performance of unenhanced axillary T2-weighted and diffusion-weighted (DW) magnetic resonance (MR) imaging for axillary nodal staging in patients with newly diagnosed breast cancer, with node-by-node and patient-by-patient validation.

**MATERIALS AND METHODS:** Institutional review board approval and informed consent were obtained. Fifty women (mean age, 60 years; range, 22-80 years) underwent high-spatial-resolution axillary 3.0-T T2-weighted imaging without fat suppression and DW imaging ( $b = 0, 500, \text{ and } 800 \text{ sec/mm}^2$ ), followed by either sentinel lymph node biopsy (SLNB) or axillary lymph node dissection. Two radiologists independently scored each lymph node on a confidence level scale from 0 (benign) to 4 (malignant), first on T2-weighted MR images, then on DW MR images. Two researchers independently measured the mean apparent diffusion coefficient (ADC) of each lymph node. Diagnostic performance parameters were calculated on the basis of node-by-node and patient-by-patient validation.

**RESULTS:** With respective node-by-node and patient-by-patient validation, T2-weighted MR imaging had a specificity of 93%-97% and 87%-95%, sensitivity of 32%-55% and 50%-67%, negative predictive value (NPV) of 88%-91% and 86%-89%, positive predictive value (PPV) of 60%-70% and 62%-75%, and area under the receiver operating characteristic curve (AUC) of 0.78 and 0.80-0.88, with good interobserver agreement ( $\kappa = 0.70$ ). The addition of DW MR

imaging resulted in lower specificity (59%-88% and 50%-84%), higher sensitivity (45%-64% and 75%-83%), comparable NPV (89% and 90%-91%), lower PPV (23%-42% and 34%-60%), and lower AUC (0.68-0.73 and 0.70-0.86). ADC measurement resulted in a specificity of 63%-64% and 61%-63%, sensitivity of 41% and 67%, NPV of 85% and 85%-86%, PPV of 18% and 35%-36%, and AUC of 0.54-0.58 and 0.69-0.74, respectively, with excellent interobserver agreement (intraclass correlation coefficient, 0.83).

**CONCLUSION:** Dedicated high-spatial-resolution axillary T2-weighted MR imaging showed good specificity on the basis of node-by-node and patient-by-patient validation, with good interobserver agreement. However, its NPV is still insufficient to substitute it for SLNB for exclusion of axillary lymph node metastasis. DW MR imaging and ADC measurement were of no added value.

*impactfactor:* 6.867

### **Schipper RJ**

#### **Noninvasive nodal restaging in clinically node positive breast cancer patients after neoadjuvant systemic therapy: a systematic review**

Schipper RJ\*, Moossdorff M, Beets-Tan RG, Smidt ML, Lobbes MB

Eur J Radiol. 2015 Jan;84(1):41-7

**OBJECTIVE:** To provide a systematic review of studies comparing the diagnostic performance of noninvasive techniques and axillary lymph node dissection in the identification of initially node positive patients with pathological complete response of axillary lymph nodes to neoadjuvant systemic therapy.

**METHODS:** PubMed and Embase databases were searched until May 21st, 2014. First, duplicate studies were eliminated. Next, study abstracts were read by two readers to assess eligibility. Studies were selected based on predefined inclusion criteria. Of these, data extraction was performed by two readers independently.

**RESULTS:** Of the 987 abstracts that were considered for inclusion, four were eligible for final analysis, which included a total of 572 patients. The diagnostic performance of clinical examination, axillary ultrasound, breast MRI, whole body (18)F-FDG PET-CT, and a prediction model to identify patients with pathological complete response were investigated. Studies were often limited by small sample size. Furthermore, systemic therapy regimens and definitions of clinical and pathological complete response were variable, refraining further pooling of data. The reported positive predictive value of different techniques to identify patients with axillary pathological complete response after neoadjuvant systemic therapy varied between 40% and 100%.

**CONCLUSION:** At present, there is no accurate noninvasive restaging technique able to identify patients with complete axillary response after neoadjuvant systemic therapy.

*impactfactor:* 2.369

### **Schipper RJ**

#### **The diagnostic performance of sentinel lymph node biopsy in pathologically confirmed node positive breast cancer patients after neoadjuvant systemic therapy: A systematic review and meta-analysis**

van Nijnatten TJ, Schipper RJ\*, Lobbes MB, Nelemans PJ, Beets-Tan RG, Smidt ML

Eur J Surg Oncol. 2015 Oct;41(10):1278-87

**PURPOSE:** To provide a systematic review and meta-analysis of studies investigating sentinel lymph node biopsy after neoadjuvant systemic therapy in pathologically confirmed node positive breast cancer patients.

**METHODS:** Pubmed and Embase databases were searched until June 19th, 2015. All abstracts were read and data extraction was performed by two independent readers. A random-effects model was used to pool the proportion for identification rate, false-negative rate (FNR) and axillary pCR with 95% confidence intervals. Subgroup analyses affirmed potential confounders for identification rate and FNR.

**RESULTS:** A total of 997 abstracts were identified and eventually eight studies were included. Pooled estimates were 92.3% (90.8-93.7%) for identification rate, 15.1% (12.7-17.6%) for FNR and 36.8% (34.2-39.5%) for axillary pCR. After subgroup analysis, FNR is significantly worse if one sentinel node was removed compared to two or more sentinel nodes (23.9% versus 10.4%,  $p = 0.026$ ) and if studies contained clinically nodal stage 1-3, compared to studies with clinically nodal stage 1-2 patients (21.4 versus 13.1%,  $p = 0.049$ ). Other factors, including single tracer mapping and the definition of axillary pCR, were not significantly different.

**CONCLUSION:** Based on current evidence it seems not justified to omit further axillary treatment in every clinically node positive breast cancer patients with a negative sentinel lymph node biopsy after neoadjuvant systemic therapy.

*impactfactor: 3.009*

## **Schipper RJ**

### **The role of MRI in axillary lymph node imaging in breast cancer patients: a systematic review**

Kuijs VJ, Moosdorff M, Schipper RJ\*, Beets-Tan RG, Heuts EM, Keymeulen KB, Smidt ML, Lobbes MB

Insights Imaging. 2015 Apr;6(2):203-15

**OBJECTIVES:** To assess whether MRI can exclude axillary lymph node metastasis, potentially replacing sentinel lymph node biopsy (SLNB), and consequently eliminating the risk of SLNB-associated morbidity.

**METHODS:** PubMed, Cochrane, Medline and Embase databases were searched for relevant publications up to July 2014. Studies were selected based on predefined inclusion and exclusion criteria and independently assessed by two reviewers using a standardised extraction form.

**RESULTS:** Sixteen eligible studies were selected from 1,372 publications identified by the search. A dedicated axillary protocol [sensitivity 84.7 %, negative predictive value (NPV) 95.0 %] was superior to a standard protocol covering both the breast and axilla simultaneously (sensitivity 82.0 %, NPV 82.6 %). Dynamic, contrast-enhanced MRI had a lower median sensitivity (60.0 %) and NPV (80.0 %) compared to non-enhanced T1w/T2w sequences (88.4, 94.7 %), diffusion-weighted imaging (84.2, 90.6 %) and ultrasmall superparamagnetic iron oxide (USPIO)-enhanced T2\*w sequences (83.0, 95.9 %). The most promising results seem to be achievable when using non-enhanced T1w/T2w and USPIO-enhanced T2\*w sequences in combination with a dedicated axillary protocol (sensitivity 84.7 % and NPV 95.0 %).

**CONCLUSIONS:** The diagnostic performance of some MRI protocols for excluding axillary lymph node metastases approaches the NPV needed to replace SLNB. However, current observations are based on studies with heterogeneous study designs and limited populations.

MAIN MESSAGES: • Some axillary MRI protocols approach the NPV of an SLNB procedure. • Dedicated axillary MRI is more accurate than protocols also covering the breast. • T1w/T2w protocols combined with USPIO-enhanced sequences are the most promising sequences.

impactfactor: --

## **Schipper RJ**

### **Three-Dimensional Breast Radiotherapy and the Elective Radiation Dose at the Sentinel Lymph Node Site in Breast Cancer**

van Roozendaal LM, Schipper RJ\*, Smit LH, Brans BT, Beets-Tan RG, Lobbjes MB, Boersma LJ, Smidt ML

Ann Surg Oncol. 2015 Nov;22(12):3824-30

BACKGROUND: Several trials are presently randomizing clinically node-negative breast cancer patients treated with breast-conserving therapy (BCT) to sentinel lymph node biopsy (SLNB) or watchful waiting. We aimed to investigate the elective radiation dose at the sentinel lymph node (SLN) site while evaluating two techniques for SLN localization, in breast cancer patients treated with lumpectomy and three-dimensional (3D) whole-breast radiotherapy.

METHODS: The SLN site of consecutive Tis-2N0 breast cancer patients undergoing lumpectomy and forward intensity-modulated whole-breast radiotherapy was determined by the location of the hotspot on preoperative single-photon emission computed tomography (SPECT)/computed tomography (CT) and by a surgical clip placed at the removed SLN(s) during SLNB. The radiation dose at the SLN site was subsequently determined on the postoperative radiotherapy planning CT. An elective radiation dose to the SLN site was defined as at least 95 % of the breast dose.

RESULTS: Of the 42 included patients, the mean percentage of the breast dose on the SLN site was 90 % (standard deviation 26, range 7-132, median 99), with a non-significant difference between the two techniques (surgical clip or SPECT/CT) ( $p = 0.608$ ). In 32/42 patients (76 %) the SLN site received an elective radiation dose.

CONCLUSIONS: A surgical clip placed at the removed SLN(s) during SLNB proved to be an adequate method of determining the radiation dose at the SLN site when compared with using SPECT/CT. With the use of 3D radiotherapy, the site of the SLN is treated with an elective radiation dose in the majority of patients who are treated with BCT.

impactfactor: 3.930

## **Simkens GA**

### **Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis**

Simkens GA\*, van Oudheusden TR\*, Luyer MD\*, Nienhuijs SW\*, Nieuwenhuijzen GA\*, Rutten HJ\*, de Hingh IH\*

Ann Surg Oncol. 2015 Aug;22(8):2656-62. Epub 2014 Dec 17

BACKGROUND: The prognosis of patients with peritoneally metastasized colorectal cancer has improved significantly with the introduction of cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (CRS + HIPEC). Although a macroscopically complete resection is achieved in nearly every patient, recurrence rates are high. This study aims to identify risk factors for early recurrence, thereby offering ways to reduce its occurrence.

METHODS: All patients with colorectal peritoneal carcinomatosis treated with CRS + HIPEC and a minimum follow-up of 12 months, in April 2014, were analyzed. Patient data were



compared between patients with or without recurrence within 12 months after CRS + HIPEC. Risk factors were determined using logistic regression analysis. Postoperative complications were graded according to the serious adverse events (SAEs) score, with grade 3 or higher indicating complications requiring intervention.

**RESULTS:** A complete macroscopic cytoreduction was achieved in 96 % of all patients treated with CRS + HIPEC. Forty-six of 133 patients (35 %) developed recurrence within 12 months. An SAE =3 after CRS + HIPEC was the only significant risk factor found for early recurrence (odds ratio 2.3;  $p = 0.046$ ). Median survival in the early recurrence group was 19.3 months compared with 43.2 months in the group without early recurrence ( $p < 0.001$ ). Patients with an SAE =3 showed a reduced survival compared with patients without such complications (22.1 vs. 31.0 months, respectively;  $p = 0.02$ ).

**CONCLUSIONS:** Early recurrence after CRS + HIPEC is associated with a significant reduction in overall survival. This study identifies postoperative complications requiring intervention as the only significant risk factor for early recurrence, independent of the extent of peritoneal disease, highlighting the importance of minimizing the risk of postoperative complications.

*impactfactor:* 3.930

## **Smeets B**

### **Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy**

Berkelmans GH\*, Kouwenhoven EA, Smeets BJ\*, Weijs TJ\*, Silva Corten LC, van Det MJ, Nieuwenhuijzen GA\*, Luyer MD\*

World J Gastroenterol. 2015 Aug 14;21(30):9118-25

**AIM:** To investigate the value of elevated drain amylase concentrations for detecting anastomotic leakage (AL) after minimally invasive Ivor-Lewis esophagectomy (MI-ILE).

**METHODS:** This was a retrospective analysis of prospectively collected data in two hospitals in the Netherlands. Consecutive patients undergoing MI-ILE were included. A Jackson-Pratt drain next to the dorsal side of the anastomosis and bilateral chest drains were placed at the end of the thoracoscopic procedure. Amylase levels in drain fluid were determined in all patients during at least the first four postoperative days. Contrast computed tomography scans and/or endoscopic imaging were performed in cases of a clinically suspected AL. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis on endoscopy, re-operation, radiographic investigations, post mortal examination or when gastro-intestinal contents were found in drain fluid. Receiver operator characteristic curves were used to determine the cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value, risk ratio and overall test accuracy were calculated for elevated drain amylase concentrations.

**RESULTS:** A total of 89 patients were included between March 2013 and August 2014. No differences in group characteristics were observed between patients with and without AL, except for age. Patients with AL were older than were patients without AL ( $P = 0.01$ ). One patient (1.1%) without AL died within 30 d after surgery due to pneumonia and acute respiratory distress syndrome. Anastomotic leakage that required any intervention occurred in 15 patients (16.9%). Patients with proven anastomotic leakage had higher drain amylase levels than patients without anastomotic leakage [median 384 IU/L (IQR 34-6263) vs median 37 IU/L (IQR 26-66),  $P = 0.003$ ]. Optimal cut-off values on postoperative days 1, 2, and 3 were 350 IU/L, 200 IU/L and 160 IU/L, respectively. An elevated amylase level was found in 9 of the 15 patients with AL. Five of these 9 patients had early elevations of their amylase levels, with a median of 2 d (IQR 2-5) before signs and symptoms occurred.

CONCLUSION: Measurement of drain amylase levels is an inexpensive and easy tool that may be used to screen for anastomotic leakage soon after MI-ILE. However, clinical validation of this marker is necessary.

*impactfactor:* 2.369

## **Smeets B**

### **The contribution of mast cells to postoperative ileus in experimental and clinical studies**

Peters EG\*, De Jonge WJ, Smeets BJ\*, Luyer MD\*

Neurogastroenterol Motil. 2015 Jun;27(6):743-9

*Voor abstract zie:* Chirurgie - Peters EG

*impactfactor:* --

## **Smeets B**

### **The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial**

Peters EG\*, Smeets B\*, Dekkers M\*, Buise MD\*, de Jonge WJ, Slooter GD, de Reilingh TS, Weddam JA, Nieuwenhuijzen G\*, Rutten H\*, de Hingh I\*, Hiligsmann M, Buurman WA, Luyer M\*

Trials. 2015 Jan 27;16(1):20

*Voor abstract zie:* Chirurgie - Peters EG

*impactfactor:* 1.731

## **Smulders JF**

### **Association Between Postprandial Symptoms and Gastric Emptying After Sleeve Gastrectomy**

Burgerhart JS, van Rutte PW\*, Edelbroek MA\*, Wyndaele DN\*, Smulders JF\*, van de Meeberg PC, Siersema PD, Smout AJ

Obes Surg. 2015 Feb;25(2):209-14

*Voor abstract zie:* Chirurgie - Rutte PW van

*impactfactor:* 3.747

## **Smulders JF**

### **Hiatal Hernia**

Castelijns B\*, Ponten JE\*, Van de Poll MC, Nienhuijs SW\*, Smulders JF\*, Hu ZW, Wu JM, Wang ZG, Idani H, Asami S, Nakano K, Miyake S, Harano M, Miyoshi H, Araki H, Ogawa T, Takahashi K, Shiozaki S, Ninomiya M, Prasad A, Todkar J, Asti E, Lovece A, Sironi A, Bonavina , Wright , Wurst H, Zhang C, Li HL, Ke LM, Loi K12, Hua R, Yao QY, Chen H, Okinyi W, Odende K, Ndungu B, Ndonga A, Kiragu P, Kelimu A, Alimujiang M, Tian W, Bing M

Hernia. 2015 Apr;19 Suppl 1:S13-7

*Geen abstract beschikbaar*

*impactfactor:* 2.050

**Smulders JF**

**Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial**

Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH, van Geloven AA, Gerhards MF, Govaert MJ, van Grevenstein WM, Hoofwijk AG, Kruij PM, Nienhuijs SW\*, Boermeester MA, Vermeulen J, van Dieren S, Lange JF, Bemelman WA; Ladies trial collaborators. Collaborators: de Hingh IH\*, Luyer MD\*, van Montfort G\*, Ponten EH\*, Smulders JF\*

Lancet. 2015 Sep 26;386(10000):1269-77. Epub 2015 Jul 22

Voor abstract zie: *Chirurgie - Nienhuijs SW*

impactfactor: 45.217

**Smulders JF**

**Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*

Obes Surg. 2015 Aug;25(8):1425-30

Voor abstract zie: *Chirurgie - Wezenbeek MR van*

impactfactor: 3.747

**Smulders JF**

**The Sleeve Bypass Trial: a multicentre randomized controlled trial comparing the long term outcome of laparoscopic sleeve gastrectomy and gastric bypass for morbid obesity in terms of excess BMI loss percentage and quality of life**

Biter LU, Gadiot RP, Grotenhuis BA, Dunkelgrün M, van Mil SR, Zengerink HJ, Smulders JF\*, Mannaerts GH

BMC Obes. 2015 Aug 26;2:30. eCollection 2015

**BACKGROUND:** Obesity is an increasing disease worldwide. Bariatric surgery is the only effective therapy to induce sufficient long-term weight loss for morbidly obese patients. Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) is the gold standard surgical technique. Laparoscopic Sleeve Gastrectomy (LSG) is a new promising bariatric procedure which has the advantage of maintaining an intact gastrointestinal tract. The aim of this study is to evaluate the efficiency of both techniques. Our hypothesis is that LSG has a similar percentage excess BMI loss (%EBMIL) after 5 years compared to LRYGB.

**METHODS/DESIGN:** The Sleeve Bypass Trial is a randomized multicentre clinical trial: patients eligible for bariatric surgery are randomized to either LSG or LRYGB. Patients with a body mass index (BMI)  $\geq 40$  kg/m<sup>2</sup> or BMI 35 kg/m<sup>2</sup> with obesity related comorbidity (T2 DM, sleep apnoea, hypertension) are eligible for randomization. At randomization patients are stratified for centre, sex, T2 DM and BMI  $\geq 50$  kg/m<sup>2</sup>. A total number of 620 patients will be enrolled and equally (1:1) randomized to both treatment arms. Only surgeons experienced in both operation techniques will participate in the Sleeve Bypass trial. The primary endpoint is the 5-year weight loss (%EBMIL) of LSG and LRYGB. Secondary endpoints are resolution of obesity related comorbidity, complications, revision bariatric surgery and quality of life (QOL) defined in various questionnaires.

**DISCUSSION:** Long-term %EBMIL between the two treatment strategies used to be in favour of LRYGB, but more recent results throughout the world show similar %EBMIL in both techniques. If weight loss is comparable, obesity-related comorbidity and QOL after bariatric

procedures should be taken into account when deciding on which surgical technique is to be preferred for certain subgroups in the future.

*impactfactor:* --

### **Stokmans RA**

#### **Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair**

Broos PP\*, Stokmans RA\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*; ENGAGE Investigators

J Endovasc Ther. 2015 Oct;22(5):770-7

*Voor abstract zie:* Chirurgie - Broos PP

*impactfactor:* 2.826

### **Stokmans RA**

#### **Performance of the Endurant stent graft in challenging anatomy**

Broos PP\*, Stokmans RA\*, van Sterkenburg SM, Torsello G, Vermassen F, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

J Vasc Surg. 2015 Aug;62(2):312-8

*Voor abstract zie:* Chirurgie - Broos PP

*impactfactor:* 3.021

### **Teijink JA**

#### **Agreements and discrepancies between the estimated walking distance, nongraded and graded treadmill testing, and outside walking in patients with intermittent claudication**

Fokkenrood HJ\*, van den Houten MM\*, Houterman S\*, Breek JC, Scheltinga MR, Teijink JA\*

Ann Vasc Surg. 2015 Aug;29(6):1218-24

*Voor abstract zie:* Chirurgie - Fokkenrood HJ

*impactfactor:* 1.170

### **Teijink JA**

#### **Aspects of Exercise before or after Bariatric Surgery: A Systematic Review**

ouwels S\*, Wit M\*, Teijink JA\*, Nienhuijs SW\*

Obes Facts. 2015;8(2):132-46

*Voor abstract zie:* Chirurgie - Pouwels S

*impactfactor:* 2.245

### **Teijink JA**

#### **Attitudes to supervised exercise therapy**

Gommans L\*, Teijink JA\*

Br J Surg. 2015 Sep;102(10):1153-5. Epub 2015 Jul 23

*Geen abstract beschikbaar*

*impactfactor:* 5.542

**Teijink JA**

**Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review**

Pouwels S\*, Willigendael EM, van Sambeek MR\*, Nienhuijs SW\*, Cuypers PW\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Jan;49(1):66-76

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: 3.490

**Teijink JA**

**Co-morbidity forces physiotherapists to deviate from guideline recommendations resulting in various treatments for the same patient: a Vignette study**

Dorenkamp S, Mesters I, Teijink JA, de Bie RA

Eur J PersCent Healthcare. 2015;3(1):83-89

Rational, aims and objectives: The aim of this Vignette study was to assess whether physiotherapists (PTs) make reasoned adaptations to evidence-based treatment recommendations when co-morbidity influences single disease treatment.

Method: To study the influence of co-morbidity on treatment recommendations, 3 vignettes were created based on authentic patient data. In the first vignette, a patient with a single-diseased Intermittent Claudication (IC) was described, in the second vignette, co-morbidity Chronic Obstructive Pulmonary Disease (COPD) was added. In the third vignette, Knee Osteoarthritis (OA) was additionally added. Therapists described 3 treatment plans and their decision rationale. A random selection of 100 Dutch Claudication Network members was invited to participate in this qualitative study.

Results: The response rate was 61%. Thirty percent of the physical therapists did not adjust treatment despite co-morbidity. Another 30% partly adapted the treatment plan when co-morbidity was added to the vignette. The presence of co-morbidity induced 40% to abandon guideline recommendations and to create an individualised treatment plan based on the health needs of the vignette patient.

Conclusion: This study showed that the majority of PTs makes adaptations to otherwise evidence-based recommendations when co-morbidity is present in order to tailor treatment to the specific needs of the individual patient. However, the same patient was treated in various ways by different PTs.

impactfactor: --

**Teijink JA**

**Commentary on "Supervised versus unsupervised exercise for intermittent claudication: A sytematic review and meta-analysis"**

Hageman D\*, Gommans LN\*, Fokkenrood HJ\*, Koelemay MJ, Teijink JA\*

Am Heart J. 2015 Aug;170(2):e1-3

Geen abstract beschikbaar

impactfactor: 4.463

**Teijink JA**

**Difficulties of using single-diseased guidelines to treat patients with multiple diseases**

Dörenkamp S, Mesters I, Teijink J\*, de Bie R

Front Public Health. 2015 Apr 29;3:67. eCollection 2015

*geen abstract beschikbaar*

*impactfactor: --*

**Teijink JA**

**Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair**

Broos PP\*, Stokmans RA\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*; ENGAGE Investigators

J Endovasc Ther. 2015 Oct;22(5):770-7

*Voor abstract zie: Chirurgie - Broos PP*

*impactfactor: 2.826*

**Teijink JA**

**Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*

Springerplus. 2015 Jul 7;4:322

*Voor abstract zie: Chirurgie - Pouwels S*

*impactfactor: --*

**Teijink JA**

**Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial**

Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JA\*, Hoffmann WH, Smits TM, van Brussel JP, Stultiens GN, Derom A, den Hoed PT, Ho GH, van Dijk LC, Verhofstad N\*, Orsini M, van Petersen A, Woltman K, Hulst, van Sambeek MR\*, Rizopoulos D, Rouwet EV, Hunink MG

JAMA. 2015 Nov 10;314(18):1936-44

**IMPORTANCE:** Supervised exercise is recommended as a first-line treatment for intermittent claudication. Combination therapy of endovascular revascularization plus supervised exercise may be more promising but few data comparing the 2 therapies are available.

**OBJECTIVE:** To assess the effectiveness of endovascular revascularization plus supervised exercise for intermittent claudication compared with supervised exercise only.

**DESIGN, SETTING, AND PARTICIPANTS:** Randomized clinical trial of 212 patients allocated to either endovascular revascularization plus supervised exercise or supervised exercise only. Data were collected between May 17, 2010, and February 16, 2013, in the Netherlands at 10 sites. Patients were followed up for 12 months and the data were analyzed according to the intention-to-treat principle.

**INTERVENTIONS:** A combination of endovascular revascularization (selective stenting) plus supervised exercise (n = 106) or supervised exercise only (n = 106).

**MAIN OUTCOMES AND MEASURES:** The primary end point was the difference in maximum treadmill walking distance at 12 months between the groups. Secondary end points included treadmill pain-free walking distance, vascular quality of life (VascuQoL) score (1 [worst outcome] to 7 [best outcome]), and 36-item Short-Form Health Survey (SF-36) domain

scores for physical functioning, physical role functioning, bodily pain, and general health perceptions (0 [severe limitation] to 100 [no limitation]).

**RESULTS:** Endovascular revascularization plus supervised exercise (combination therapy) was associated with significantly greater improvement in maximum walking distance (from 264 m to 1501 m for an improvement of 1237 m) compared with the supervised exercise only group (from 285 m to 1240 m for improvement of 955 m) (mean difference between groups, 282 m; 99% CI, 60-505 m) and in pain-free walking distance (from 117 m to 1237 m for an improvement of 1120 m vs from 135 m to 847 m for improvement of 712 m, respectively) (mean difference, 408 m; 99% CI, 195-622 m). Similarly, the combination therapy group demonstrated significantly greater improvement in the disease-specific VascuQoL score (1.34 [99% CI, 1.04-1.64] in the combination therapy group vs 0.73 [99% CI, 0.43-1.03] in the exercise group; mean difference, 0.62 [99% CI, 0.20-1.03]) and in the score for the SF-36 physical functioning (22.4 [99% CI, 16.3-28.5] vs 12.6 [99% CI, 6.3-18.9], respectively; mean difference, 9.8 [99% CI, 1.4-18.2]). No significant differences were found for the SF-36 domains of physical role functioning, bodily pain, and general health perceptions.

**CONCLUSIONS AND RELEVANCE:** Among patients with intermittent claudication after 1 year of follow-up, a combination therapy of endovascular revascularization followed by supervised exercise resulted in significantly greater improvement in walking distances and health-related quality-of-life scores compared with supervised exercise only.

*Comment in: Erasing Disability in Peripheral Artery Disease: The Role of Endovascular Procedures and Supervised Exercise. [JAMA. 2015]*

*impactfactor:* 35.289

## **Teijink JA**

### **Endovascular Treatment of Ruptured Abdominal Aortic Aneurysms with Hostile Aortic Neck Anatomy**

Broos PP\*, 't Mannelte YW\*, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Sep;50(3):313-9. Epub 2015 May 28

*Voor abstract zie: Chirurgie - Broos PP*

*impactfactor:* 3.490

## **Teijink JA**

### **Gender differences following supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Scheltinga MR, van Sambeek MR\*, Maas AH, Bendermacher BL, Teijink JA\*

J Vasc Surg. 2015 Sep;62(3):681-8

*Voor abstract zie: Chirurgie - Gommans L*

*impactfactor:* 3.021

## **Teijink JA**

### **Performance of the Endurant stent graft in challenging anatomy**

Broos PP\*, Stokmans RA\*, van Sterkenburg SM, Torsello G, Vermassen F, Cuypers PW\*, van Sambeek MR\*, Teijink JA\*

J Vasc Surg. 2015 Aug;62(2):312-8

*Voor abstract zie: Chirurgie - Broos PP*

*impactfactor:* 3.021

## **Teijink JA**

### **Preoperative exercise therapy in lung surgery patients: A systematic review**

Pouwels S\*, Fiddelaers J, Teijink JA\*, Woorst JF\*, Siebenga J, Smeenk FW\*

Respir Med. 2015 Dec;109(12):1495-504. Epub 2015 Aug 15

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: *3.086*

## **Teijink JA**

### **Risk Factors for Proximal Neck Complications After Endovascular Aneurysm Repair Using the Endurant Stentgraft**

Bastos Goncalves F, Hoeks SE, Teijink JA\*, Moll FL, Castro JA, Stolker RJ, Forbes TL, Verhagen HJ

Eur J Vasc Endovasc Surg. 2015 Feb;49(2):156-62. Epub 2014 Nov 7

**OBJECTIVE:** To assess the incidence and risk factors for proximal aneurysm neck related complications with a late generation device for endovascular abdominal aneurysm repair (EVAR).

**METHODS:** Data were retrieved from a prospective registry (Endurant Stent Graft Natural Selection Global Postmarket Registry) involving 79 institutions worldwide. The risk factors tested were age, gender, surgical risk profile, proximal neck length (<10 mm), diameter (>30 mm), supra- and infrarenal angulation (>60° and 75°), mural thrombus/calcification (>50%) and taper (>10%), and AAA diameter (>65 mm). Two neck related composite endpoints were used, for intra-operative (type-1a endoleak, conversion, deployment/retrieval complication or unintentional renal coverage) and post-operative (type-1a endoleak or migration) adverse events. Independent risk factors were identified using multivariable backwards modeling.

**RESULTS:** The study included 1263 patients (mean age 73, 10.3% female) from March 2009 to May 2011. Twenty three (1.8%) intra-operative adverse events occurred. Neck length <10 mm (OR 4.9, 95% CI 1.1-22.6) and neck thrombus/calcification >50% (OR 4.8, 95% CI 1.7-13.5) were risk factors for intra-operative events. The planned 1 year follow up visit was reached for the entire cohort, and the 2 year visit for 431 patients. During this time, 99 (7.8%) events occurred. Female gender (HR 1.9, 95% CI 1.1-3.2), aneurysm diameter >65 mm (HR 2.8, 95% CI 1.9-4.2), and neck length <10 mm (HR 2.8, 95% CI 1.1-6.9) were significant post-operative risk factors. Neck angulation, neck taper, large diameter neck, and presence of thrombus/calcification were not predictors of adverse outcome in this study.

**CONCLUSION:** These results support the adequacy of this device in the face of adverse neck anatomy, and confirm neck length as the most relevant anatomical limitation for EVAR. Additionally, the study confirms the decline in early to mid-term intervention rates with a newer generation device in a large patient sample. Lastly, it suggests that neck related risk factors affect outcome and impact on prognosis in varying degrees.

impactfactor: *3.490*

## **Teijink JA**

### **Safety of supervised exercise therapy in patients with intermittent claudication**

Gommans LN\*, Fokkenrood HJ\*, van Dalen HC\*, Scheltinga MR, Teijink JA\*, Peters RJ

J Vasc Surg. 2015 Feb;61(2):512-518.e2

Voor abstract zie: *Chirurgie - Gommans L*

impactfactor: *3.021*



**Teijink JA**

**Site-specific association between distal aortic pulse wave velocity and peripheral arterial stenosis severity: a prospective cardiovascular magnetic resonance study**

van den Bosch HC\*, Westenberg JJ, Setz-Pels W\*, Wondergem J\*, Wolterbeek R, Duijm LE\*, Teijink JA\*, de Roos A\*

J Cardiovasc Magn Reson. 2015 Jan 20;17(1):2

Voor abstract zie: *Radiologie - Bosch HC van den*

impactfactor: 4.556

**Teijink JA**

**The effect of supervised exercise therapy on physical activity and ambulatory activities in patients with intermittent claudication**

Fokkenrood HJ\*, Lauret GJ, Verhofstad N\*, Bendermacher BL, Scheltinga MR,

Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Feb;49(2):184-91. Epub 2014 Dec 12

Voor abstract zie: *Chirurgie - Fokkenrood HJ*

impactfactor: 3.490

**Teijink JA**

**Vascular complications and surgical interventions after world's largest Q fever outbreak**

Broos PP\*, Hagens JC, Kampschreur LM, Wever PC, Bleeker-Rovers CP, Koning OH, Teijink JA\*, Wegdam-Blans MC\*

J Vasc Surg. 2015 Nov;62(5):1273-80. Epub 2015 Sep 10

Voor abstract zie: *Chirurgie - Broos PP*

impactfactor: 3.021

**Teijink JA**

**Venous Side Branch Ligation as a First Step Treatment for Haemodialysis Access Induced Hand Ischaemia: Effects on Access Flow Volume and Digital Perfusion**

Vaes RH, Wouda R, Teijink JA\*, Scheltinga MR

Eur J Vasc Endovasc Surg. 2015 Dec;50(6):810-4. Epub 2015 Sep 19

OBJECTIVE: Haemodialysis access induced distal ischemia (HAIDI) induced by an autogenous arteriovenous fistula (AVF) is caused by loss of blood pressure somewhere along the arterial blood supply of the arm. In some patients, side branches of the access' venous outflow tract may contribute to this blood pressure loss. Beneficial effects of side branch ligation (SBL) as a first step approach to ischemic symptoms have been reported. However, effects on access flow and AVF function after prolonged follow up are unknown.

MATERIALS AND METHODS: Prior to SBL, HAIDI patients with a brachial artery based AVF were studied using a questionnaire quantifying hand ischemia, digital brachial index (DBI, finger plethysmography), and Duplex analysis. Access flow volume, patency rates, hand perfusion, and complications were determined during a 12 month observation period following SBL.

RESULTS: In 9 years, SBLs were performed in 20 haemodialysis patients, either as a single operative procedure (n = 10) or supplemented (n = 10) with additional surgical techniques during the same procedure (banding, n = 5; basilic vein transposition, n = 4; DRIL, n = 1). Follow up data after 12 months were available in 18 patients. One patient with progressive hand ischemia required access ligation 3 months after SBL. Hand ischemia was attenuated or

abolished in the remaining 17 patients (94% clinical success rate). DBI improved from  $0.51 \pm 0.05$  (pre-operative) to  $0.68 \pm 0.04$  (immediate post-operative) and  $0.83 \pm 0.07$  (at 1 year follow up). One year primary, assisted primary, and secondary patency rates were 67% (12/18), 83% (15/18), and 94% (17/18), respectively, while mean access flows remained acceptable at  $710 \pm 70$  mL/min.

**CONCLUSIONS:** Ligation of non-functional venous side branches of an autogenous brachial artery AVF causing hand ischemia leads to prolonged attenuation of hand ischemia whereas access flow volumes are maintained after 1 year of follow up. Side branch ligation must be considered prior to embarking on more invasive surgery for HAIDI.

*impactfactor:* 3.490

## **Veen AH van der**

### **Wound Infections Following Implant removal below the knee: the effect of antibiotic prophylaxis; the WIFI-trial, a multi-centre randomized controlled trial**

Backes M, Dingemans SA, Schep NW, Bloemers FW, Van Dijkman B, Garssen FP, Haverlag R, Hoogendoorn JM, Joosse P, Mirck B, Postma V, Ritchie E, Roerdink WH, Sintenie JB, Soesman NM, Sosef NL, Twigt BA, Van Veen RN, Van der Veen AH\*, Van Velde R, Vos DI, De Vries MR, Winkelhagen J, Goslings JC, Schepers T

BMC Surg. 2015 Feb 6;15(1):12

**BACKGROUND:** In the Netherlands about 18,000 procedures with implant removal are performed annually following open or closed reduction and fixation of fractures, of which 30-80% concern the foot, ankle and lower leg region. For clean surgical procedures, the rate of postoperative wound infections (POWI) should be less than ~2%. However, rates of 10-12% following implant removal have been reported, specifically after foot, ankle and lower leg fractures. Currently, surgeons individually decide if antibiotics prophylaxis is given, since no guideline exists. This leads to undesirable practice variation. The aim of the study is to assess the (cost-)effectiveness of a single intravenous gift of Cefazolin prior to implant removal following surgical fixation of foot, ankle and/or lower leg fractures.

**METHODS:** This is a double-blind randomized controlled trial in patients scheduled for implant removal following a foot, ankle or lower leg fracture. Primary outcome is a POWI within 30 days after implant removal. Secondary outcomes are quality of life, functional outcome and costs at 30 days and 6 months after implant removal. With 2 x 250 patients a decrease in POWI rate from 10% to 3.3% (expected rate in clean-contaminated elective orthopaedic trauma procedures) can be detected (Power=?80%, 2-sided alpha=?5%, including 15% lost to follow up).

**DISCUSSION:** If administration of prophylactic antibiotics prior to implant removal reduces the infectious complication rate, this will offer a strong argument to adopt this as standard practice of care. This will consequently lead to less physical and social disabilities and health care use. A preliminary, conservative estimation suggests yearly cost savings in the Netherlands of € 3.5 million per year.

*impactfactor:* 1.397

## **Verhofstad N**

### **Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial**

Fakhry F, Spronk S, van der Laan L, Wever JJ, Teijink JA\*, Hoffmann WH, Smits TM, van Brussel JP, Stultiens GN, Derom A, den Hoed PT, Ho GH, van Dijk LC, Verhofstad N\*, Orsini M, van Petersen A, Woltman K, Hulst , van Sambeek MR\*, Rizopoulos D, Rouwet EV, Hunink MG

JAMA. 2015 Nov 10;314(18):1936-44

Voor abstract zie: *Chirurgie - Teijink JA*

impactfactor: 35.289

## **Verhofstad N**

### **The effect of supervised exercise therapy on physical activity and ambulatory activities in patients with intermittent claudication**

Fokkenrood HJ\*, Lauret GJ, Verhofstad N\*, Bendermacher BL, Scheltinga MR, Teijink JA\*

Eur J Vasc Endovasc Surg. 2015 Feb;49(2):184-91. Epub 2014 Dec 12

Voor abstract zie: *Chirurgie - Fokkenrood HJ*

impactfactor: 3.490

## **Vermeer TA**

### **Does extended surgery influence health-related quality of life in patients with rectal cancer?**

Orsini RG\*, Vermeer TA\*, Traa MJ, Nieuwenhuijzen GA\*, de Hingh IH\*, Rutten HJ\*

Dis Colon Rectum. 2015 Feb;58(2):179-85

Voor abstract zie: *Chirurgie - Orsini RG*

impactfactor: 2.615

## **Vermeer TA**

### **Effect of preoperative treatment strategies on the outcome of patients with clinical T3, non-metastasized rectal cancer: A comparison between Dutch and Canadian expert centers**

Breugom AJ, Vermeer TA\*, van den Broek CB, Vuong T, Bastiaannet E, Azoulay L, Dekkers OM, Niazi T, van den Berg HA\*, Rutten HJ\*, van de Velde CJ

Eur J Surg Oncol. 2015 Aug;41(8):1039-44

AIM: High-dose-rate brachytherapy (HDRBT) appears to be associated with less treatment-related toxicity compared with external beam radiotherapy in patients with rectal cancer. The present study compared the effect of preoperative treatment strategies on overall survival, cancer-specific deaths, and local recurrences between a Dutch and Canadian expert center with different preoperative treatment strategies.

PATIENTS AND METHODS: We included 145 Dutch and 141 Canadian patients with cT3, non-metastasized rectal cancer. All patients from Canada were preoperatively treated with HDRBT. The preoperative treatment strategy for Dutch patients consisted of either no preoperative treatment, short-course radiotherapy, or chemoradiotherapy. Cox proportional hazards models were used to estimate hazard ratios (HR) with 95% confidence intervals (CIs) comparing overall survival. We adjusted for age, cN stage, (y)pT stage, comorbidity, and type

of surgery. Primary endpoint was overall survival. Secondary endpoints were cancer-specific deaths and local recurrences.

RESULTS: Five-year overall survival was 70.9% (95% CI 62.6%-77.7%) in Dutch patients compared with 86.9% (80.1%-91.6%) in Canadian patients, resulting in an adjusted HR of 0.70 (95% CI 0.39-1.26;  $p = 0.233$ ). Of 145 Dutch patients, 6.9% (95% CI 2.8%-11.0%) had a local recurrence and 17.9% (95% CI 11.7%-24.2%) patients died of rectal cancer, compared with 4.3% (95% CI 0.9%-7.5%) local recurrences and 10.6% (95% CI 5.5%-15.7%) rectal cancer deaths out of 141 Canadian patients.

CONCLUSION: We did not detect statistically significant differences in overall survival between a Dutch and Canadian expert center with different treatment strategies. This finding needs to be further investigated in a randomized controlled trial.

impactfactor: 3.009

## Verwaal VJ

### Evolution of Treatments for Peritoneal Metastases From Colorectal Cancer

O'Dwyer S, Verwaal VJ, Sugarbaker PH

J Clin Oncol. 2015 Jun 20;33(18):2122-3

Geen abstract beschikbaar

impactfactor: 18.428

## Verwaal VJ

### Peritoneal metastases from small bowel cancer: Results of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in The Netherlands

van Oudheusden TR\*, Lemmens VE, Braam HJ, van Ramshorst B, Meijerink J, te Velde EA, Mehta AM, Verwaal VJ<sup>∞</sup>, de Hingh IH\*.

Surgery. 2015 Jun;157(6):1023-7. Epub 2015 Mar 25

<sup>∞</sup> = Ten tijde van publicatie werkzaam bij: Department of Surgical Oncology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, The Netherlands.

Voor abstract zie: Chirurgie - Oudheusden TR van

impactfactor: 3.380

## Verwaal VJ

### [Peritonitis carcinomatosa from colorectal carcinoma: new treatment options] -

### Peritonitis carcinomatosa van colorectaal carcinoom : nieuwe behandel mogelijkheden

Verwaal VJ\*, De Hingh IH\*, Boot H

Ned Tijdschr Geneesk. 2015;159:A9319

Peritonitis carcinomatosa occurs in 10% of patients with colorectal carcinoma.- Compared with patients with lung and liver metastases, survival in patients with peritonitis carcinomatosa is worse if treated with systemic chemotherapy. However, treatment with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) offers longer survival than systemic chemotherapy.- A Dutch registration study shows that the 3- and 5-year survival of patients treated with cytoreductive surgery and HIPEC had a 3-year survival of 46% and a 5-year survival of 31%.- Mortality and morbidity have dropped greatly due to standardisation of the intervention in accordance with the Dutch protocol.

impactfactor: --

## Verwaal VJ

### **Stability of oxaliplatin in chloride-containing carrier solutions used in hyperthermic intraperitoneal chemotherapy**

Mehta AM, Van den Hoven JM, Rosing H, Hillebrand MJ, Nuijen B, Huitema AD, Beijnen JH, Verwaal VJ\*

Int J Pharm. 2015 Feb 1;479(1):23-7

**PURPOSE:** Oxaliplatin is increasingly becoming the chemotherapeutic drug of choice for the treatment of peritoneal malignancies using cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Oxaliplatin is unstable in chloride-containing media, resulting in the use of 5% dextrose as the carrier solution in these procedures. Exposure of the peritoneum to 5% dextrose during perfusion times varying from 30 min to 90 min is associated with serious hyperglycemias and electrolyte disturbances. This can result in significant postoperative morbidity and mortality. In order to find out whether safer, chloride-containing carrier solutions can be used, we report the results of in-vitro analysis of oxaliplatin stability in both chloride-containing and chloride-deficient carrier solutions and discuss the implications for oxaliplatin-based CRS-HIPEC procedures.

**METHODS:** 5 mg of oxaliplatin was added to 50 mL of various carrier solutions at 42 °C: 5% dextrose, 0.9% sodium chloride, Ringer lactate, Dianeal(®) PD4 glucose 1.36% solution for peritoneal dialysis and 0.14 M sterile phosphate buffer pH 7.4. Samples were collected at standardized intervals and oxaliplatin concentration was determined using a stability indicating high-performance liquid chromatographic method, coupled to an UV detector (HPLC-UV); oxaliplatin degradation products were identified using HPLC-mass spectrometry.

**RESULTS:** In 5% dextrose, oxaliplatin concentration remained stable over a 2-hour period. Increasing chloride concentrations were associated with increasing degradation rates; however, this degradation was limited to <10% degradation after 30 min (the standard peritoneal perfusion time in most clinical CRS-HIPEC protocols) and <20% degradation after 120 min at 42 °C. In addition, oxaliplatin degradation was associated with the formation of its active drug form [Pt(dach)Cl<sub>2</sub>].

**CONCLUSIONS:** The use of chloride-containing carrier solutions for oxaliplatin does not relevantly affect its concentrations under the tested in-vitro conditions. Chloride seems to promote formation of the active cytotoxic drug form of oxaliplatin and therefore could enhance its cytotoxic effect. These data show that more physiological, chloride-containing carrier solutions can be used safely and effectively as a medium for oxaliplatin in CRS-HIPEC procedures.

*impactfactor:* 3.650

## Verwaal VJ

### **The colon shuffle: A modified urinary diversion**

Meijer RP, Mertens LS, Meinhardt W, Verwaal VJ<sup>∞</sup>, Dik P, Horenblas S

Eur J Surg Oncol. 2015 Sep;41(9):1264-8

**AIM:** To assess the results of a urinary diversion in patients who already have a colostomy or simultaneously require a (rectum) colon resection. The diversion is created from the distal part of the transected colon with a simultaneously created new colostomy contra-laterally (if necessary). This procedure is known in our institute as the 'colon shuffle'.

**MATERIALS AND METHODS:** All patients who underwent a colon shuffle in the period of 2003 and 2013 in our institute (Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital) were identified. Comorbidity was scored using the Charlson comorbidity index. Local or systemic treatment prior to surgery was reported (e.g. external beam radiotherapy,

systemic chemotherapy). Surgical complications were reported according to the Clavien-Dindo classification.

**RESULTS:** Twenty-one patients (14 male; 7 female) underwent a colon shuffle procedure in our institute, with a mean age of 61.5 years. The majority (90.4%) of these patients had been subjected to radiotherapy on the pelvic region in the past. Although short-term complications (<30 days) were seen in 52.4% of these patients, major complications such as anastomotic leakage of the bowel and fecal peritonitis were not seen in this high-risk group of patients.

**CONCLUSION:** The colon shuffle offers an elegant solution for patients who require a urinary diversion simultaneously with a colostomy or for patients who already have a colostomy from previous surgery.

∞ = Ten tijde van publicatie werkzaam bij: Department of Surgery, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

impactfactor: 3.009

## **Vugts G**

### **Contralateral lymph node recurrence in breast cancer: Regional event rather than distant metastatic disease. A systematic review of the literature**

Moosdorff M, Vugts G\*, Maaskant-Braat AJ\*, Strobbe LJ, Voogd AC, Smidt ML, Nieuwenhuijzen GA\*

Eur J Surg Oncol. 2015 Sep;41(9):1128-36

**AIMS:** After treatment for breast cancer, some patients experience a contralateral lymph node recurrence (CLNR). Traditionally, contralateral nodes are considered a distant site. However, aberrant lymph drainage after previous surgery is common. This might indicate that CLNR is a regional event. This study aimed to review the literature to determine prognosis after CLNR.**METHODS:** PubMed was searched up until July 2014. Articles on CLNR with or without ipsilateral breast tumour recurrence (IBTR), and repeat sentinel node (SN) studies reporting on positive contralateral nodes were included. Exclusion criteria were synchronous contralateral breast cancer and synchronous distant events.

**RESULTS:** 24 articles were included, describing 48 patients. Of these 48, 26 patients had an isolated CLNR, 7 IBTR and clinically detected CLNR, and 15 IBTR with a positive contralateral repeat SN. Isolated CLNR occurred earlier (45.9 months) than IBTR with CLNR (126.6 months,  $p < 0.001$ ) or with a positive contralateral repeat SN (217.2,  $p = 0.02$ ). Surgical treatment was described for 38 patients, and consisted of axillary lymph node dissection for 34 (89.5%). Information on adjuvant therapy was available for 27 patients, 21 (77.8%) received chemotherapy. Follow-up information after CLNR was available for 23 patients (47.9%). Mean follow-up was 50.3 months. Overall survival and disease-free survival were 82.6% [95% CI 67.1-98.1] and 65.2% [45.7-84.7] respectively at last follow-up.

**CONCLUSIONS:** Although observed in a small population, the survival of CLNR is not comparable to distant disease. Most patients received locoregional and systemic treatment suggesting a curative approach. This indicates that CLNR should be regarded as a regional event.

impactfactor: 3.009

## **Vugts G**

### **Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

**PURPOSE:** Repeat sentinel node biopsy (SNB) is an alternative to axillary lymph node dissection (ALND) for axillary staging in recurrent breast cancer. This study was conducted to determine factors associated with technical success of repeat SNB.

**METHODS:** A total of 536 patients with locally recurrent nonmetastatic breast cancer underwent lymphatic mapping (LM) and repeat SNB in 29 Dutch hospitals.

**RESULTS:** A total of 179 patients previously underwent breast-conserving surgery (BCS) with SNB, 262 patients BCS with ALND and 61 patients mastectomy, 35 with SNB and 26 with ALND. Another 34 patients underwent breast surgery without axillary interventions. A repeat sentinel node (SN) was identified in 333 patients (62.1 %) and was successfully removed in 235 (53.5 %). The overall repeat SN identification rate was 62.1 %, varying from 35 to 100 % in the participating hospitals. Previous radiotherapy of the breast [odds ratio (OR) 0.16; 95 % confidence interval (CI) 0.03-0.84], subareolar tracer injection (OR 0.34; 95 % CI 0.16-0.73), and a 2-day LM protocol (OR 0.57; 95 % CI 0.33-0.97) after previous BCS were independently associated with failure of SN identification. Injection of a larger amount of tracer (>180 MBq) led to a higher identification rate (OR 4.40; 95 % CI 1.45-13.32).

**CONCLUSIONS:** Repeat SNB is a technically feasible procedure for axillary staging in recurrent breast cancer patients. Previous radiotherapy appears to be associated with failure of SN identification. Injection with a larger amount of tracer (>180 MBq) leads to a higher identification rate; subareolar injection and a 2-day LM protocol after previous BCS appear to be less adequate.

*impactfactor:* 3.930

## **Vugts G**

### **Repeat sentinel node biopsy should be considered in patients with locally recurrent breast cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Luiten EJ, Rutgers EJ, Rutten HJ\*, Roumen RM, Nieuwenhuijzen GA\*

Breast Cancer Res Treat. 2015 Oct;153(3):549-56

Most patients with locally recurrent breast cancer undergo axillary lymph node dissection (ALND). However, repeat sentinel node biopsy (SNB) could provide regional nodal staging and obviate the need for standard ALND. The Sentinel Node and Recurrent Breast Cancer (SNARB) study is a Dutch nationwide registration study conducted to determine feasibility, aberrant drainage rates, and clinical consequences of repeat SNB. A total of 536 patients with locally recurrent non-metastatic breast cancer underwent lymphatic mapping and repeat SNB in 29 Dutch hospitals. A repeat sentinel node (SN) was identified in 333 of 536 patients (62.1 %) and surgically harvested in 287 patients (53.5 %). Aberrant lymph drainage was observed in 180 (54.1 %) of the 333 patients, more often after previous ALND (81.9 %) than SNB (28.4 %;  $P < 0.001$ ). In 230 patients (80.1 %), the retrieved SN was tumor negative; 17 SNs (5.9 %) contained a micrometastasis and 29 (10.1 %) a macrometastasis. Confirmation ALND in 31 repeat SN-negative patients revealed a macrometastasis in two patients (6.5 %). The negative predictive value (NPV) of repeat SNB was 93.6 %, and ALND was omitted in 109 of the 248 patients (44.0 %) with a negative repeat SN. In 29 of the 44

patients (63.0 %) with a positive SN, adjuvant treatment plans were altered based on the repeat SNB. Repeat SNB is a feasible procedure with a high NPV, leading to a change in management in a substantial proportion of patients. Therefore, repeat SNB should replace routine ALND and serve as the standard of care in recurrent breast cancer.

*impactfactor:* 3.940

## **Weijts TJ**

### **Diagnostic value of drain amylase for detecting intrathoracic leakage after esophagectomy**

Berkelmans GH\*, Kouwenhoven EA, Smeets BJ\*, Weijts TJ\*, Silva Corten LC, van Det MJ, Nieuwenhuijzen GA\*, Luyer MD\*

World J Gastroenterol. 2015 Aug 14;21(30):9118-25

**AIM:** To investigate the value of elevated drain amylase concentrations for detecting anastomotic leakage (AL) after minimally invasive Ivor-Lewis esophagectomy (MI-ILE).

**METHODS:** This was a retrospective analysis of prospectively collected data in two hospitals in the Netherlands. Consecutive patients undergoing MI-ILE were included. A Jackson-Pratt drain next to the dorsal side of the anastomosis and bilateral chest drains were placed at the end of the thorascopic procedure. Amylase levels in drain fluid were determined in all patients during at least the first four postoperative days. Contrast computed tomography scans and/or endoscopic imaging were performed in cases of a clinically suspected AL. Anastomotic leakage was defined as any sign of leakage of the esophago-gastric anastomosis on endoscopy, re-operation, radiographic investigations, post mortal examination or when gastro-intestinal contents were found in drain fluid. Receiver operator characteristic curves were used to determine the cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value, risk ratio and overall test accuracy were calculated for elevated drain amylase concentrations.

**RESULTS:** A total of 89 patients were included between March 2013 and August 2014. No differences in group characteristics were observed between patients with and without AL, except for age. Patients with AL were older than were patients without AL ( $P = 0.01$ ). One patient (1.1%) without AL died within 30 d after surgery due to pneumonia and acute respiratory distress syndrome. Anastomotic leakage that required any intervention occurred in 15 patients (16.9%). Patients with proven anastomotic leakage had higher drain amylase levels than patients without anastomotic leakage [median 384 IU/L (IQR 34-6263) vs median 37 IU/L (IQR 26-66),  $P = 0.003$ ]. Optimal cut-off values on postoperative days 1, 2, and 3 were 350 IU/L, 200 IU/L and 160 IU/L, respectively. An elevated amylase level was found in 9 of the 15 patients with AL. Five of these 9 patients had early elevations of their amylase levels, with a median of 2 d (IQR 2-5) before signs and symptoms occurred.

**CONCLUSION:** Measurement of drain amylase levels is an inexpensive and easy tool that may be used to screen for anastomotic leakage soon after MI-ILE. However, clinical validation of this marker is necessary.

*impactfactor:* 2.369

## **Weijts TJ**

### **Leaving a Mobilized Thoracic Esophagus In Situ When Incurable Cancer Is Discovered Intraoperatively**

Weijts TJ\*, Toxopeus EL, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, Schraepen MC, Sosef MN, Wijnhoven BP, Schets IR, Bleys RL, van Hillegersberg R

Ann Thorac Surg. 2015 Feb;99(2):490-4. Epub 2014 Dec 10



**BACKGROUND:** Occasionally incurable cancer is encountered after completion of the thoracic (first) phase of a three-phase esophagectomy. The outcome of aborting the operation at this stage, leaving the mobilized thoracic esophagus in situ, is unknown.

**METHODS:** A multicenter retrospective analysis was performed of patients in whom a completely mobilized thoracic esophagus was left in situ when incurable disease was discovered intraoperatively. The occurrence of esophageal necrosis or perforation, mortality, and all other adverse events were recorded and graded by severity.

**RESULTS:** Some 18 patients were included. The median admission time was 9 days. All patients had resumed oral intake at discharge, except for 1 patient who was fed through a nasojejunal tube. After the operation, the median overall survival was 2.9 months. Postoperatively, 7 patients (39%) experienced major surgical adverse events, and 11 patients (61%) had no or only minor adverse events. Major adverse events were associated with the patient's death in 6 patients (33%), within 5 to 34 days postoperatively. Esophageal perforation or ischemia developed in 4 patients (22%) and 1 patient (6%), respectively. No predictive factors could be identified.

**CONCLUSIONS:** Leaving a completely mobilized thoracic esophagus in situ when incurable cancer was discovered intraoperatively was a successful strategy in more than half of the patients. However, one third experienced major adverse events leading to mortality.

*impactfactor:* 3.849

## **Weijs TJ**

### **Routes for early enteral nutrition after esophagectomy. A systematic review**

Weijs TJ\*, Berkelmans GH\*, Nieuwenhuijzen GA\*, Ruurda JP, Hillegersberg RV, Soeters PB, Luyer MD\*

Clin Nutr. 2015 Feb;34(1):1-6. Epub 2014 Aug 1

**BACKGROUND:** Early enteral feeding following surgery can be given orally, via a jejunostomy or via a nasojejunal tube. However, the best feeding route following esophagectomy is unclear.

**OBJECTIVES:** To determine the best route for enteral nutrition following esophagectomy regarding anastomotic leakage, pneumonia, percentage meeting the nutritional requirements, weight loss, complications of tube feeding, mortality, patient satisfaction and length of hospital stay.

**DESIGN:** A systematic literature review following PRISMA and MOOSE guidelines.

**RESULTS:** There were 17 eligible studies on early oral intake, jejunostomy or nasojejunal tube feeding. Only one nonrandomized study (N = 133) investigated early oral feeding specifically following esophagectomy. Early oral feeding was associated with a reduced length of stay with delayed oral feeding, without increased complication rates. Postoperative nasojejunal tube feeding was not significantly different from jejunostomy tube feeding regarding complications or catheter efficacy in the only randomised trial on this subject (N = 150). Jejunostomy tube feeding outcome was reported in 12 non-comparative studies (N = 3293). It was effective in meeting short-term nutritional requirements, but major tube-related complications necessitated relaparotomy in 0-2.9% of patients. In three non-comparative studies (N = 135) on nasojejunal tube feeding only minor complications were reported, data on nutritional outcome was lacking. Data on patient satisfaction and long-term nutritional outcome were not found for any of the feeding routes investigated.

**CONCLUSION:** It is unclear what the best route for early enteral nutrition is after esophagectomy. Especially data regarding early oral intake are scarce, and phase 2 trials are needed for further investigation.

*impactfactor:* 4.476

**Weijs TJ**

**Topography and extent of pulmonary vagus nerve supply with respect to transthoracic oesophagectomy**

Weijs TJ\*, Ruurda JP, Luyer MD\*, Nieuwenhuijzen GA\*, van Hillegersberg R, Bleys RL  
J Anat. 2015 Oct;227(4):431-9

Pulmonary complications are frequently observed after transthoracic oesophagectomy. These complications may be reduced by sparing the vagus nerve branches to the lung. However, current descriptions of the regional anatomy are insufficient. Therefore, we aimed to provide a highly detailed description of the course of the pulmonary vagus nerve branches. In six fixed adult human cadavers, bilateral microscopic dissection of the vagus nerve branches to the lungs was performed. The level of branching and the number, calibre and distribution of nerve branches were described. Nerve fibres were identified using neurofilament immunohistochemistry, and the nerve calibre was measured using computerized image analysis. Both lungs were supplied by a predominant posterior and a smaller anterior nerve plexus. The right lung was supplied by 13 (10-18) posterior and 3 (2-3) anterior branches containing 77% (62-100%) and 23% (0-38%) of the lung nerve supply, respectively. The left lung was supplied by a median of 12 (8-13) posterior and 3 (2-4) anterior branches containing 74% (60-84%) and 26% (16-40%) of the left lung nerve supply, respectively. During transthoracic oesophagectomy with en bloc lymphadenectomy and transection of the vagus nerves at the level of the azygos vein, 68-100% of the right lung nerve supply and 86-100% of the inferior left lung lobe nerve supply were severed. When vagotomy was performed distally to the last large pulmonary branch, 0-8% and 0-13% of the nerve branches to the right middle/inferior lobes and left inferior lobe, respectively, were lost. In conclusion, this study provides a detailed description of the extensive pulmonary nerve supply provided by the vagus nerves. During oesophagectomy, extensive mediastinal lymphadenectomy denervates the lung to a great extent; however, this can be prevented by performing the vagotomy distal to the caudalmost large pulmonary branch. Further research is required to determine the feasibility of sparing the pulmonary vagus nerve branches without compromising the completeness of lymphadenectomy.

*impactfactor:* 2.097

**Wezenbeek MR van**

**Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*

Obes Surg. 2015 Aug;25(8):1425-30

**BACKGROUND:** The vertical banded gastroplasty (VBG) used to be a common restrictive bariatric procedure but has been abandoned by many due to a high failure rate, a high incidence of long-term complications, and the newer adjustable gastric band (AGB) and sleeve. However, potential favorable long-term results and the upcoming banded gastric bypass, with a similar mechanical outlet restriction and control of the pouch size, renewed our interest in the VBG. Therefore, we investigated the long-term outcome of primary VBG at the Catharina Hospital in the Netherlands.

**METHODS:** Patients that underwent a primary VBG between 1998 and 2008 were included. Patients' characteristics, operative details, evolution on weight and comorbidities, complications, and outcome of revisions were reviewed.

**RESULTS:** A total of 392 patients (80 % female) were reviewed with a mean age of 40±7.9 years and body mass index of 44±7.5 kg/m<sup>2</sup>. Mean follow-up after VBG was 66±7.50 months and showed a mean excess weight loss (EWL) of 53±7.27 % and comorbidity

reduction of 54 %. One hundred fifty-two patients (39 %) out of 227 patients (58 %) with long-term complaints underwent revisional surgery. Main reasons for revision were weight regain and vomiting/food intolerance. Analysis before revision showed an outlet dilatation (17 %), pouch dilatation (16 %), and outlet stenosis (10 %). After revision, an additional EWL of 23 % and 33 % further reduction in comorbidities was seen.

CONCLUSIONS: Primary VBG has an acceptable EWL of 53 % and 55 % of comorbidities were improved. However, the high complication rate, often necessitating revision, underlines the limits of this procedure.

*impactfactor:* 3.747

## **Zoete JP de**

### **Long-Term Results of Primary Vertical Banded Gastroplasty**

van Wezenbeek MR\*, Smulders JF\*, de Zoete JP\*, Luyer MD\*, van Montfort G\*, Nienhuijs SW\*

Obes Surg. 2015 Aug;25(8):1425-30

Voor abstract zie: *Chirurgie - Wezenbeek MR van*

*impactfactor:* 3.747

\* = Werkzaam in het Catharina Ziekenhuis

## **Dermatologie**

**Kelleners - Smeets N**

**Epidermal Cyst Formation and Hyperkeratosis in a Patient Treated with Vismodegib for Locally Advanced Basal Cell Carcinoma**

Reinders MG, Brinkhuizen T, Soetekouw PM, Kelleners-Smeets NW\*, Abdul Hamid MA, Mosterd K\*

Acta Derm Venereol. 2015 May;95(5):618-9

*Geen abstract beschikbaar*

*impactfactor: 3.025*

**Kelleners - Smeets N**

**Photodynamic Therapy in Bowen's Disease: Influence of Histological Features and Clinical Characteristics on Its Success**

Westers-Attema A, Lohman BG, van den Heijkant F, Nelemans PJ, Winnepenninckx VJ, Kelleners-Smeets NW\*, Mosterd K\*

Dermatology. 2015;230(1):55-61. Epub 2014 Nov 13

**BACKGROUND:** In Bowen's disease (BD) there is no consensus on optimal treatment. Photodynamic therapy (PDT) is an effective non-invasive treatment modality for BD with excellent cosmetic results.

**OBJECTIVE:** This retrospective study examines whether clinical and histological features of BD impact PDT response.

**METHODS:** Patients with previously untreated BD from 2002 until 2007 were identified at the Maastricht University Medical Centre. Patients treated with PDT were included. All histological slides were re-examined.

**RESULTS:** During the study period 98 tumours were treated with PDT. In univariate analysis severe atypia and higher age were associated with decreased probability of clinical clearance. Higher age was also associated with an increased risk of recurrence. In multivariate analysis severe atypia remained the only independent risk factor for therapy failure.

**CONCLUSION:** In patients with BD, severe atypia and higher age are associated with an increased risk of treatment failure after PDT.

*impactfactor: 1.569*

**Kelleners - Smeets N**

**Photodynamic therapy versus topical imiquimod for treatment of superficial basal cell carcinoma: a subgroup analysis within a non-inferiority randomised controlled trial**

Roozeboom MH, Nelemans PJ, Mosterd K\*, Steijlen PM, Arits AH, Kelleners-Smeets NW\*

Br J Dermatol. 2015 Mar;172(3):739-45. Epub 2014 Nov 30

*voor abstract zie: Dermatologie – Mosterd K*

*impactfactor: 4.275*

### **Kelleners - Smeets N**

#### **Preoperative Management of Antithrombotic Medication in Mohs Micrographic Surgery**

Liu X, Lammers L, Nelemans PJ, Mosterd K\*, Kelleners-Smeets NW\*

Acta Derm Venereol. 2015 Oct 5;95(7):845-847

*Geen abstract beschikbaar*

*impactfactor: 3.025*

### **Kelleners - Smeets N**

#### **Subtyping Basal Cell Carcinoma by Clinical Diagnosis Versus Punch Biopsy**

Roozeboom MH, Kreukels H, Nelemans PJ, Mosterd K\*, Winnepenninckx VJ,

Abdul Hamid MA, de Haas ER, Kelleners-Smeets NW\*

Acta Derm Venereol. 2015 Nov 4;95(8):996-998

*Voor abstract zie: Dermatologie - Mosterd K*

*impactfactor: 3.025*

### **Kelleners - Smeets N**

#### **Tumor thickness and adnexal extension of superficial basal cell carcinoma (sBCC) as determinants of treatment failure for methyaminolevulinate (MAL)-photodynamic therapy (PDT), imiquimod, and 5-fluorouracil (FU)**

Roozeboom MH, van Kleef L, Arits AH, Mosterd K\*, Winnepenninckx VJ, van Marion AM, Nelemans PJ, Kelleners-Smeets NW\*

J Am Acad Dermatol. 2015 Jul;73(1):93-8

**BACKGROUND:** Noninvasive treatments are frequently used in treatment of superficial basal cell carcinoma (sBCC) because of better cosmetic results, lower costs, and less burden on health care services when compared with surgical excision. However, probability of treatment failure is higher after noninvasive therapies and may depend on histologic tumor characteristics.

**OBJECTIVE:** We sought to investigate whether tumor thickness and adnexal extension are determinants of treatment failure in sBCC treated with topical methyaminolevulinate-photodynamic therapy, imiquimod, or 5-fluorouracil.

**METHODS:** Data were derived from a randomized controlled trial on the effectiveness of methyaminolevulinate photodynamic therapy, imiquimod, and 5-fluorouracil for treatment of sBCC (ISRCTN79701845). For tumors with treatment failure (n = 112) and a randomly selected control group of tumors without treatment failure (n = 224) data on tumor thickness and adnexal extension were retrospectively collected. Treatment failure was defined as a clinically and histologically persistent or recurrent tumor within 1-year posttreatment.

**RESULTS:** Tumor thickness of included patients ranged from 0.2 to 1.0 mm. Tumor thickness and adnexal extension of sBCC were not significantly associated with treatment failure of methyaminolevulinate photodynamic therapy, imiquimod, or 5-fluorouracil.

**LIMITATIONS:** Follow-up period of 1 year is a limitation.

**CONCLUSION:** There seems to be no need to determine tumor thickness or adnexal extension in sBCC before treatment.

*impactfactor: 4.449*

**Mosterd K****Epidermal Cyst Formation and Hyperkeratosis in a Patient Treated with Vismodegib for Locally Advanced Basal Cell Carcinoma**

Reinders MG, Brinkhuizen T, Soetekouw PM, Kelleners-Smeets NW\*, Abdul Hamid MA, Mosterd K\*

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*Voor abstract zie: Dermatologie - Kelleners-Smeets NW*

*impactfactor: 1.569*

**Mosterd K****Photodynamic therapy versus topical imiquimod for treatment of superficial basal cell carcinoma: a subgroup analysis within a non-inferiority randomised controlled trial**

Roozeboom MH, Nelemans PJ, Mosterd K\*, Steijlen PM, Arits AH, Kelleners-Smeets

NW\*

Br J Dermatol. 2015 Mar;172(3):739-45. Epub 2014 Nov 30

**BACKGROUND:** A recent non-inferiority randomised controlled trial (RCT) indicated that imiquimod can be considered as superior to methylaminolevulinate photodynamic therapy (MAL-PDT) in treatment of superficial basal cell carcinoma (sBCC). Knowledge of treatment effectiveness in subgroup of patients is of great value in clinical practice to select the most effective treatment for an individual patient with sBCC.

**OBJECTIVES:** To explore whether the relative treatment effect of MAL-PDT and imiquimod is consistent across subgroups defined by patient and tumour characteristics.

**METHODS:** Data were derived from a single-blinded, non-inferiority, multicentre RCT comparing MAL-PDT, topical imiquimod and fluorouracil (ISRCTN79701845). Treatment success was defined as free of tumour-recurrence at 12-months follow-up. Subgroup analyses were performed for subgroups defined by gender, age, tumour location and tumour size.

**RESULTS:** 202 patients received MAL-PDT and 198 received imiquimod. Superiority of imiquimod versus MAL-PDT was observed in subgroups of females, sBCC on the trunk and large tumours with risk differences in favour of imiquimod of 18.4% (95%CI:7.8-29.0%), 21.0% (95%CI:10.9-31.1%), 18.9% (95%CI:7.1-30.7%), respectively. Higher probability of treatment success for imiquimod versus MAL-PDT was consistently found in all other subgroups with exception of sBCC localised on the lower extremities in older patients. In the latter subgroup, the risk difference at the expense of imiquimod was -57.3% (95%CI:-81.7 to -32.9%).

**CONCLUSIONS:** Imiquimod remains the first choice treatment for sBCC in terms of effectiveness. In older patients with sBCC on the lower extremities MAL-PDT might be

preferred. Results should be interpreted carefully as subgroup analyses were exploratory and not driven by prior hypotheses.

*impactfactor:* 4.275

## **Mosterd K**

### **Preoperative Management of Antithrombotic Medication in Mohs Micrographic Surgery**

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*impactfactor:* 3.025

## **Mosterd K**

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*impactfactor:* 3.025

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**METHODS:** Data were derived from a randomized controlled trial on the effectiveness of methylaminolevulinate photodynamic therapy, imiquimod, and 5-fluorouracil for treatment of sBCC (ISRCTN79701845). For tumors with treatment failure (n = 112) and a randomly selected control group of tumors without treatment failure (n = 224) data on tumor thickness and adnexal extension were retrospectively collected. Treatment failure was defined as a clinically and histologically persistent or recurrent tumor within 1-year posttreatment. **RESULTS:** Tumor thickness of included patients ranged from 0.2 to 1.0 mm. Tumor thickness and adnexal extension of sBCC were not significantly associated with treatment failure of methylaminolevulinate photodynamic therapy, imiquimod, or 5-fluorouracil.

**LIMITATIONS:** Follow-up period of 1 year is a limitation.

**CONCLUSION:** There seems to be no need to determine tumor thickness or adnexal extension in sBCC before treatment.

*impactfactor:* 4.449



**Steensel M van**

**Cerebral lipid accumulation in Chanarin-Dorfman Syndrome**

Huigen MC, van der Graaf M, Morava E, Dassel AC, van Steensel MA\*, Seyger MM, Wevers RA, Willemsen MA

Mol Genet Metab. 2015 Jan;114(1):51-4

Chanarin-Dorfman Syndrome (CDS) is caused by a defect in the CGI-58/ABHD5 gene resulting in a deficiency of CGI-58 and in intracellular accumulation of triacylglycerol in skin and liver. Patients are mainly characterized by congenital ichthyosis, but the clinical phenotype is very heterogeneous. Distinct brain involvement has never been described. We present a clinical description of two patients with congenital ichthyosis. On suspicion of Sjögren-Larsson syndrome (SLS) single-voxel 1H-MR spectroscopy of the brain was performed and biochemical testing of fatty aldehyde dehydrogenase (FALDH) to establish this diagnosis gave normal results. Vacuolisation in a peripheral blood smear has led to the CDS suspicion. In both patients the diagnosis CDS was confirmed by ABHD5 mutation analysis. Interestingly, a clear lipid accumulation in the cerebral white matter, cortex and basal ganglia was demonstrated in both CDS-patients. These results demonstrate, for the first time, cerebral involvement in CDS and give new insights in the complex phenotype. Since the clinical implications of this abnormal cerebral lipid accumulation are still unknown, further studies are warranted.

*impactfactor:* 2.625

**Steensel M van**

**Comment on Zhao et al. "Palmoplantar Keratoderma of the Gamborg-Nielsen Type is Caused by Mutations in the SLURP1 Gene and Represents a Variant of Mal de Meleda"**

Nellen RG, Steijlen PM\*, van Geel M, van Steensel MA\*

Acta Derm Venereol. 2015 Nov 4;95(8):1034-1035

*Letter to the editor*

*impactfactor:* 3.025

**Steensel M van**

**Connexins and skin disease: insights into the role of beta connexins in skin homeostasis**

Martin PE, van Steensel M\*

Cell Tissue Res. 2015 Jun;360(3):645-58. Epub 2015 Jan 24

Cell-to-cell communication triggered by connexin channels plays a central role in maintaining epidermal homeostasis. Here, we discuss the role of the beta connexin subgroup, where site-specific mutations in at least 4 of these proteins lead to distinctive non-inflammatory and inflammatory hyperproliferative epidermal disorders. Recent advances in the molecular pathways evoked and correlation with clinical outcome are discussed. The latest data provide increasing evidence that connexins in the epidermis are sensors to environmental stress and that targeting aberrant hemichannel activity holds significant therapeutic potential for inflammatory skin disorders.

*impactfactor:* 3114

**Steensel M van**

**Darier disease: discrete phenotype in a Sinhalese patient with Darier disease**

Nellen RG, Arits AH, van Geel M, Steijlen PM, van Steensel MA\*

J Eur Acad Dermatol Venereol. 2015 Aug;29(8):1641-2. Epub 2014 Jul 1

*geen abstract beschikbaar*

*impactfactor:* 2.826

**Steensel M van**

**Novel KRT83 and KRT86 mutations associated with monilethrix**

van Steensel M\*, Vreeburg M, Urbina MT, López P, Morice-Picard F, van Geel M

Exp Dermatol. 2015 Mar;24(3):222-4.

Monilethrix is an autosomal dominant hair disorder caused by mutations in the hard keratins KRT81, KRT83 and KRT86. The affected hairs are fragile and break easily, leading to scarring alopecia. Follicular hyperkeratosis in the neck and on extensor sides of extremities is a frequently associated finding. The disorder is rare, but probably underreported because its manifestations may be mild. Mutations in KRT81 and KRT86 are the most common. Here, we report new cases from Venezuela, the Netherlands, Belgium and France. The Venezuelan kindred is special for having patients with digenic novel nucleotide changes, a KRT86 mutation associated with monilethrix and a KRT81 variant of unknown clinical significance. In the French and Dutch patients, we found novel KRT86 and KRT83 mutations. Our findings expand the mutational spectrum associated with monilethrix.

*impactfactor:* 3.762

**Steensel M van**

**Novel TGM5 mutations in acral peeling skin syndrome**

van der Velden J, van Geel M, Nellen R, Jonkman M, McGrath J, Nanda A, Sprecher E, van Steensel M\*, McLean W, Cassidy A

Exp Dermatol. 2015 Apr;24(4):285-9

Acral peeling skin syndrome (APSS, MIM #609796) is a rare autosomal recessive disorder characterized by superficial exfoliation and blistering of the volar and dorsal aspects of hands and feet. The level of separation is at the junction of the stratum granulosum and stratum corneum. APSS is caused by mutations in the TGM5 gene encoding transglutaminase-5, which is important for structural integrity of the outermost epidermal layers. The majority of patients originate from Europe and carry a p.(Gly113Cys) mutation in TGM5. In this study we report both European and non-European families carrying other mutations in the TGM5 gene. In 5 patients we found 3 novel mutations: c.1001+2\_1001+3del, c.1171G>A and c.1498C>T. To confirm their pathogenicity we performed functional analyses with a transglutaminase activity assay, determined alternative splicing by reverse transcribed-PCR analysis and used databases and in silico prediction tools.

*impactfactor:* 3.762

**Steijlen P**

**Comment on Zhao et al. "Palmoplantar Keratoderma of the Gamborg-Nielsen Type is Caused by Mutations in the SLURP1 Gene and Represents a Variant of Mal de Meleda**

Nellen RG, Steijlen PM\*, van Geel M, van Steensel MA\*

Acta Derm Venereol. 2015 Nov 4;95(8):1034-1035

*impactfactor:* 3.025

\* = *Werkzaam in het Catharina Ziekenhuis*

## **Fysiotherapie**

**Wit M**

**Aspects of Exercise before or after Bariatric Surgery: A Systematic Review**

Pouwels S\*, Wit M\*, Teijink JA\*, Nienhuijs SW\*

Obes Facts. 2015;8(2):132-46

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: 2.245

\* = Werkzaam in het Catharina Ziekenhuis

## Gynaecologie

## **Boll D**

### **Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial**

Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, Boll D\*, Boss EA, Hermans RH\*, Engelhart KC, Haartsen JE, Pijlman BM, van Loon-Baelemans IE, Mertens HJ, Nolting WE, van Beek JJ, Roukema JA, Zijlstra WP, Kruitwagen RF, van de Poll-Franse LV

J Clin Oncol. 2015 Nov 1;33(31):3550-9

**PURPOSE:** This study was conducted to longitudinally assess the impact of an automatically generated survivorship care plan (SCP) on patient-reported outcomes in routine clinical practice. Primary outcomes were patient satisfaction with information and care. Secondary outcomes included illness perceptions and health care use.

**METHODS:** Twelve hospitals were randomly assigned to SCP care or usual care in a pragmatic, cluster randomized trial. Newly diagnosed patients with endometrial cancer completed questionnaires after diagnosis (n = 221; 75% response), 6 months (n = 158), and 12 months (n = 147). An SCP application was built in the Web-based ROGY (Registration System Oncological Gynecology). By clicking the SCP button, a patient-tailored SCP was generated.

**RESULTS:** In the SCP care arm, 74% of patients received an SCP. They reported receiving more information about their treatment (mean [M] = 57, standard deviation [SD] = 20 v M = 47, SD = 24; P = .03), other services (M = 35, SD = 22 v M = 25, SD = 22; P = .03), and different places of care (M = 27, SD = 25 v M = 23, SD = 26; P = .04) than the usual care arm (scales, 0 to 100). However, there were no differences regarding satisfaction with information or care. Patients in the SCP care arm experienced more symptoms (M = 3.3, SD = 2.0 v M = 2.6, SD = 1.6; P = .03), were more concerned about their illness (M = 4.4, SD = 2.3 v M = 3.9, SD = 2.1; P = .03), were more affected emotionally (M = 4.0, SD = 2.2 v M = 3.7, SD = 2.2; P = .046), and reported more cancer-related contact with their primary care physician (M = 1.8, SD = 2.0 v M = 1.1, SD = 0.9; P = .003) than those in the usual care arm (scale, 1 to 10). These effects did not differ over time.

**CONCLUSION:** The present trial showed no evidence of a benefit of SCPs on satisfaction with information and care. Furthermore, SCPs increased patients' concerns, emotional impact, experienced symptoms, and the amount of cancer-related contact with the primary care physician. Whether this may ultimately lead to more empowered patients should be investigated further.

*impactfactor:* 18.428

## **Dietz V**

### **Prolapse and continence surgery in countries of the Organization for Economic Cooperation and Development in 2012**

Haya N, Baessler K, Christmann-Schmid C, de Tayrac R4, Dietz V\*, Guldberg R, Mascarenhas T, Nussler E, Ballard E, Ankardal M, Boudemaghe T, Wu JM, Maher CF

Am J Obstet Gynecol. 2015 Jun;212(6):755.e1-755.e27. Epub 2015 Feb 25.

**OBJECTIVE:** The purpose of this study was to report the rates and types of pelvic organ prolapse (POP) and female continence surgery performed in member countries of the Organization for Economic Co-operation and Development (OECD) in 2012.

**STUDY DESIGN:** The published health outcome data sources of the 34 OECD countries were contacted for data on POP and female continence interventions from 2010-2012. In nonresponding countries, data were sought from national or insurer databases. Extracted

data were entered into an age-specific International Classification of Disease, edition 10 (ICD-10)-compliant Excel spreadsheet by 2 authors independently in English-speaking countries and a single author in non-English-speaking countries. Data were collated centrally and discrepancies were resolved by mutual agreement.

**RESULTS:** We report on 684,250 POP and 410,352 continence procedures that were performed in 15 OECD countries in 2012. POP procedures (median rate, 1.38/1000 women; range, 0.51-2.55 prolapse procedures/1000 women) were performed 1.8 times more frequently than continence procedures (median rate, 0.75/1000 women; range, 0.46-1.65 continence procedures/1000 women). Repairs of the anterior vaginal compartment represented 54% of POP procedures; posterior repairs represented 43% of the procedures, and apical compartment repairs represented 20% of POP procedures. Median rate of graft usage was 15.7% of anterior vaginal repairs (range, 3.3-25.6%) and 8.5% (range, 3.2-17%) of posterior vaginal repairs. Apical compartment repairs were repaired vaginally at a median rate of 70% (range, 35-95%). Sacral colpopexy represented a median rate of 17% (range, 5-65%) of apical repairs; 61% of sacral colpopexies were performed minimally invasively. Between 2010 and 2012, there was a 3.7% median reduction in transvaginal grafts, a 4.0% reduction in midurethral slings, and a 25% increase in sacral colpopexies that were performed per 1000 women. Midurethral slings represented 82% of female continence surgeries.

**CONCLUSION:** The 5-fold variation in the rate of prolapse interventions within OECD countries needs further evaluation. The significant heterogeneity (>10 times) in the rates at which individual POP procedures are performed indicates a lack of uniformity in the delivery of care to women with POP and demands the development of uniform guidelines for the surgical management of prolapse. In contrast, the midurethral slings were the standard female continence surgery performed throughout OECD countries in 2012.

*impactfactor:* 4.704

## **Hasaart TH**

### **Increased maternal TSH and decreased maternal FT4 are associated with a higher operative delivery rate in low-risk pregnancies: A prospective cohort study**

Monen L, Pop VJ, Hasaart TH\*, Wijnen H, Oei SG, Kuppens SM\*

BMC Pregnancy Childbirth. 2015 Oct 16;15(1):267.

**BACKGROUND:** The increasing number of operative deliveries is a topic of major concern in modern obstetrics. Maternal thyroid function is of known influence on many obstetric parameters. Our objective was to investigate a possible relation between maternal thyroid function, and operative deliveries. Secondary aim was to explore whether thyroid function was related to specific reasons for operative deliveries.

**METHODS:** In this prospective cohort study, low-risk Caucasian women, pregnant of a single cephalic fetus were included. Women with known auto-immune disease, a pre-labour Caesarean section, induction of labour, breech presentation or preterm delivery were excluded. In all trimesters of pregnancy the thyroid function was assessed. Differences in mean TSH and FT4 were assessed using t-test. Mean TSH and FT4 levels for operative deliveries were determined by one way ANOVA. Repeated measurement analyses were performed (ANOVA), adjusting for BMI, partly, maternal age and gestational age at delivery.

**RESULTS:** In total 872 women were included, of which 699 (80.2 %) had a spontaneous delivery. At 36 weeks gestation women who had an operative delivery had a significantly higher mean TSH (1.63mIU/L versus 1.46mIU/L,  $p=0.025$ ) and lower mean FT4 (12.9pmol/L versus 13.3pmol/L,  $p=0.007$ ) compared to women who had a spontaneous delivery. Mean TSH was significantly higher ( $p=0.026$ ) and mean FT4 significantly lower ( $p=0.030$ )



throughout pregnancy for women with an operative delivery due to failure to progress in second stage of labour, compared to women with a spontaneous delivery or operative delivery for other reasons.

**CONCLUSIONS:** Increased TSH and decreased FT4 seem to be associated with more operative vaginal deliveries and Caesarean sections. After adjusting for several confounders the association remained for operative deliveries due to failure to progress in second stage of labour, possibly to be explained by less efficient uterine action.

*impactfactor:* 2.190

## **Hasaart TH**

### **Maternal thyrotropin is independently related to Small for Gestational Age neonates at term**

Monen L\*, Kuppens S\*, Hasaart T\*, Oosterbaan H, Oei S, Wijnen H, Hutton K, Vader H, Pop V

Clin Endocrinol (Oxf). 2015 Feb;82(2):254-9. Epub 2014 Sep 26

*Voor abstract zie:* Gynaecologie - Monen L

*impactfactor:* 3.457

## **Kuijsters N**

### **Hysteroscopische operaties onder sedatie op de polikliniek**

Van Vliet HA\*, Kuijsters N\*, Braam L\*, Schoot BC\*

NTOG 2015; 128: 412-7

*impactfactor:* --

## **Kuppens SM**

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BMC Pregnancy Childbirth. 2015 Oct 16;15(1):267

*Voor abstract zie:* Gynaecologie - Hasaart TH

*impactfactor:* 2.190

## **Kuppens SM**

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Clin Endocrinol (Oxf). 2015 Feb;82(2):254-9. Epub 2014 Sep 26

*Voor abstract zie:* Gynaecologie - Monen L

*impactfactor:* 3.457

## **Maesele N**

### **Pijn na endometriumablatie, het postablatiesyndroom?**

Maesele N\*, van Vliet HA\*, Schoot BC\*

NTOG 2015; 128: 27-31

*impactfactor:* --

**Monen L**

**Maternal thyrotropin is independently related to Small for Gestational Age neonates at term**

Monen L\*, Kuppens S\*, Hasaart T\*, Oosterbaan H, Oei S, Wijnen H, Hutton K, Vader H, Pop V

Clin Endocrinol (Oxf). 2015 Feb;82(2):254-9. Epub 2014 Sep 26

**OBJECTIVE:** Small for gestational age (SGA) newborns constitute still a major cause of perinatal morbidity and mortality. Overt thyroid disease is a known cause of preterm birth and low birth weight but in its untreated condition it is rare today. In the present study we investigated the possible relation between maternal thyroid function assessed in euthyroid women at each trimester and the incidence of term born SGA neonates.

**DESIGN:** A prospective cohort study was performed.

**PATIENTS:** Thyroid function was assessed at 12, 24 and 36 weeks gestation in 1051 healthy Caucasian women who delivered at > 37 weeks gestation.

**MEASUREMENTS:** One-way ANOVA was used to compare mean TSH and FT4 levels between women with SGA neonates and controls. Multiple logistic regression analysis was performed in order to adjust for known risk factors of SGA.

**RESULTS:** Seventy (6.7%) SGA neonates were identified and they were significantly more often born to women with a TSH >97.5th at first and third trimester. Multiple logistic regression analysis showed that smoking (O.R: 4.4, 95% CI: 2.49 - 7.64), pre-eclampsia (O.R.: 2.8, 95% CI: 1.19 - 6.78) and TSH >97.5th percentile (OR 3.3, 95% CI 1.39 - 7.53) were significantly related to SGA. Maternal FT4 levels and TPO-Ab status were not associated with SGA offspring.

**CONCLUSIONS:** Our data show that TSH levels in the upper range of the reference interval at different trimesters (3.0 to 3.29 mIU/L) are independently related to an increased risk of delivering SGA neonates at term.

*impactfactor: 3.457*

**Piek JW**

**Early salpingectomy (Tubectomy) with delayed oophorectomy to improve quality of life as alternative for risk-reducing salpingo-oophorectomy in BRCA1/2 mutation carriers (TUBA study): a prospective non-randomised multicentre study**

Harmsen MG, Arts-de Jong M, Hoogerbrugge N, Maas AH, Prins JB, Bulten J, Teerenstra S, Adang EM, Piek JM\*, van Doorn HC, van Beurden M, Mourits MJ, Zweemer RP, Gaarenstroom KN, Slangen BF, Vos MC, van Lonkhuijzen LR, Massuger LF, Hermens RP, de Hullu JA

BMC Cancer. 2015 Aug 19;15(1):593

**BACKGROUND:** Risk-reducing salpingo-oophorectomy (RRSO) around the age of 40 is currently recommended to BRCA1/2 mutation carriers. This procedure decreases the elevated ovarian cancer risk by 80-96 % but it initiates premature menopause as well. The latter is associated with short-term and long-term morbidity, potentially affecting quality of life (QoL). Based on recent insights into the Fallopian tube as possible site of origin of serous ovarian carcinomas, an alternative preventive strategy has been put forward: early risk-reducing salpingectomy (RRS) and delayed oophorectomy (RRO). However, efficacy and safety of this alternative strategy have to be investigated.

**METHODS:** A multicentre non-randomised trial in 11 Dutch centres for hereditary cancer will be conducted. Eligible patients are premenopausal BRCA1/2 mutation carriers after completing childbearing without (a history of) ovarian carcinoma. Participants choose

between standard RRSO at age 35-40 (BRCA1) or 40-45 (BRCA2) and the alternative strategy (RRS upon completion of childbearing and RRO at age 40-45 (BRCA1) or 45-50 (BRCA2)). Women who opt for RRS but do not want to postpone RRO beyond the currently recommended age are included as well. Primary outcome measure is menopause-related QoL. Secondary outcome measures are ovarian/breast cancer incidence, surgery-related morbidity, histopathology, cardiovascular risk factors and diseases, and cost-effectiveness. Mixed model data analysis will be performed.

DISCUSSION: The exact role of the Fallopian tube in ovarian carcinogenesis is still unclear. It is not expected that further fundamental research will elucidate this role in the near future. Therefore, this clinical trial is essential to investigate RRS with delayed RRO as alternative risk-reducing strategy in order to improve QoL.

*impactfactor:* 3.362

### **Putten HW van der**

#### **Lymphovascular space invasion and the treatment of stage I endometrioid endometrial cancer**

van der Putten LJ, Geels YP, Ezendam NP, van der Putten HW\*, Snijders MP, van de Poll-Franse LV, Pijnenborg JM

Int J Gynecol Cancer. 2015 Jan;25(1):75-80

OBJECTIVES: Treatment of clinical early-stage endometrioid endometrial cancer (EEC) in The Netherlands consists of primary hysterectomy and bilateral salpingo-oophorectomy. Adjuvant radiotherapy is given when 2 or more the following risk factors are present: 60 years or older, grade 3 histology, and 50% or more myometrial invasion. Lymphovascular space invasion (LVSI) is a predictor of poor prognosis and early distant spread. It is unclear whether adjuvant radiotherapy is sufficient in patients with LVSI-positive EEC. METHODS/MATERIALS: Eighty-one patients treated from 1999 until 2011 for stage I LVSI-positive EEC in 11 Dutch hospitals were included. The outcomes of patients with 0 to 1 risk factors were compared with those with 2 to 3 risk factors, and both were compared with the known literature.

RESULTS: Eighteen patients presented with recurrent disease, and 12 of those recurrences had a distant component. Overall and distant recurrence rates were 19.2% and 11.5% in patients with 0 to 1 risk factors followed by observation and 25.5% and 17% in patients with 2 to 3 risk factors who received adjuvant radiotherapy. Only 1 patient with grade 1 disease had a recurrence.

CONCLUSIONS: In stage I LVSI-positive EEC with 0 to 1 risk factors, observation might not be adequate. Moreover, despite adjuvant radiotherapy, a high overall and distant recurrence rate was observed in patients with 2 to 3 risk factors. The use of systemic treatment in these patients, with the exception of patients with grade 1 disease, should be investigated.

*impactfactor:* 1.958

### **Schoot BC**

#### **Hysteroscopische operaties onder sedatie op de polikliniek**

Van Vliet HA\*, Kuijsters N\*, Braam L\*, Schoot BC\*

NTOG 2015; 128: 412-7

*impactfactor:* --

**Schoot BC**

**Pijn na endometriümblatie, het postablatiesyndroom?**

Maesele N\*, van Vliet HA\*, Schoot BC\*

NTOG 2015; 128: 27-31

*impactfactor:* --

**Schoot BC**

**Removal of endometrial polyps: hysteroscopic morcellation vs bipolar resectoscopy, a randomized trial**

Hamerlynck TW\*, Schoot BC\*, van Vliet HA\*, Weyers S J Minim Invasive Gynecol. 2015 Nov-Dec;22(7):1237-43. Epub 2015 Jul 17

**STUDY OBJECTIVE:** To compare hysteroscopic morcellation with bipolar resectoscopy for removal of endometrial polyps, in terms of procedure time, peri- and post-operative adverse events, tissue availability, and short-term effectiveness.

**DESIGN:** Multicenter, open label, randomized controlled trial (Canadian Task Force classification I).

**SETTING:** Day surgery setting of a teaching and a university hospital.

**PATIENTS:** Women with larger (= 1 cm) endometrial polyps.

**INTERVENTIONS:** Hysteroscopic morcellation with the TRUCLEAR 8.0 Tissue Removal System (Smith & Nephew, Inc., Andover (MA), United States) or bipolar resectoscopy with a rigid 8.5 mm bipolar resectoscope (Karl Storz GmbH, Tuttlingen, Germany).

**MEASUREMENTS AND MAIN RESULTS:** Eighty-four women were included in the intention-to-treat analysis. Median operating time was 4.0 min (2.5 - 7.1 min) and 6.0 min (3.8 - 11.7 min) in the hysteroscopic morcellation and resectoscopy group, respectively. Operating time was reduced by 38% (95% CI 5 - 60%,  $p = .028$ ) in the hysteroscopic morcellation group. Procedure time, defined as the sum of the installation and operating time, tended to be less for the hysteroscopic morcellation group (median 9.5 min (7.6 - 12.2 min) versus 12.2 min (8.8 - 16.0 min),  $p = .072$ ). In 3 patients of the resectoscopy group perforation occurred at dilation or hysteroscope (re)introduction resulting in procedure discontinuation or prolongation of the hospital stay. In 1 patient of the hysteroscopic morcellation group perforation occurred at dilation, nevertheless the procedure was successfully completed. Postoperatively, 2 patients of the hysteroscopic morcellation group were diagnosed with a urinary tract infection. Tissue was available for pathology analysis in all patients except for 2 patients of the resectoscopy group in whom the procedure was discontinued due to perforation.

**CONCLUSION:** Hysteroscopic morcellation is a fast, effective and safe alternative to bipolar resectoscopy for removal of endometrial polyps.

*impactfactor:* 1.830

**Slappendel E**

**Is IVF-served two different ways-more cost-effective than IUI with controlled ovarian hyperstimulation?**

Tjon-Kon-Fat RI, Bensdorp AJ, Bossuyt PM, Koks C, Oosterhuis GJ, Hoek A, Hompes P, Broekmans FJ, Verhoeve HR, de Bruin JP, van Golde R, Repping S, Cohlen BJ, Lambers MD, van Bommel PF, Slappendel E\*, Perquin D, Smeenk J, Pelinck MJ, Gianotten J, Hoozemans DA, Maas JW, Groen H, Eijkemans MJ, van der Veen F, Mol BW, van Wely M

Hum Reprod. 2015 Oct;30(10):2331-9. Epub 2015 Aug 12

**STUDY QUESTION:** What is the cost-effectiveness of in vitro fertilization (IVF) with conventional ovarian stimulation, single embryo transfer (SET) and subsequent cryocycles or IVF in a modified natural cycle (MNC) compared with intrauterine insemination with controlled ovarian hyperstimulation (IUI-COH) as a first-line treatment in couples with unexplained subfertility and an unfavourable prognosis on natural conception?.

**SUMMARY ANSWER:** Both IVF strategies are significantly more expensive when compared with IUI-COH, without being significantly more effective. In the comparison between IVF-MNC and IUI-COH, the latter is the dominant strategy. Whether IVF-SET is cost-effective depends on society's willingness to pay for an additional healthy child.

**WHAT IS KNOWN ALREADY:** IUI-COH and IVF, either after conventional ovarian stimulation or in a MNC, are used as first-line treatments for couples with unexplained or mild male subfertility. As IUI-COH is less invasive, this treatment is usually offered before proceeding to IVF. Yet, as conventional IVF with SET may lead to higher pregnancy rates in fewer cycles for a lower multiple pregnancy rate, some have argued to start with IVF instead of IUI-COH. In addition, IVF in the MNC is considered to be a more patient friendly and less costly form of IVF.

**STUDY DESIGN, SIZE, DURATION:** We performed a cost-effectiveness analysis alongside a randomized noninferiority trial. Between January 2009 and February 2012, 602 couples with unexplained infertility and a poor prognosis on natural conception were allocated to three cycles of IVF-SET including frozen embryo transfers, six cycles of IVF-MNC or six cycles of IUI-COH. These couples were followed until 12 months after randomization.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** We collected data on resource use related to treatment, medication and pregnancy from the case report forms. We calculated unit costs from various sources. For each of the three strategies, we calculated the mean costs and effectiveness. Incremental cost-effectiveness ratios (ICER) were calculated for IVF-SET compared with IUI-COH and for IVF-MNC compared with IUI-COH. Nonparametric bootstrap resampling was used to investigate the effect of uncertainty in our estimates.

**MAIN RESULTS AND THE ROLE OF CHANCE:** There were 104 healthy children (52%) born in the IVF-SET group, 83 (43%) the IVF-MNC group and 97 (47%) in the IUI-COH group. The mean costs per couple were €7187 for IVF-SET, €8206 for IVF-MNC and €5070 for IUI-COH. Compared with IUI-COH, the costs for IVF-SET and IVF-MNC were significantly higher (mean differences €2117; 95% CI: €1544-€2657 and €3136, 95% CI: €2519-€3754, respectively). The ICER for IVF-SET compared with IUI-COH was €43 375 for the birth of an additional healthy child. In the comparison of IVF-MNC to IUI-COH, the latter was the dominant strategy, i.e. more effective at lower costs.

**LIMITATIONS, REASONS FOR CAUTION:** We only report on direct health care costs. The present analysis is limited to 12 months.

**WIDER IMPLICATIONS OF THE FINDINGS:** Since we found no evidence in support of offering IVF as a first-line strategy in couples with unexplained and mild subfertility, IUI-COH should remain the treatment of first choice.

*impactfactor:* 4.569

## Slappendel E

### **Prevention of multiple pregnancies in couples with unexplained or mild male subfertility: randomised controlled trial of in vitro fertilisation with single embryo transfer or in vitro fertilisation in modified natural cycle compared with intrauterine insemination with controlled ovarian hyperstimulation**

Bensdorp AJ, Tjon-Kon-Fat RI, Bossuyt PM, Koks CA, Oosterhuis GJ, Hoek A, Hompes PG, Broekmans FJ, Verhoeve HR, de Bruin JP, van Golde R, Repping S, Cohlen BJ, Lambers MD, van Bommel PF, Slappendel E\*, Perquin D, Smeenk JM, Pelinck MJ, Gianotten J, Hoozemans DA, Maas JW, Eijkemans MJ, van der Veen F, Mol BW, van Wely M

BMJ. 2015 Jan 9;350:g7771.

**OBJECTIVES:** To compare the effectiveness of in vitro fertilisation with single embryo transfer or in vitro fertilisation in a modified natural cycle with that of intrauterine insemination with controlled ovarian hyperstimulation in terms of a healthy child. **DESIGN:** Multicentre, open label, three arm, parallel group, randomised controlled non-inferiority trial. **SETTING:** 17 centres in the Netherlands. **PARTICIPANTS:** Couples seeking fertility treatment after at least 12 months of unprotected intercourse, with the female partner aged between 18 and 38 years, an unfavourable prognosis for natural conception, and a diagnosis of unexplained or mild male subfertility. **INTERVENTIONS:** Three cycles of in vitro fertilisation with single embryo transfer (plus subsequent cryocycles), six cycles of in vitro fertilisation in a modified natural cycle, or six cycles of intrauterine insemination with ovarian hyperstimulation within 12 months after randomisation. **MAIN OUTCOME MEASURES:** The primary outcome was birth of a healthy child resulting from a singleton pregnancy conceived within 12 months after randomisation. Secondary outcomes were live birth, clinical pregnancy, ongoing pregnancy, multiple pregnancy, time to pregnancy, complications of pregnancy, and neonatal morbidity and mortality. **RESULTS:** 602 couples were randomly assigned between January 2009 and February 2012; 201 were allocated to in vitro fertilisation with single embryo transfer, 194 to in vitro fertilisation in a modified natural cycle, and 207 to intrauterine insemination with controlled ovarian hyperstimulation. Birth of a healthy child occurred in 104 (52%) couples in the in vitro fertilisation with single embryo transfer group, 83 (43%) in the in vitro fertilisation in a modified natural cycle group, and 97 (47%) in the intrauterine insemination with controlled ovarian hyperstimulation group. This corresponds to a risk, relative to intrauterine insemination with ovarian hyperstimulation, of 1.10 (95% confidence interval 0.91 to 1.34) for in vitro fertilisation with single embryo transfer and 0.91 (0.73 to 1.14) for in vitro fertilisation in a modified natural cycle. These 95% confidence intervals do not extend below the predefined threshold of 0.69 for inferiority. Multiple pregnancy rates per ongoing pregnancy were 6% (7/121) after in vitro fertilisation with single embryo transfer, 5% (5/102) after in vitro fertilisation in a modified natural cycle, and 7% (8/119) after intrauterine insemination with ovarian hyperstimulation (one sided  $P=0.52$  for in vitro fertilisation with single embryo transfer compared with intrauterine insemination with ovarian hyperstimulation; one sided  $P=0.33$  for in vitro fertilisation in a modified natural cycle compared with intrauterine insemination with controlled ovarian hyperstimulation). **CONCLUSIONS:** In vitro fertilisation with single embryo transfer and in vitro fertilisation in a modified natural cycle were non-inferior to intrauterine insemination with controlled ovarian hyperstimulation in terms of the birth of a healthy child and showed comparable, low multiple pregnancy rates.

*impactfactor:* 17.445

**Vandenput, I**

**Pipelle Prospective ENDometrial carcinoma (PIPENDO) study, pre-operative recognition of high risk endometrial carcinoma: a multicentre prospective cohort study**

Visser NC, Bulten J, van der Wurff AA, Boss EA, Bronkhorst CM, Feijen HW, Haartsen JE, van Herk HA, de Kievit IM, Klinkhamer PJ\*, Pijlman BM, Snijders MP, Vandenput I\*, Vos MC, de Wit PE, van de Poll-Franse LV,, Massuger LF, Pijnenborg JM  
BMC Cancer. 2015 Jun 30;15:487

Voor abstract zie: Pamm - Klinkhamer PJ

impactfactor: 3.362

**Vergeldt T**

**Risk factors for pelvic organ prolapse and its recurrence: a systematic review**

Vergeldt TF\*, Weemhoff M, IntHout J, Kluivers KB

Int Urogynecol J. 2015 Nov;26(11):1559-73. Epub 2015 May 13

INTRODUCTION AND HYPOTHESIS: Pelvic organ prolapse (POP) is a common condition with multifactorial etiology. The purpose of this systematic review was to provide an overview of literature on risk factors for POP and POP recurrence. METHODS: PubMed and Embase were searched with "pelvic organ prolapse" combined with "recurrence" and combined with "risk factors," with Medical Subject Headings and Thesaurus terms and text words variations until 4 August 2014, without language or publication date restrictions. Only cohort or cross-sectional studies carried out in western developed countries containing multivariate analyses and with a definition of POP based on anatomical references were included. POP recurrence had to be defined as anatomical recurrence after native tissue repair without mesh. Follow-up after surgery should have been at least 1 year. Articles were excluded if POP was not a separate entity or if it was unclear whether the outcome was primary POP or recurrence. RESULTS: PubMed and Embase revealed 2,988 and 4,449 articles respectively. After preselection, 534 articles were independently evaluated by two researchers, of which 15 met the selection criteria. In 10 articles on primary POP, 30 risk factors were investigated. Parity, vaginal delivery, age, and body mass index (BMI) were significantly associated in at least two articles. In 5 articles on POP recurrence, 29 risk factors were investigated. Only preoperative stage was significantly associated in at least two articles. CONCLUSION: Parity, vaginal delivery, age, and BMI are risk factors for POP and preoperative stage is a risk factor for POP recurrence.

impactfactor: 1.961

**Vliet HA van**

**Hysteroscopische operaties onder sedatie op de polikliniek**

Van Vliet HA\*, Kuijsters N\*, Braam L\*, Schoot BC\*

NTOG 2015; 128: 412-7.

impactfactor: --

**Vliet HA van**

**Immediate postpartum insertion of intrauterine device for contraception**

Lopez LM, Bernholc A, Hubacher D, Stuart G, Van Vliet HA\*

Cochrane Database Syst Rev. 2015 Jun 26;6:CD003036

**BACKGROUND:** Women who want to start intrauterine contraception (IUC) during the postpartum period might benefit from IUC insertion immediately after delivery. Postplacental insertion greatly reduces the risk of subsequent pregnancy and eliminates the need for a return visit to start contraception. Without the option of immediate insertion, many women may never return for services or may adopt less effective contraception.

**OBJECTIVES:** Our aim was to examine the outcomes of IUC insertion immediately after placenta delivery (within 10 minutes), especially when compared with insertion at other postpartum times. We focused on successful IUC placement (insertion), subsequent expulsion, and method use.

**SEARCH METHODS:** We searched for trials until 1 April 2015. Sources included PubMed (MEDLINE), the Cochrane Central Register of Controlled Trials (CENTRAL), POPLINE, Web of Science, EMBASE, LILACS, ClinicalTrials.gov, and ICTRP. For the original review, the authors contacted investigators to identify other trials.

**SELECTION CRITERIA:** We sought randomized controlled trials (RCTs) with at least one treatment arm that involved immediate IUC placement (i.e., within 10 minutes of placenta delivery). Comparison arms could have included early postpartum insertion (from 10 minutes postplacental to hospital discharge) or standard insertion (during a postpartum visit). Trials could also have compared different IUC methods or insertion techniques. Delivery may have been vaginal or cesarean. Primary outcomes were placement (insertion), subsequent expulsion, and method use at study assessment.

**DATA COLLECTION AND ANALYSIS:** For dichotomous outcomes, we used the Mantel-Haenszel odds ratio (OR) with 95% confidence interval (CI). Earlier studies primarily reported results as life-table rates. We aggregated trials in a meta-analysis if they had similar interventions and outcome measures. A sensitivity analysis included studies with moderate or high quality evidence and sufficient outcome data.

**MAIN RESULTS:** We included 15 trials. Seven studies reported from 2010 to 2014 were added to eight from the original 2001 review. Newer trials compared immediate postplacental insertion versus early (10 minutes to 48 hours) or standard insertion (during the postpartum visit). Of four with full reports, three were small trials. The other three studies had conference abstracts. The eight early trials examined immediate insertion of different devices or insertion techniques. Most studies were published in the 1980s, some with limited reporting. Our sensitivity analysis included trials with sufficient outcome data and moderate or high quality evidence. Four newer trials comparing insertion times met the inclusion criteria. Two studies used the levonorgestrel-releasing intrauterine system (LNG-IUS) after vaginal delivery. The other two trials placed IUC after cesarean section; one used the CuT 380A intrauterine device (IUD) and the other used the LNG-IUS. A pilot trial compared immediate insertion versus early or standard insertion. In groups comparing immediate versus early insertion (N = 30), all women had the LNG-IUS inserted. By six months, the groups had the same expulsion rate and did not differ significantly in IUC use. For immediate versus standard insertion, we conducted meta-analyses of four trials. Insertion rates did not differ significantly between study arms. However, the trial from Uganda showed insertion was more likely for the immediate group, although the estimate was imprecise. In the meta-analysis, expulsion by six months was more likely for the immediate group, but the confidence interval was wide (OR 4.89, 95% CI 1.47 to 16.32; participants = 210; studies = 4). IUC use at six months was more likely with immediate insertion than with standard insertion (OR 2.04, 95% CI 1.01 to 4.09; participants = 243; studies = 4). Study arms did not differ in use at 3 or 12 months in individual small trials.

**AUTHORS' CONCLUSIONS:** Recent trials compared different insertion times after vaginal or cesarean delivery. Evidence was limited because studies with full reports generally had small sample sizes. Overall, the quality of evidence was moderate; abstracts and older studies had



limited reporting. Ongoing trials will add to the evidence, although some are small. Trials of adequate power are needed to estimate expulsion rates and side effects. The benefit of effective contraception immediately after delivery may outweigh the disadvantage of increased risk for expulsion. Frequent prenatal visits during the third trimester provide the opportunity to discuss effective contraceptive methods and desired timing for initiation. Clinical follow-up can help detect early expulsion, as can educating women about expulsion signs and symptoms. Update of Immediate post-partum insertion of intrauterine devices. [Cochrane Database Syst Rev. 2010]

*impactfactor:* 6.032

## **Vliet HA van**

### **Pijn na endometriümblatie, het postablatiesyndroom?**

Maesele N\*, van Vliet HA\*, Schoot BC\*

NTOG 2015; 128: 27-31

*impactfactor:* --

## **Vliet HA van**

### **Removal of endometrial polyps: hysteroscopic morcellation vs bipolar resectoscopy, a randomized trial**

Hamerlynck TW\*, Schoot BC\*, van Vliet HA\*, Weyers S

J Minim Invasive Gynecol. 2015 Nov-Dec;22(7):1237-43. Epub 2015 Jul 17

*Voor abstract zie: Gynaecologie - Schoot BC*

*impactfactor:* 1.830

## **Vliet HA van**

### **The HysNiche trial: hysteroscopic resection of uterine caesarean scar defect (niche) in patients with abnormal bleeding, a randomised controlled trial**

Vervoort AJ, Van der Voet LF, Witmer M, Thirkow AL, Radder CM, van Kesteren PJ, Quarero HW, Kuchenbecker WK, Bongers MY, Geomini PM, de Vleeschouwer LH, van Hooft MH, van Vliet HA\*, Veersema S, Renes WB, van Meurs HS1, Bosmans J, Oude Rengerink K, Brölmann HA, Mol BW, Huirne JA

BMC Womens Health. 2015 Nov 12;15(1):103

**BACKGROUND:** A caesarean section (CS) can cause a defect or disruption of the myometrium at the site of the uterine scar, called a niche. In recent years, an association between a niche and postmenstrual spotting after a CS has been demonstrated. Hysteroscopic resection of these niches is thought to reduce spotting and menstrual pain. However, there are no randomised trials assessing the effectiveness of a hysteroscopic niche resection.

**METHODS/DESIGN:** We planned a multicentre randomised trial comparing hysteroscopic niche resection to no intervention. We study women with postmenstrual spotting after a CS and a niche with a residual myometrium of at least 3 mm during sonohysterography. After informed consent is obtained, eligible women will be randomly allocated to hysteroscopic resection of the niche or expectant management for 6 months. The primary outcome is the number of days with postmenstrual spotting during one menstrual cycle 6 months after randomisation. Secondary outcomes are menstrual characteristics, menstruation related pain and experienced discomfort due to spotting or menstrual pain, quality of life, patient satisfaction, sexual function, urological symptoms, medical consultations, medication use, complications, lost productivity and medical costs. Measurements will be performed at

baseline and at 3 and 6 months after randomisation. A cost-effectiveness analysis will be performed from a societal perspective at 6 months after randomisation.

**DISCUSSION:** This trial will provide insight in the (cost)effectiveness of hysteroscopic resection of a niche versus expectant management in women who have postmenstrual spotting and a niche with sufficient residual myometrium to perform a hysteroscopic niche resection.

*impactfactor:* 1.495

## **Wilms FF**

### **Prescribing patterns of antenatal corticosteroids in women with threatened preterm labor**

Wilms FF\*, van Baaren GJ, Vis JY, Oudijk MA, Kwee A, Porath MM, Scheepers HC, Spaanderman ME, Bloemenkamp KW, Bolte AC, Bax CJ, Cornette JM, Duvekot JJ, Nij Bijvank BW, van Eyck J, Franssen MT, Sollie KM, Vandenbussche FP, Woiski MD, van der Post JA, Bossuyt PM, Opmeer BC, Mol BW

Eur J Obstet Gynecol Reprod Biol. 2015 Jun 17;192:47-53

**OBJECTIVE:** To assess the impact of cervical length (CL) measurement and fetal fibronectin testing (fFN) on the clinicians' decision to prescribe antenatal corticosteroids (ACS) to women with symptoms of preterm labor.

**STUDY DESIGN:** This is a secondary analysis of a prospective cohort study including women with symptoms of preterm labor and intact membranes between 24 and 34 weeks' gestation. We compared the proportion prescribed and completed ACS courses, preterm delivery within seven days and median intervals from ACS to delivery in four groups: group 1 CL<10mm, group 2 CL 10-30mm and positive fFN, group 3 CL 10-30mm and negative fFN, group 4 CL>30mm.

**RESULTS:** ACS were prescribed to 63/65 (97%) women in group 1, 176/192 (91%) in group 2, 111/172 women (65%) in group 3 and 55/242 (23%) in group 4. In group 1, 42 (65%) women delivered within seven days, compared to 34 (18%) in group 2, 6 (3%) in group 3 and 3 (1%) in group 4. Median intervals between ACS and delivery were 6 days (IQR 3-61 days), 44 days (IQR 17-69 days), 53 days (IQR 37-77 days) and 66 days (IQR 43-78 days) in group 1, 2, 3 and 4 respectively.

**CONCLUSION:** ACS were prescribed frequently to women with a CL of 10-30mm and a negative fFN test or a CL>30mm. There is room for improvement in the prescription of ACS in these low risk women.

*impactfactor:* 1.695

## **Wilms FF**

### **Risk factors for preterm delivery: do they add to fetal fibronectin testing and cervical length measurement in the prediction of preterm delivery in symptomatic women?**

van Baaren GJ, Bruijn MM2, Vis JY, Wilms FF\*, Oudijk MA, Kwee A, Porath MM Oei G, Scheepers HC, Spaanderman ME, Bloemenkamp KW, Haak MC, Bolte AC, Bax CJ, Cornette JM, Duvekot JJ, Nij Bijvanck BW, van Eijck J, Franssen MT, Sollie KM, Vandenbussche FP, Woiski M, Bossuyt PM, Opmeer BC, Mol BW

Eur J Obstet Gynecol Reprod Biol. 2015 Jun 10;192:79-85

**OBJECTIVE:** To assess whether patient characteristics add to the fetal fibronectin test and cervical length measurement in the prediction of preterm delivery in symptomatic women.

**STUDY DESIGN:** A nationwide prospective cohort study was conducted in all ten perinatal centres in the Netherlands. Women with symptoms of preterm labour between 24 and 34

weeks gestation with intact membranes were invited. In all women qualitative fibronectin testing (0.050µg/mL cut-off) and cervical length measurement were performed. Only singleton pregnancies were included in this analysis. Logistic regression was used to construct two multivariable models to predict spontaneously delivery within 7 days: a model including cervical length and fetal fibronectin as predictors, and an extended model including all potential predictors. The models were internally validated using bootstrapping techniques. Predictive performances were assessed as the area under the receiver operator characteristic curve (AUC) and calibration plots. We compared the models' capability to identify women with a low risk to deliver within 7 days. A risk less than 5%, corresponding to the risk for women with a cervical length of at least 25mm, was considered as low risk. RESULTS: Seventy-three of 600 included women (12%) had delivered spontaneously within 7 days. The extended model included maternal age, parity, previous preterm delivery, vaginal bleeding, C-reactive protein, cervical length, dilatation and fibronectin status. Both models had high discriminative performances (AUC of 0.92 (95% CI 0.88-0.95) and 0.95 (95% CI 0.92-0.97) respectively). Compared to the model with fibronectin and cervical length, our extended model reclassified 38 women (6%) from low risk to high risk and 21 women (4%) from high risk to low risk. Preterm delivery within 7 days occurred once in both the reclassification groups.

CONCLUSION: In women with symptoms of preterm labour before 34 weeks gestation, a model that integrates maternal characteristics, clinical signs and laboratory tests, did not predict delivery within 7 days better than a model with only fibronectin and cervical length.

*impactfactor: 1.695*

**ICMT**

**Cheung A**

**The organizational and clinical impact of integrating bedside equipment to an information system: A systematic literature review of patient data management systems (PDMS)**

Cheung A\*, van Velden FH, Lagerburg V\*, Minderman N

Int J Med Inform. 2015 Mar;84(3):155-165

**OBJECTIVE:** The introduction of an information system integrated to bedside equipment requires significant financial and resource investment; therefore understanding the potential impact is beneficial for decision-makers. However, no systematic literature reviews (SLRs) focus on this topic. This SLR aims to gather evidence on the impact of the aforementioned system, also known as a patient data management system (PDMS) on both organizational and clinical outcomes.

**MATERIALS AND METHODS:** A literature search was performed using the databases Medline/PubMed and CINAHL for English articles published between January 2000 and December 2012. A quality assessment was performed on articles deemed relevant for the SLR.

**RESULTS:** Eighteen articles were included in the SLR. Sixteen articles investigated the impact of a PDMS on the organizational outcomes, comprising descriptive, quantitative and qualitative studies. A PDMS was found to reduce the charting time, increase the time spent on direct patient care and reduce the occurrence of errors. Only two articles investigated the clinical impact of a PDMS. Both reported an improvement in clinical outcomes when a PDMS was integrated with a clinical decision support system (CDSS).

**CONCLUSIONS:** A PDMS has shown to offer many advantages in both the efficiency and the quality of care delivered to the patient. In addition, a PDMS integrated to a CDSS may improve clinical outcomes, although further studies are required for validation.

*impactfactor:* 2.004

\* = Werkzaam in het Catharina Ziekenhuis

## **Intensive Care**

**Bindels AJ****122: Predicting fluid responsiveness in post-cardiac surgery patients**

Meijs L\*, Bindels A\*, Roos A\*, Lima A, Bakker J.

Crit Care Med. 2015 Dec;43(12 Suppl 1):32

*Geen abstract beschikbaar*

*impactfactor:* 6.312

**Bindels AJ****Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

Boer AK\*, Kreeftenberg H\*, Bindels A\*, Roos A\*, Houterman S\*, Korsten E\*, van Dijk-van Berkel M\*

Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

*Geen abstract beschikbaar*

*impactfactor:* --

**Bindels AJ****Cholesterol in the ICU: a cheap and reliable marker for illness severity?**

Kreeftenberg HG\*, Roos AN\*, Bindels AJ\*, Scharnhorst V\*

Neth J Crit Care 2015;20(2):17-20

*Voor abstract zie: Inwendige geneeskunde - Kreeftenberg HG*

*impactfactor:* --

**Bindels AJ****Cholesterol in the ICU: a cheap and reliable marker for illness severity? : case report**

Kreeftenberg HG\*, Roos AN\*, Bindels AJ\*, Scharnhorst V\*

Neth J Crit Care 2015;20(2):7-20

*Voor abstract zie: Inwendige geneeskunde - Kreeftenberg HG*

*impactfactor:* --

**Meijs L****122: Predicting fluid responsiveness in post-cardiac surgery patients**

Meijs L\*, Bindels A\*, Roos A\*, Lima A, Bakker J

Crit Care Med. 2015 Dec;43(12 Suppl 1):32

*Geen abstract beschikbaar*

*impactfactor:* 6.312

**Roos AN****122: Predicting fluid responsiveness in post-cardiac surgery patients**

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*Geen abstract beschikbaar*

*impactfactor:* 6.312

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*geen abstract beschikbaar*

*impactfactor:* --

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Neth J Crit Care 2015;20(2):17-20

*Voor abstract zie: Inwendige geneeskunde - Kreeftenberg HG*

*impactfactor:* --

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Kreeftenberg HG\*, Roos AN\*, Bindels AJ\*, Scharnhorst V\*

Neth J Crit Care 2015;20(2):7-20

*Voor abstract zie: Inwendige geneeskunde - Kreeftenberg HG*

*impactfactor:* --

**Roos AN**

**Iatrogenic anemia/Twenty-five million liters of blood into the sewer: comment**

Coene KL\*, Roos AN\*, Scharnhorst V\*

J Thromb Haemost. 2015 Jun;13(6):1160-1

Comment in Iatrogenic anemia/Twenty-five million liters of blood into the sewer: reply. [J Thromb Haemost. 2015]

Hospital-acquired anemia: the contribution of diagnostic blood loss. [J Thromb Haemost. 2015]

Comment on Twenty-five million liters of blood into the sewer. [J Thromb Haemost. 2014]

Iatrogenic anemia (can it be prevented?). [J Thromb Haemost. 2014]

*impactfactor:* 5.720

\* = Werkzaam in het Catharina Ziekenhuis



## **Inwendige Geneeskunde**

**Aarnoudse AJ**

**Long-term sequelae of severe acute kidney injury in the critically ill patient without comorbidity: a retrospective cohort study.**

Fortrie G, Stads S, Aarnoudse AJ\*, Zietse R, Betjes MG

PLoS One. 2015 Mar 23;10(3):e0121482. eCollection 2015

**BACKGROUND AND OBJECTIVES:** Acute kidney injury (AKI) necessitating renal replacement therapy (RRT) is associated with high mortality and increased risk for end stage renal disease. However, it is unknown if this applies to patients with a preliminary unremarkable medical history. The purpose of this study was to describe overall and renal survival in critically ill patients with AKI necessitating RRT stratified by the presence of comorbidity.

**DESIGN, SETTING, PARTICIPANTS, AND MEASUREMENTS:** A retrospective cohort study was performed, between 1994 and 2010, including all adult critically ill patients with AKI necessitating RRT, stratified by the presence of comorbidity. Logistic regression, survival curve and cox proportional hazards analyses were used to evaluate overall and renal survival. Standardized mortality rate (SMR) analysis was performed to compare long-term survival to the predicted survival in the Dutch population.

**RESULTS:** Of the 1067 patients included only 96(9.0%) had no comorbidity. Hospital mortality was 56.6% versus 43.8% in patients with and without comorbidity, respectively. In those who survived hospitalization 10-year survival was 45.0% and 86.0%, respectively. Adjusted for age, sex and year of treatment, absence of comorbidity was not associated with hospital mortality (OR=0.74, 95%-CI=0.47-1.15), while absence of comorbidity was associated with better long-term survival (adjusted HR=0.28, 95%-CI = 0.14-0.58). Compared to the Dutch population, patients without comorbidity had a similar mortality risk (SMR=1.6, 95%-CI=0.7-3.2), while this was increased in patients with comorbidity (SMR=4.8, 95%-CI=4.1-5.5). Regarding chronic dialysis dependency, 10-year renal survival rates were 76.0% and 92.9% in patients with and without comorbidity, respectively. Absence of comorbidity was associated with better renal survival (adjusted HR=0.24, 95%-CI=0.07-0.76).

**CONCLUSIONS:** While hospital mortality remains excessively high, the absence of comorbidity in critically ill patients with RRT-requiring AKI is associated with a relative good long-term prognosis in those who survive hospitalization.

*impactfactor:* 3.234

**Aarnoudse AL**

**ABCB1 gene variants, digoxin and risk of sudden cardiac death in a general population**

Niemeijer MN, van den Berg ME, Deckers JW, Aarnoudse AL\*, Hofman A, Franco OH, Uitterlinden AG, Rijnbeek PR, Eijgelsheim M, Stricker BH

Heart. 2015 Dec 15;101(24):1973-9

**OBJECTIVE:** The ATP-binding cassette B1 (ABCB1) gene encodes P-glycoprotein, a transport protein, which plays an important role in the bioavailability of digoxin. We aimed to investigate the interaction between variants within the ABCB1 gene and digoxin on the risk of sudden cardiac death (SCD).

**METHODS:** Within the Rotterdam Study, a population-based cohort study in persons 45 years of age and older, we used Cox regression to analyse the association between three polymorphisms that have been associated with digoxin bioavailability, extracted from 1000-Genomes imputed ABCB1 genotypes and the risk of SCD, stratified by digoxin use.

**RESULTS:** In a total study population of 10 932 persons, 419 SCDs occurred during a median follow-up of 9.8 years. In non-users of digoxin, the risk of SCD was not different across genotypes. In digoxin users, homozygous T allele carriers of C1236T (HR 1.90; 95% CI 1.09 to

3.30; allele frequency 0.43), G2677T (HR 1.89; 95% CI 1.10 to 3.24; allele frequency 0.44) and C3435T (HR 1.72; 95% CI 1.03 to 2.87; allele frequency 0.53) had a significantly increased risk of SCD in a recessive model. Interaction between the ABCB1 polymorphisms and digoxin use was significant for C1236T and G2677T in the age-adjusted and sex-adjusted model.

**CONCLUSIONS:** In this study, we showed that in digoxin users variant alleles at each of the three loci in the ABCB1 gene were associated with an increased risk of SCD compared with digoxin users with none or one T allele. If replicated, the findings imply that the ABCB1 genotype modifies the risk of cardiac digoxin toxicity.

*impactfactor:* 5.595

## **Ammerlaan H**

### **Efficacy of tenofovir and efavirenz in combination with lamivudine or emtricitabine in antiretroviral-naïve patients in Europe**

Swartz JE, Vandekerckhove L, Ammerlaan H\*, de Vries AC, Begovac J, Bierman WF, Boucher CA, van der Ende ME7, Grossman Z, Kaiser R, Levy I, Mudrikova T, Paredes R, Perez-Bercoff D, Pronk M\*, Richter C, Schmit JC, Vercauteren J, Zazzi M, Židovec Lepej S, De Luca A, Wensing AM; European Society for translational Antiviral Research (ESAR) J Antimicrob Chemother. 2015;70(6):1850-7

**BACKGROUND:** The combination of tenofovir and efavirenz with either lamivudine or emtricitabine (TELE) has proved to be highly effective in clinical trials for first-line treatment of HIV-1 infection. However, limited data are available on its efficacy in routine clinical practice.

**METHODS:** A multicentre cohort study was performed in therapy-naïve patients initiating ART with TELE before July 2009. Efficacy was studied using ITT (missing or switch?=failure) and on-treatment (OT) analyses. Genotypic susceptibility scores (GSSs) were determined using the Stanford HIVdb algorithm.

**RESULTS:** Efficacy analysis of 1608 patients showed virological suppression to <50 copies/mL at 48 weeks in 91.5% (OT) and 70.6% (ITT). Almost a quarter of all patients (22.9%) had discontinued TELE at week 48, mainly due to CNS toxicity. Virological failure within 48 weeks was rarely observed (3.3%, n=?53). In multilevel, multivariate analysis, infection with subtype B (P=?0.011), baseline CD4 count <200 cells/mm<sup>3</sup> (P=?0.001), GSS <3 (P=?0.002) and use of lamivudine (P=?0.001) were associated with a higher risk of virological failure. After exclusion of patients using co-formulated compounds, virological failure was still more often observed with lamivudine. Following virological failure, three-quarters of patients switched to a PI-based regimen with GSS <3. After 1 year of second-line therapy, viral load was suppressed to <50 copies/mL in 73.5% (OT).

**CONCLUSIONS:** In clinical practice, treatment failure on TELE regimens is relatively frequent due to toxicity. Virological failure is rare and more often observed with lamivudine than with emtricitabine. Following virological failure on TELE, PI-based second-line therapy was often successful despite GSS <3.

*impactfactor:* 5.313

## **Ammerlaan H**

### **Predictive value of prior colonization and antibiotic use for third-generation cephalosporin-resistant enterobacteriaceae bacteremia in patients with sepsis**

Rottier WC, Bamberg YR, Dorigo-Zetsma JW, van der Linden PD, Ammerlaan HS\*, Bonten MJ

Clin Infect Dis. 2015 Jun 1;60(11):1622-30

**BACKGROUND:** To prevent inappropriate empiric antibiotic treatment in patients with bacteremia caused by third-generation cephalosporin (3GC)-resistant Enterobacteriaceae (3GC-R EB), Dutch guidelines recommend  $\beta$ -lactam and aminoglycoside combination therapy or carbapenem monotherapy in patients with prior 3GC-R EB colonization and/or recent cephalosporin or fluoroquinolone usage. Positive predictive values (PPVs) of these determinants are unknown.

**METHODS:** We retrospectively studied patients with a clinical infection in whom blood cultures were obtained and empiric therapy with broad-spectrum  $\beta$ -lactams and/or aminoglycosides and/or fluoroquinolones was started. We determined the PPVs of prior colonization and antibiotic use for 3GC-R EB bacteremia, and the consequences of guideline adherence on appropriateness of empiric treatment.

**RESULTS:** Of 9422 episodes, 773 (8.2%) were EB bacteremias and 64 (0.7%) were caused by 3GC-R EB. For bacteremia caused by 3GC-R EB, PPVs of prior colonization with 3GC-R EB (90-day window) and prior usage of cephalosporins or fluoroquinolones (30-day window) were 7.4% and 1.3%, respectively, and PPV was 1.8% for the presence of any of these predictors. Adherence to Dutch sepsis guideline recommendations was 27%. Of bacteremia episodes caused by 3GC-R and 3GC-sensitive EB, 56% and 94%, respectively, were initially treated with appropriate antibiotics. Full adherence to guideline recommendations would hardly augment proportions of appropriate therapy, but could considerably increase carbapenem use.

**CONCLUSIONS:** In patients receiving empiric treatment for sepsis, prior colonization with 3GC-R EB and prior antibiotic use have low PPV for infections caused by 3GC-R EB. Strict guideline adherence would unnecessarily stimulate broad-spectrum antibiotic use.

*impactfactor:* 8.886

## **Bernards N**

### **Ten weeks to live: A population-based study on treatment and survival of patients with metastatic pancreatic cancer in the south of the Netherlands**

Bernards N\*, Haj Mohammad N, Creemers GJ\*, de Hingh IH\*, van Laarhoven HW, Lemmens VE

Acta Oncol. 2015 Mar;54(3):403-10. Epub 2014 Sep 29

**Background.** A large proportion of patients with pancreatic cancer presents with metastatic disease. We conducted a population-based study to evaluate trends in treatment and survival of patients with metastatic pancreatic cancer. **Methods.** We included all patients diagnosed with pancreatic cancer between 1993 and 2010 in the South of the Netherlands (N = 3099). Multivariable logistic regression analysis was conducted to evaluate trends in treatment with chemotherapy. Crude overall survival according to period of diagnosis was analyzed, and independent risk factors for death were identified. **Results.** Forty-eight percent of the patients (N = 1494) were diagnosed with metastatic disease. The percentage of patients being diagnosed with metastatic disease increased during the study period from 35% in 1993-1996 to 59% in 2009-2010 (p < 0.0001). Overall, 18% of these patients received chemotherapy. The prescription of palliative chemotherapy almost tripled from 10% to 27%

( $p < 0.0001$ ). Treatment largely depended on age, ranging from 38% among patients aged < 50 years [compared to 60-69 years: adjusted odds ratio (ORadj) 2.5 (95% CI 1.4-4.2)] to 1% among patients aged = 80 years [compared to 60-69 years: ORadj 0.04 (95% CI 0.0-0.2)]. Patients were more likely to receive chemotherapy if they had a high socioeconomic status [ORadj 2.0 (95% CI 1.3-3.1)], and if diagnosis was pathologically verified [no verification vs. verification: ORadj 0.3 (95% CI 0.2-0.5)]. The administration of chemotherapy varied widely between 10 hospitals (5-34%,  $p < 0.0001$ ). The median overall survival of patients with metastatic pancreatic cancer remained 9-11 weeks. Conclusion. A growing proportion of pancreatic cancer patients presented with metastatic disease. Usage of palliative chemotherapy increased over time, but median survival remained 9-11 weeks. In the near future, it should be evaluated if the recently introduced regimens have an impact on population-based survival.

Voor abstract zie: *Inwendige geneeskunde - Creemers GJ*  
*impactfactor: 2.997*

## **Bernards N**

### **The relevance of pathological verification in suspected pancreatic cancer**

Bernards N\*, Creemers GJ\*, Huysentruyt CJ, de Hingh IH\*, van der Schelling GP, de Bruïne AP\*, Lemmens VE\*

Cancer Epidemiol. 2015 Apr;39(2):250-5

**OBJECTIVES:** This population-based study assessed which factors were associated with pathological verification of pancreatic cancer.

**METHODS:** All patients diagnosed with a malignancy of the pancreas between 1993 and 2010 in the South of the Netherlands (N=3321) were included.

**RESULTS:** Pancreatic cancer was pathologically verified in 59% of patients. The proportion of verification increased over time from 56% in 1993-1996 to 69% in 2009-2010 ( $p < 0.0001$ ). High rates of verification were found among young patients (<50 years vs. 60-69 yrs: adjusted odds ratio (ORadj) 3.2 (95% CI: 1.9-5.4)), patients with a high socioeconomic status (high vs. low: ORadj 1.3 (95% CI: 1.1-1.7)), patients with metastatic disease (metastatic vs locoregional: ORadj 3.2 (95% CI: 2.7-3.8)) and patients treated with chemotherapy (yes vs. no: ORadj 2.4 (95% CI: 1.8-3.2)). The most favorable prognosis was found in patients with verified locoregional disease (median overall survival (mOS) 7.6 months, 95% CI: 7.1-8.6). Patients with unverified metastatic disease carried the worst prognosis (mOS 1.7 months, 95% CI: 1.4-2.0).

**CONCLUSION:** Verification by pathology remains preferable and desirable whenever possible. However, the median survival rate exhibited by patients without verification suggests that the vast majority of patients suffered from true invasive pancreatic cancer. This may justify treatment decisions even in the absence of pathologic verification in selected patients.

*impactfactor: 2.711*

**Bie AJ de**

**Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S\*, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

Isolated pancreatic involvement is a rare initial presentation in patients with ANCA-associated vasculitis. We report a patient with a suspected malignant pancreatic mass, referred to our hospital for pancreaticoduodenectomy. However, the pancreatic mass proved to be the initial manifestation of ANCA-associated vasculitis.

*impactfactor:* 1.969

**Blaauw M**

**Characteristics associated with the presence and development of extra-articular manifestations in ankylosing spondylitis: 12-year results from OASIS**

Essers I, Ramiro S, Stolwijk C, Blaauw M\*, Landewé R, van der Heijde D, Van den Bosch F, Dougados M, van Tubergen A

Rheumatology (Oxford). 2015 Apr;54(4):633-40. Epub 2014 Sep 17

**OBJECTIVE:** The aim of this study was to identify characteristics associated with the presence and development of extra-articular manifestations (EAMs) in a prevalence cohort of patients with AS.

**METHODS:** Twelve-year follow-up data from the Outcome in Ankylosing Spondylitis International Study (OASIS) were used. In addition, medical charts were checked for the presence of acute anterior uveitis (AAU), IBD and psoriasis. Demographic, clinical and radiographic characteristics associated with the presence of (any) EAM at baseline or new development during follow-up were identified.

**RESULTS:** Two hundred and sixteen patients were included [mean age 43.6 years (s.d. 12.7), 154 (71%) men, mean symptom duration 20.5 years (s.d. 11.7), mean follow-up 8.3 years (s.d. 4.3)]. At baseline, 39 (18%) patients had AAU, 15 (7%) had IBD and 9 (4%) had psoriasis. The history of AAU was univariably associated with increased age [odds ratio (OR) 1.04 (95% CI 1.01, 1.07)], longer symptom duration [OR 1.05 (95% CI 1.02, 1.08)] and more radiographic damage [OR 1.02 (95% CI 1.00, 1.04)]. The history of psoriasis was associated with greater age [OR 1.05 (95% CI 1.00, 1.11)] and lower CRP [OR 0.77 (95% CI 0.59, 1.00)]. At follow-up, 27 patients developed a new EAM. Newly developed IBD was associated with a higher time-varying AS Disease Activity Score [hazard ratio (HR) 2.80 (95% CI 1.43, 5.52)], worse physical function [HR 1.40 (95% CI 1.09, 1.80)] and worse patient global well-being [HR 1.46 (95% CI 1.10, 1.93)]. Newly developed AAU was associated with an elevated time-varying CRP [HR 1.02 (95% CI 1.01, 1.04)].

**CONCLUSION:** Development of EAMs was infrequent in this cohort, despite relatively long follow-up. In particular, markers of disease activity were associated with the development of IBD.

*impactfactor:* 4.475

**Creemers GJ**

**Deciding on adjuvant chemotherapy for elderly stage III colon cancer patients: A qualitative insight into the perspectives of surgeons and medical oncologists**

van Erning FN, Janssen-Heijnen ML, Creemers GJ\*, Pruijt HF, Maas HA, Lemmens VE

J Geriatr Oncol. 2015 May;6(3):219-24. Epub 2015 Feb 20

**OBJECTIVE:** The aim of this study is to identify doctor-related factors determining the decision-making for adjuvant chemotherapy for stage III colon cancer patients aged  $\geq 75$  years.

**MATERIALS AND METHODS:** 21 surgeons and 15 medical oncologists from 10 community hospitals were asked to complete a short questionnaire including tick-box questions regarding motives for non-referral/non-treatment, consultation of geriatricians, chemotherapy schemes prescribed and an open question regarding tolerability of chemotherapy.

**RESULTS:** 29 medical specialists returned a completed questionnaire (response 81%). The motives for non-referral/non-treatment reported most often were comorbidity/bad general health condition of the patient; surgical complications; and treatment offered but refused by patient/family. 39% of the surgeons and 55% of the medical oncologists reported consultation of a geriatrician in 2-30% of their decisions. CAPOX and capecitabine were reported by medical oncologists as the most frequently prescribed regimens. Factors that influenced the decision for monotherapy or combination therapy were comorbidity; general health condition of the patient; and toxicity profile of the chemotherapeutics. In general, medical oncologists defined grade  $\geq 2$  toxicities as tolerable, with the exception of neuropathy, for which grade  $\geq 1$  toxicity was accepted.

**CONCLUSIONS:** In case medical oncologists prescribe adjuvant chemotherapy to elderly stage III colon cancer patients, the chemotherapy schemes used are in line with clinical guidelines and they agree on acceptable levels of toxicity. However, the variation among surgeons and medical oncologists in motives for non-referral, non-treatment and consultation of geriatricians when deciding on adjuvant chemotherapy for elderly stage III colon cancer patients, shows the complexity and need for specific knowledge.

*impactfactor:* 1.859

**Creemers GJ**

**Maintenance treatment with capecitabine and bevacizumab in metastatic colorectal cancer (CAIRO3): a phase 3 randomised controlled trial of the Dutch Colorectal Cancer Group**

Simkens LH, van Tinteren H, May A, ten Tije AJ, Creemers GJ\*, Loosveld OJ, de Jongh FE, Erdkamp FL, Erjavec Z, van der Torren AM, Tol J, Braun HJ, Nieboer P, van der Hoeven JJ, Haasjes JG, Jansen RL, Wals J, Cats A, Derleyn VA, Honkoop AH, Mol L, Punt CJ, Koopman M

Lancet. 2015 May 9;385(9980):1843-52. Epub 2015 Apr 7

**BACKGROUND:** The optimum duration of first-line treatment with chemotherapy in combination with bevacizumab in patients with metastatic colorectal cancer is unknown. The CAIRO3 study was designed to determine the efficacy of maintenance treatment with capecitabine plus bevacizumab versus observation.

**METHODS:** In this open-label, phase 3, randomised controlled trial, we recruited patients in 64 hospitals in the Netherlands. We included patients older than 18 years with previously untreated metastatic colorectal cancer, with stable disease or better after induction treatment with six 3-weekly cycles of capecitabine, oxaliplatin, and bevacizumab (CAPOX-B),

WHO performance status of 0 or 1, and adequate bone marrow, liver, and renal function. Patients were randomly assigned (1:1) to either maintenance treatment with capecitabine and bevacizumab (maintenance group) or observation (observation group). Randomisation was done centrally by minimisation, with stratification according to previous adjuvant chemotherapy, response to induction treatment, WHO performance status, serum lactate dehydrogenase concentration, and treatment centre. Both patients and investigators were aware of treatment assignment. We assessed disease status every 9 weeks. On first progression (defined as PFS1), patients in both groups were to receive the induction regimen of CAPOX-B until second progression (PFS2), which was the study's primary endpoint. All endpoints were calculated from the time of randomisation. Analyses were done by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00442637.

**FINDINGS:** Between May 30, 2007, and Oct 15, 2012, we randomly assigned 558 patients to either the maintenance group (n=279) or the observation group (n=279). Median follow-up was 48 months (IQR 36-57). The primary endpoint of median PFS2 was significantly improved in patients on maintenance treatment, and was 8.5 months in the observation group and 11.7 months in the maintenance group (HR 0.67, 95% CI 0.56-0.81, p<0.0001). This difference remained significant when any treatment after PFS1 was considered. Maintenance treatment was well tolerated, although the incidence of hand-foot syndrome was increased (64 [23%] patients with hand-foot skin reaction during maintenance). The global quality of life did not deteriorate during maintenance treatment and was clinically not different between treatment groups.

**INTERPRETATION:** Maintenance treatment with capecitabine plus bevacizumab after six cycles of CAPOX-B in patients with metastatic colorectal cancer is effective and does not compromise quality of life.

*impactfactor:* 45.217

## **Creemers GJ**

### **Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial**

Shapiro J, van Lanschot JJ, Hulshof MC, van Hagen P, van Berge Henegouwen MI, Wijnhoven BP, van Laarhoven HW, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Ten Kate FJ, Creemers GM\*, Punt CJ, Plukker JT, Verheul HM, Bilgen EJ, van Dekken H, van der Sangen MJ, Rozema T, Biermann K, Beukema JC, Piet AH, van Rij CM, Reinders JG, Tilanus HW, Steyerberg EW, van der Gaast A; CROSS study group

Lancet Oncol. 2015 Sep;16(9):1090-8. Epub 2015 Aug 5

*Voor abstract zie:* Chirurgie - Nieuwenhuijzen GA

*impactfactor:* 24.690

## **Creemers GJ**

### **Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin**

van Oudheusden TR\*, Razenberg LG\*, van Gestel YR, Creemers GJ\*, Lemmens VE, de Hingh IH\*

Sci Rep. 2015 Dec 21;5:18632

*Voor abstract zie:* Chirurgie - Oudheusden TR van

*impactfactor:* 5.578



**Creemers GJ**

**Ten weeks to live: A population-based study on treatment and survival of patients with metastatic pancreatic cancer in the south of the Netherlands**

Bernards N, Haj Mohammad N, Creemers GJ\*, de Hingh IH\*, van Laarhoven HW, Lemmens VE

Acta Oncol. 2015 Mar;54(3):403-10. Epub 2014 Sep 29

Voor abstract zie: *Inwendige geneeskunde - Bernards N*

impactfactor: 2.997

**Creemers GJ**

**The Prognostic Relevance of Histological Subtype in Patients With Peritoneal Metastases From Colorectal Cancer: A Nationwide Population-Based Study**

Razenberg LG\*, van Gestel YR, Lemmens VE, de Wilt JH, Creemers GJ\*, de Hingh IH\*

Clin Colorectal Cancer. 2015 Dec;14(4):e13-9. Epub 2015 Jun 6

Voor abstract zie: *Oncologie - Razenberg LG*

impactfactor: 2.813

**Creemers GJ**

**The relevance of pathological verification in suspected pancreatic cancer**

Bernards N\*, Creemers GJ\*, Huysentruyt CJ, de Hingh IH\*, van der Schelling GP, de Bruïne AP\*, Lemmens VE\*

Cancer Epidemiol. 2015 Apr;39(2):250-5

Voor abstract zie: *Inwendige geneeskunde - Bernards N*

impactfactor: 2.711

**Creemers GJ**

**Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

Voor abstract zie: *Inwendige geneeskunde - Bie AJ de*

impactfactor: 1.969

**Creemers GJ**

**Timing of adjuvant chemotherapy and its relation to survival among patients with stage III colon cancer**

Bos AC, van Erning FN, van Gestel YR, Creemers GJ\*, Punt CJ, van Oijen MG, Lemmens VE

Eur J Cancer. 2015 Nov;51(17):2553-61. Epub 2015 Sep 7

BACKGROUND: Currently available data suggest that delaying the start of adjuvant chemotherapy in colon cancer patients has a detrimental effect on survival. We analysed which factors impact on the timing of adjuvant chemotherapy and evaluated the influence on overall survival (OS).

PATIENTS AND METHODS: Stage III colon cancer patients who underwent resection and received adjuvant chemotherapy between 2008 and 2013 were selected from the Netherlands Cancer Registry. Timing of adjuvant chemotherapy was subdivided into: ?4, 5-6,

7-8, 9-10, 11-12 and 13-16weeks post-surgery. Multivariable regressions were performed to assess the influence of several factors on the probability of starting treatment within 8weeks post-surgery and to evaluate the association of timing of adjuvant chemotherapy with 5-year OS.

RESULTS: 6620 patients received adjuvant chemotherapy, 14% commenced after 8weeks. Factors associated with starting treatment after 8weeks were older age (Odds ratio (OR) 65-74 versus <65years 1.3 (95% confidence interval (CI): 1.14-1.58); OR ≥75 versus <65years 1.6 (1.25-1.94)), emergency resection (OR 1.8 (1.41-2.32)), anastomotic leakage (OR 8.1 (6.14-10.62)), referral to another hospital for adjuvant chemotherapy (OR 1.9 (1.36-2.57)) and prolonged postoperative hospital admission (OR 4.7 (3.30-6.68)). Starting 5-8weeks post-surgery showed no decrease in OS compared to initiation within 4weeks (Hazard ratio (HR) 5-6weeks 0.9 (0.79-1.11); HR 7-8weeks 1.1 (0.91-1.30)). However, commencing beyond 8weeks was associated with decreased OS compared to initiation within 8weeks (HR 9-10weeks 1.4 (1.21-1.68); HR 11-12weeks 1.3 (1.06-1.59); HR 13-16weeks 1.7 (1.23-2.23)).

CONCLUSION: Our data support initiating adjuvant chemotherapy in stage III colon cancer patients within 8weeks post-surgery

impactfactor: 5.417

## Creemers GJ

### **Trends in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for the treatment of synchronous peritoneal carcinomatosis of colorectal origin in the Netherlands**

Razenberg LG\*, van Gestel YR, Creemers GJ\*, Verwaal VJ, Lemmens VE, de Hingh IH\*

Eur J Surg Oncol. 2015 Apr;41(4):466-71. Epub 2015 Jan 29

Voor abstract zie: Oncologie - Razenberg LG

impactfactor: 3.009

## Dekker MJ

### **Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S\*, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

Voor abstract zie: Inwendige geneeskunde - Bie AJ de

impactfactor: 1.969

## Konings CJ

### **The Effect of Online Hemodiafiltration on Infections: Results from the CONvective TRANsport SStudy**

den Hoedt CH, Grooteman MP, Bots ML, Blankestijn PJ, van der Tweel I, van der Weerd NC, Penne EL, Mazairac AH, Levesque R, ter Wee PM, Nubé MJ, van den Dorpel MA; CONTRAST investigators; Konings CJ\*, collaborator

PLoS One. 2015 Aug 19;10(8):e0135908

BACKGROUND: Hemodialysis (HD) patients have a high risk of infections. The uremic milieu has a negative impact on several immune responses. Online hemodiafiltration (HDF) may reduce the risk of infections by ameliorating the uremic milieu through enhanced clearance of middle molecules. Since there are few data on infectious outcomes in HDF, we compared the effects of HDF with low-flux HD on the incidence and type of infections.

**PATIENTS AND METHODS:** We used data of the 714 HD patients (age  $64 \pm 14$ , 62% men, 25% Diabetes Mellitus, 7% catheters) participating in the CONvective TRANsport STudy (CONTRAST), a randomized controlled trial evaluating the effect of HDF as compared to low-flux HD. The events were adjudicated by an independent event committee. The risk of infectious events was compared with Cox regression for repeated events and Cox proportional hazard models. The distributions of types of infection were compared between the groups.

**RESULTS:** Thirty one percent of the patients suffered from one or more infections leading to hospitalization during the study (median follow-up 1.96 years). The risk for infections during the entire follow-up did not differ significantly between treatment arms (HDF 198 and HD 169 infections in 800 and 798 person-years respectively, hazard ratio HDF vs. HD 1.09 (0.88-1.34),  $P = 0.42$ ). No difference was found in the occurrence of the first infectious event (either fatal, non-fatal or type specific). Of all infections, respiratory infections (25% in HDF, 28% in HD) were most common, followed by skin/musculoskeletal infections (21% in HDF, 13% in HD).

**CONCLUSIONS:** HDF as compared to HD did not result in a reduced risk of infections, larger studies are needed to confirm our findings.

*impactfactor:* 3.234

### **Konings CJ**

#### **Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

*Voor abstract zie: Inwendige geneeskunde - Bie AJ de*

*impactfactor:* 1.969

### **Kreeftenberg HG**

#### **Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

Boer AK\*, Kreeftenberg H\*, Bindels A\*, Roos A\*, Houterman S\*, Korsten E\*, van Dijk-van Berkel M\*

Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

*Geen abstract beschikbaar*

*impactfactor:* --

### **Kreeftenberg HG**

#### **Cholesterol in the ICU: a cheap and reliable marker for illness severity?**

Kreeftenberg HG\*, Roos AN\*, Bindels AJ\*, Scharnhorst V\*

Neth J Crit Care 2015;20(2):17-20

Several markers as C-reactive protein and procalcitonin are used in the ICU to monitor the success of the treatment. Recently, studies about the prognostic value of cholesterol have been reported. In this case series we discuss cholesterol as a cheap and reliable marker for daily follow up, to monitor improvement or deterioration of patients in the ICU.

*impactfactor:* --

**Peters WG**

**The standardised mortality ratio: the proper quality indicator in acute leukaemia?**

Saes L, Peters WG\*, Schaafsma R, van Spronsen DJ, van der Velden AW, van den Bosch WF, Meijer E

Neth J Med. 2015 Mar;73(3):119-23

**BACKGROUND:** The standardised mortality ratio (SMR) is a quality indicator used to measure quality of care in the Netherlands. It is subject to much criticism, which was the reason to study the value of the SMR as a quality indicator for the treatment of acute leukaemia.

**METHODS:** A retrospective analysis was performed in patients with acute leukaemia admitted to a Santeon hospital during the period 2005-2009. SMR values were calculated and compared with the overall survival (OS).

**RESULTS:** During the study period, 455 unique patients were admitted with acute leukaemia. SMR calculation was based on 992 admissions. SMR analysis yielded a high mortality ratio in hospital 1, 2, 3 and 4 in comparison with the national average (100), significant for hospital 1 and 4 (180 [CI 95% 126-257] and 187 [CI 95% 134-261], respectively) OS analysis also showed a significantly different outcome between hospitals. However, using OS as outcome parameter, hospital 2 and 6 showed the lowest performance as compared with hospital 1 and 4 using SMR as parameter. After multivariate analysis, age (HR 1.04; CI 95% 1.03-1.05;  $p < 0.001$ ) and hospital (hospital 5 compared with 6: HR 0.54; CI 95% 0.30- .98;  $p = 0.043$ ; hospital 2 compared with 1: HR 1.51; CI 95% 1.02-2.23;  $p = 0.039$ ) were the only significant variables that influenced OS.

**CONCLUSION:** Outcome according to SMR is not equivalent to outcome according to OS. This study shows that the use of the SMR as a quality indicator for the treatment of acute leukaemia does not appear to be justified.

*impactfactor:* 1.969

**Pronk MJ**

**Efficacy of tenofovir and efavirenz in combination with lamivudine or emtricitabine in antiretroviral-naïve patients in Europe**

Swartz JE, Vandekerckhove L, Ammerlaan H\*, de Vries AC, Begovac J, Bierman WF, Boucher CA, van der Ende ME7, Grossman Z, Kaiser R, Levy I, Mudrikova T, Paredes R, Perez-Bercoff D, Pronk M\*, Richter C, Schmit JC, Vercauteren J, Zazzi M, Židovec Lepej S, De Luca A, Wensing AM; European Society for translational Antiviral Research (ESAR) J Antimicrob Chemother. 2015;70(6):1850-7

*Voor abstract zie:* Inwendige geneeskunde - Ammerlaan H

*impactfactor:* 5.313

**Pronk MJ**

**Specific in vitro interferon-gamma and IL-2 production as biomarkers during treatment of chronic Q fever**

Schoffelen T, Wegdam-Blans MC\*, Ammerdorffer A, Pronk MJ\*, Soethoudt YE, Netea MG, van der Meer JW, Bleeker-Rovers CP, van Deuren M

Front Microbiol. 2015 Feb 12;6:93. eCollection 2015

*Voor abstract zie:* Pamm - Wegdam-Blans MC

*impactfactor:* 3.989

## **Razenberg LG**

### **Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin**

van Oudheusden TR\*, Razenberg LG\*, van Gestel YR, Creemers GJ\*, Lemmens VE, de Hingh IH\*

Sci Rep. 2015 Dec 21;5:18632

Voor abstract zie: *Chirurgie - Oudheusden TR van*

*impactfactor: 5.578*

## **Razenberg LG**

### **The Prognostic Relevance of Histological Subtype in Patients With Peritoneal Metastases From Colorectal Cancer: A Nationwide Population-Based Study**

Razenberg LG\*, van Gestel YR, Lemmens VE, de Wilt JH, Creemers GJ\*, de Hingh IH\*

Clin Colorectal Cancer. 2015 Dec;14(4):e13-9. Epub 2015 Jun 6

**BACKGROUND:** With evolving treatment possibilities for peritoneal metastases (PM) from colorectal cancer (CRC), adequate prognostication and patient selection for treatment becomes increasingly important. We investigated the prognostic relevance of commonly identified histological subtypes in PM of CRC (adenocarcinoma [AC], mucinous AC [MC], and signet-ring cell carcinoma [SC]), which is currently unclear.

**PATIENTS AND METHODS:** This study involved 4277 patients diagnosed with synchronous PM from CRC between 2005 and 2012 in The Netherlands. Kaplan-Meier analysis and log-rank testing were performed to estimate survival. Subsequently a Cox proportional hazard model was used to calculate hazard ratios for the risk of death.

**RESULTS:** Most of the CRC patients were diagnosed with AC (n = 3008; 70%), whereas MC and SC were found in 958 (22%) and 311 (7%) patients, respectively. SC was associated with the highest risk of death in colon and rectal cancer, with median survival rates of respectively, 6.6 and 6.9 months. For MC, median survival varied from 10.9 months in colon and 9.8 months in rectal cancer (P > .05). In colon cancer, MC was associated with a significantly lower risk of death compared with AC (hazard ratio, 0.9; 95% confidence interval, 0.79-0.95). In rectal cancer, no such effect was observed. AC was associated with a significantly poorer survival rate in the case of primary colonic tumor localization (7.4 months in colon vs. 10.9 months in rectal cancer).

**CONCLUSION:** Histological subtype is an important prognostic factor in patients with synchronous PM of colorectal origin. This knowledge will aid clinicians in counseling of patients and clinical decision-making regarding possible treatment options.

*impactfactor: 2.813*

## **Razenberg LG**

### **Trends in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for the treatment of synchronous peritoneal carcinomatosis of colorectal origin in the Netherlands**

Razenberg LG\*, van Gestel YR, Creemers GJ\*, Verwaal VJ, Lemmens VE, de Hingh IH\*

Eur J Surg Oncol. 2015 Apr;41(4):466-71. Epub 2015 Jan 29

**BACKGROUND:** Population-based data on the percentage of colorectal cancer (CRC) patients with synchronous peritoneal carcinomatosis (PC) being treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are currently lacking. The current population-based study describes trends in the use of CRS-HIPEC in the Netherlands, one of the first countries where CRS and HIPEC was introduced. **METHODS:** All patients

diagnosed with synchronous PC of CRC between 2005 and 2012 were extracted from the Netherlands Cancer Registry (n = 4623). Patients with primary appendiceal cancer were excluded resulting in a study population of 4430 patients. Trends in the use of CRS-HIPEC over time were analyzed by means of a Cochrane-Armitage trend test. Survival proportions were calculated as the time between diagnosis and date of death or last follow-up (January 2014). RESULTS: Of the total 4430 patients with synchronous PC, 297 (6.4%) underwent treatment with CRS-HIPEC. The proportion of colorectal PC patients receiving CRS-HIPEC increased significantly over time from 3.6% in 2005-2006 to 9.7% in 2011-2012 ( $p < 0.0001$ ). Overall median survival (MS) for patients treated with CRS-HIPEC was 32.3 months, whereas MS rates were respectively 12.6, 6.1 and 1.5 for months palliative chemotherapy with/without surgery, palliative surgery and best supportive care. CONCLUSION: The proportion of patients diagnosed with synchronous PC from CRC treated with CRS-HIPEC has increased significantly over time and currently almost 10% of PC patients are treated with CRS-HIPEC. Median survival in this population based group is 32.3 months.

*impactfactor:* 3.009

## Wlazlo N

### **Iron metabolism is prospectively associated with insulin resistance and glucose intolerance over a 7-year follow-up period: the CODAM study**

Wlazlo N\*, van Greevenbroek MM, Ferreira I, Jansen EH, Feskens EJ, van der Kallen CJ, Schalkwijk CG, Bravenboer B\*, Stehouwer CD

Acta Diabetol. 2015 Apr;52(2):337-48. Epub 2014 Oct 1

OBJECTIVES: Several markers of iron metabolism have been associated with insulin resistance (IR) and type 2 diabetes mellitus in cross-sectional studies. However, prospective data on these associations are scarce, and it is currently unclear in which tissues iron metabolism may contribute to IR. Therefore, we investigated whether markers of iron metabolism were associated with IR in muscle, liver, and adipocytes, and with glucose intolerance over a 7-year follow-up period.

DESIGN AND METHODS: Serum ferritin, transferrin, total iron, non-transferrin-bound iron, and transferrin saturation were determined at baseline of a prospective cohort study in 509 individuals (60 % men, age  $59 \pm 6.9$  years, body mass index  $28.5 \pm 4.3$ ). Both at baseline and after a 7-year follow-up (n = 386), measures of glucose, insulin (during glucose tolerance tests), and non-esterified fatty acids were obtained. Using generalized estimating equations, we investigated associations between baseline iron markers and indices of muscle, liver, and adipocyte insulin resistance (adipocyte IR), as well as glucose intolerance, over the 7-year period.

RESULTS: Over a 7-year period, baseline serum ferritin (per 10  $\mu\text{g/L}$  increase) was positively associated with homeostasis model assessment insulin resistance (HOMA2-IR) [ $\beta = 0.77$  % (95 % CI 0.50-1.03)], hepatic insulin resistance (hepatic IR) [ $\beta = 0.39$  % (0.23-0.55)], adipocyte IR [ $\beta = 1.00$  % (0.65-1.35)], and AUCglucose [ $\beta = 0.32$  % (0.18-0.46)] after adjustment for several covariates, including inflammatory markers (all  $p < 0.001$ ). Similarly, serum transferrin (per 0.1 g/L) was associated with HOMA2-IR [ $\beta = 2.66$  % (1.55-3.78)], hepatic IR [ $\beta = 1.16$  % (0.47-1.85)], adipocyte IR [ $\beta = 3.75$  % (2.27-5.25)], and AUCglucose [ $\beta = 1.35$  % (0.74-1.96)] over 7 years.

CONCLUSIONS: Iron metabolism and related factors may contribute to IR in muscle, liver, and adipocytes, eventually leading to impaired glucose metabolism and hyperglycaemia.

*impactfactor:* 2.399

\* = Werkzaam in het Catharina Ziekenhuis

## Kindergeneeskunde

**Brackel HJ**

**Fractional Exhaled Nitric Oxide Monitoring Does Not Improve Asthma Management in Children with Concordant and Discordant Asthma Phenotypes**

Voorend-van Bergen S, Vaessen-Verberne AA, Landstra AM, Brackel HJ\*, van den Berg NJ, Merkus PJ, de Jongste JC, Pijnenburg MW

Am J Respir Crit Care Med. 2015 Oct 15;192(8):1016-8.

*Geen abstract beschikbaar*

*impactfactor:* 12.996

**Brackel HJ**

**Monitoring strategies in children with asthma: a randomised controlled trial**

Voorend-van Bergen S, Vaessen-Verberne AA, Brackel HJ\*, Landstra AM, van den Berg NJ, Hop WC, de Jongste JC, Merkus PJ, Pijnenburg MW

Thorax. 2015 Jun;70(6):543-50. Epub 2015 Mar 30

**BACKGROUND:** Asthma guidelines recommend monitoring of asthma control. However, in a substantial proportion of children, asthma is poorly controlled and the best monitoring strategy is not known.

**OBJECTIVES:** We studied two monitoring strategies for their ability to improve asthma outcomes in comparison with standard care (SC): web-based monthly monitoring with the (Childhood) Asthma Control Test (ACT or C-ACT) and 4-monthly monitoring of FENO.

**METHODS:** In this randomised controlled, partly blinded, parallel group multicentre trial with a 1-year follow-up, children aged 4-18 years with a doctor's diagnosis of asthma treated in seven hospitals were randomised to one of the three groups. In the web group, treatment was adapted according to ACT obtained via a website at 1-month intervals; in the FENO group according to ACT and FENO, and in the SC group according to the ACT at 4-monthly visits. The primary endpoint was the change from baseline in the proportion of symptom-free days (SFD).

**RESULTS:** Two-hundred and eighty children (mean age 10.4 years, 66% boys) were included; 268 completed the study. Mean changes from baseline in SFD were similar between the groups: -2.1% (web group, n=90), +8.9% (FENO group, n=91) versus 0.15% (SC, n=87), p=0.15 and p=0.78. Daily dose of inhaled corticosteroids (ICS) decreased more in the web-based group compared with both other groups (-200 µg/day, p<0.01), while ACT and SFD remained similar.

**CONCLUSIONS:** The change from baseline in SFD did not differ between monitoring strategies. With web-based ACT monitoring, ICS could be reduced substantially while control was maintained.

*impactfactor:* 8.290

**Bunt JE**

**Transient anti-NMDAR encephalitis in a newborn infant due to transplacental transmission**

Hilderink M\*, Titulaer MJ, Schreurs MW, Keizer K\*, Bunt JE\*

Neurol Neuroimmunol Neuroinflamm. 2015 Jun 18;2(4):e126 eCollection 2015

*Geen abstract beschikbaar*

*impactfactor:* --



**Hilderink M**

**Transient anti-NMDAR encephalitis in a newborn infant due to transplacental transmission**

Hilderink M\*, Titulaer MJ, Schreurs MW, Keizer K\*, Bunt JE\*

Neurol Neuroimmunol Neuroinflamm. 2015 Jun 18;2(4):e126 eCollection 2015

*Geen abstract beschikbaar*

*impactfactor:* --

**Janssen EJ**

**Dutch paediatrician's opinions about acute care for critically ill children in general hospitals**

van Sambeek SJ, Martens SJ, Hundscheid T, Janssen EJ\*, Vos GD

Eur J Pediatr. 2015 May;174(5):607-13. Epub 2014 Oct 23

Paediatricians in general hospitals have limited experience with critically ill children, due to the low incidence and their diversity in age, pathology and presentation. Consequently, adequate organization, training and materials and medication are of major importance. This voluntary and anonymous survey-based study was conducted to gain insight in the current status of these aspects. In June 2012, all 687 paediatricians employed at 84 general hospitals in The Netherlands received a hardcopy questionnaire with questions relating to demographics, organization, training and materials and medication concerning the acute care for critically ill children. Of the sent questionnaires, 41.3 % were eligible for analysis. According to the organization of the acute care of critically ill children, 73.9 % of the respondents indicated verbal agreements were made, of which 77.0 % stated that these were recorded in written protocols. Taskforces were present according to 64.5 % of our respondents. Of the respondents, 64.4 % were Advanced Paediatric Life Support (APLS) certified. Of the stated training scenarios, 90.8 % were available in their hospital, which were followed on a regular basis by 63.9 % of the paediatricians. Paediatric resuscitation carts were present on both emergency department and paediatric ward according to 95.1 %. Materials (37.7 %) and medication (45.3 %) were frequently lacking.

Conclusion: Paediatricians from general hospitals in The Netherlands consider that acute care for critically ill children has to be improved in terms of organization, training and teamwork, and medication and materials. National guidelines concerning the organization and training may contribute to this improvement, as well as a standardized inventory list for paediatric resuscitation carts.

*impactfactor:* 1.907

**Odink RJ**

**Bone Mineral Density in Children and Adolescents with Prader-Willi syndrome: A longitudinal study during puberty and 9 years of Growth Hormone treatment**

Bakker NE, Kuppens RJ, Siemensma EP, Tummers-de Lind van Wijngaarden RF, Festen DA, Bindels-de Heus GC, Bocca G, Haring DA, Hoorweg-Nijman JJ, Houdijk EC, Jira PE, Lunshof L, Odink RJ\*, Oostdijk W, Rotteveel J, Van Alfen AA, Van Leeuwen M, Van Wieringen H, Wegdam-den Boer ME, Zwaveling-Soonawala N, Hokken-Koelega AC

J Clin Endocrinol Metab. 2015 Apr;100(4):1609-18. Epub 2015 Feb 10

Context: Longitudinal data on bone mineral density (BMD) in children and adolescents with PWS during long-term GH treatment are not available. Objective: To determine effects of long-term GH treatment and puberty on BMD of total body (BMDTB), lumbar spine (BMDLS) and bone mineral apparent density of the lumbar spine (BMADLS) in children with PWS.

Design: Prospective longitudinal study. Setting: Dutch PWS Cohort. Participants: Seventy-seven children with PWS who remained prepubertal during GH treatment for 4 years and 64 children with PWS who received GH treatment for 9 years. Intervention: GH treatment 1 mg/m<sup>2</sup>/day (~0.035 mg/kg/day). Main outcome measures: BMDTB, BMDLS and BMADLS by using the same dual-energy x-ray absorptiometry (DXA) machine for all annual measurements. Results: In the prepubertal group, BMDTBSDS and BMDLSSDS significantly increased during 4 years of GH treatment while BMADLSSDS remained stable. During adolescence, BMDTBSDS and BMADLSSDS decreased significantly, in girls from the age of 11 years and in boys from the age of 14 and 16 years, resp., but all BMDs remained within the normal range. Higher Tanner stage tended to be associated with lower BMDTB-SDS (P=0.083) and a significantly lower BMADLSSDS (P=0.016). After 9 years of GH treatment, lean body mass SDS was the most powerful predictor of BMDTBSDS and BMDLSSDS in adolescents with PWS. Conclusions: This long-term GH study demonstrates that BMDTB, BMDLS and BMADLS remains stable in prepubertal children with PWS but decreases during adolescence, parallel to incomplete pubertal development. Based on our findings, clinicians should start sex hormone therapy from the age of 11 in girls and 14 in boys, unless there is a normal progression of puberty

impactfactor: 6.209

## Odink R

### **Metabolic Health in short children born SGA treated with GH and GnRHa: Results of a randomized, dose-response trial**

van der Steen M, Lem AJ, van der Kaay DC, Bakker-van Waarde WM, van der Hulst FJ, Neijens FS, Noordam C, Odink RJ\*, Oostdijk W, Schroor EJ, Westerlaken C, Hokken-Koelega AC

J Clin Endocrinol Metab. 2015 Oct;100(10):3725-34. Epub 2015 Aug 10

CONTEXT: Previously we showed that pubertal children born small for gestational age (SGA) with a poor adult height (AH) expectation can benefit from treatment with growth hormone (GH) 1mg/m<sup>2</sup>/day (~0.033mg/kg/day) in combination with 2 years of GnRH analogue (GnRHa) and even more so with a double GH dose. GnRHa treatment is thought to have negative effects on body composition and blood pressure. Long-term effects and GH-dose effects on metabolic health in children treated with combined GH/GnRHa are unknown.

OBJECTIVE: To investigate body composition, blood pressure and lipid profile during GH treatment, either with or without 2 years of additional GnRHa. To assess whether GH 2mg/m<sup>2</sup>/day (~0.067mg/kg/day) results in a similar or even more favorable metabolic health at AH than GH 1mg/m<sup>2</sup>/day.

METHODS: Longitudinal, randomized, dose-response GH trial involving 107 short SGA children (58 girls) treated with GH until AH (GH randomized 1 or 2mg/m<sup>2</sup>/day during puberty). Sixty-four children received additional GnRHa. At AH, metabolic parameters were compared between children treated with combined GH/GnRHa and those with only GH. The GH-dose effect on metabolic health was evaluated in a subgroup of 47 children who started GH treatment in early puberty (randomized 1 or 2mg/m<sup>2</sup>/day) with 2 years of GnRHa.

RESULTS: At AH, fat mass percentage (FM%) SDS, lean body mass (LBM) SDS, blood pressure SDS and lipid profile were similar between children treated with combined GH/GnRHa and those with only GH. In the pubertal subgroup, FM% SDS was lower during treatment with GH 2mg/m<sup>2</sup>/day. There was no GH dose-dependent effect on LBM SDS, blood pressure and lipid profile.

CONCLUSIONS: Combined GH/GnRHa treatment has no long-term negative effects on metabolic health compared to only GH. Started in early puberty, a GH dose of 2mg/m<sup>2</sup>/day results in a similar metabolic health at AH and a more favorable FM% than GH 1mg/m<sup>2</sup>/day.

*impactfactor:* 6.209

## **Odink RJ**

### **New insights into factors influencing adult height in short SGA children: Results of a large multicenter growth hormone trial**

Renes JS, Willemsen RH, Mulder JC, Bakker-van Waarde WM, Rotteveel J, Oostdijk W, Houdijk EC, Westerlaken C, Noordam C, Verrijn Stuart AA, Odink RJ\*, de Ridder MA, Hokken-Koelega AC

Clin Endocrinol (Oxf). 2015 Jun;82(6):854-61. Epub 2015 Feb 9

BACKGROUND: Growth hormone (GH) treatment is effective in improving adult height (AH) in short children born SGA. However, there is a wide variation in height gain, even after adjustment for predictive variables. It is therefore important to investigate new factors which can influence the response to GH.

OBJECTIVE: To investigate the efficacy of GH treatment (1 mg/m<sup>2</sup>/ day) in short SGA children on AH. To assess the relation between spontaneous catch-up growth after birth and growth during puberty on the total height gain SDS to AH.

PATIENTS: Longitudinal GH trial in 170 children.

RESULTS: Median age at start of GH was 7.1 years and height -3.0 SDS. AH was -1.8 SDS (TH-corrected AH -1.1 SDS) in boys, and -1.9 SDS (TH-corrected AH -1.3 SDS) in girls. Spontaneous catch-up growth after birth was =0.5 SDS in 42% of children. In contrast to expectation, spontaneous catch-up growth was negatively correlated with total height gain SDS during GH (P=0.009). During puberty, height SDS declined (-0.4 SDS in boys and -0.5 SDS in girls) resulting in a lower total height gain SDS than expected. Pubertal height gain was 25.5 cm in boys and 15.3 cm in girls, significantly lower compared to AGA children (P<0.001). At onset of puberty, BA for boys and girls was moderately advanced (P=0.02 and P<0.001, respectively). Growth velocity was comparable to AGA children during the first two years of puberty, but thereafter significantly lower until reaching AH (P<0.001).

CONCLUSION: In contrast to our hypothesis, children with greater spontaneous catch-up growth after birth show a lower total height gain SDS during GH. Height SDS declines from mid-puberty, due to a marked early deceleration of growth velocity.

*impactfactor:* 3.457

## **Pelleboer RA**

### **Adalimumab therapy in children with crohn disease previously treated with infliximab**

Cozijnsen M, Duif V, Kokke F, Kindermann A, van Rheenen P, de Meij T, Schaart M, Damen G, Norbruis O, Pelleboer R\*, Van den Neucker A, van Wering H, Hummel T, Oudshoorn J, Escher J, de Ridder L; Dutch PIBD Working Group Kids with Crohn and Colitis

J Pediatr Gastroenterol Nutr. 2015 Feb;60(2):205-10

OBJECTIVES: Adalimumab, a humanised anti-tumour necrosis factor antibody, is an effective treatment in adult patients with refractory Crohn disease (CD). The available literature on its efficacy in children remains limited. We aimed to evaluate the real-world efficacy in paediatric patients with CD and compare the efficacy between infliximab (IFX) nonresponders and patients who lost response to IFX. METHODS: All Dutch patients with CD

receiving adalimumab before the age of 18 years after previous IFX therapy were identified. We analysed longitudinal disease activity, assessed by the mathematically weighted Pediatric Crohn's Disease Activity Index (wPCDAI) or the physician global assessment (PGA), and adverse events (AEs). RESULTS: Fifty-three patients with CD were included. Twelve patients received monotherapy and the others received combination treatment with thiopurines (n=?21), methotrexate (n=?11), steroids (n=?7), or exclusive enteral nutrition (n=?2). Median follow-up was 12 months (interquartile range 5-23). Remission was reached in 34 patients (64%, wPCDAI?<?12.5 or PGA=?0) after a median of 3.3 months, and maintained by 50% for 2 years. Eleven patients (21%) reached response but not remission (decrease in wPCDAI=?17.5 or decrease in PGA). Eighteen patients (34%) failed adalimumab treatment because of nonresponse (n=?4), lost response (n=?11), or AEs (n=?3). More IFX nonresponders failed adalimumab treatment than patients who lost response to IFX (2/3 vs 8/34, hazard ratio 18.8, 95% confidence interval 1.1-303.6). Only 1 patient encountered a serious AE, a severe but nonfatal infection. CONCLUSIONS: In clinical practice, adalimumab induces remission in two-thirds of children with IFX refractory CD.

*impactfactor:* 2.625

## **Pelleboer RA**

### **Are Carbohydrate-Deficient Transferrin Assays Useful for the Detection of Recurrent 'Binge Drinking' in Children with an Alcohol Intoxication in the Emergency Department?**

Stokbroekx MA\*, Houterman S\*, Coolen SA, van der Lely N, Pelleboer RA\*

Alcohol Alcohol. 2014 Nov;49(6):635-8. Epub 2014 Sep 15

*Voor abstract zie: Kindergeneeskunde - Stokbroekx, MA*

*impactfactor:* 2.889

## **Stokbroekx, MA**

### **Are Carbohydrate-Deficient Transferrin Assays Useful for the Detection of Recurrent 'Binge Drinking' in Children with an Alcohol Intoxication in the Emergency Department?**

Stokbroekx MA\*, Houterman S\*, Coolen SA, van der Lely N, Pelleboer RA\*

Alcohol Alcohol. 2014 Nov;49(6):635-8. Epub 2014 Sep 15

AIMS: The aim of this study was to evaluate different carbohydrate-deficient transferrin (CDT) assays for the detection of recurrent excessive alcohol abuse in adolescents prior to acute alcohol intoxication. METHODS: Data on drinking behaviour and CDT levels of adolescents (13-18 years) registered at the outpatient clinic for youth and alcohol at three major district general hospitals in the Netherlands were retrospectively collected. CDT and disialotransferrin (DST) levels of binge-drinking teenagers were compared with non-binge-drinking teenagers. RESULTS: In total 198 samples were collected for the N Latex CDT method (N = 83), no differences were found in mean CDT levels for binge versus non-binge drinkers (P = 0.8). The Helander HPLC (N = 78) showed significantly higher values for binge drinkers than for non-binge drinkers (mean 1.20%DST, SD 0.28 and mean 1.01%DST, SD 0.31, respectively (P = 0.01)). The Recipe ClinRep method (N = 37) also showed significantly higher values for binge drinkers (mean 1.17%DST, SD 0.36 and mean 0.89%DST, SD 0.34, respectively (P = 0.03)). CONCLUSION: With the Helander HPLC method and the Recipe ClinRep assay higher levels are measured in binge drinkers than in non-binge drinkers.

*In 2015 is pas bekend geworden dat dit artikel in November 2014 is verschenen*

*impactfactor:* 2.889

\* = Werkzaam in het Catharina Ziekenhuis

## Klinische fysica

## **Arends AJ**

### **FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0**

Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, Verzijlbergen FJ, Barrington SF, Pike LC, Weber WA, Stroobants S, Delbeke D, Donohoe KJ, Holbrook S, Graham MM, Testanera G, Hoekstra OS, Zijlstra J, Visser E, Hoekstra CJ, Pruim J, Willemsen A, Arends B\*, Kotzerke J, Bockisch A, Beyer T, Chiti A, Krause BJ  
Eur J Nucl Med Mol Imaging. 2015 Feb;42(2):328-54

The purpose of these guidelines is to assist physicians in recommending, performing, interpreting and reporting the results of FDG PET/CT for oncological imaging of adult patients. PET is a quantitative imaging technique and therefore requires a common quality control (QC)/quality assurance (QA) procedure to maintain the accuracy and precision of quantitation. Repeatability and reproducibility are two essential requirements for any quantitative measurement and/or imaging biomarker. Repeatability relates to the uncertainty in obtaining the same result in the same patient when he or she is examined more than once on the same system. However, imaging biomarkers should also have adequate reproducibility, i.e. the ability to yield the same result in the same patient when that patient is examined on different systems and at different imaging sites. Adequate repeatability and reproducibility are essential for the clinical management of patients and the use of FDG PET/CT within multicentre trials. A common standardised imaging procedure will help promote the appropriate use of FDG PET/CT imaging and increase the value of publications and, therefore, their contribution to evidence-based medicine. Moreover, consistency in numerical values between platforms and institutes that acquire the data will potentially enhance the role of semiquantitative and quantitative image interpretation. Precision and accuracy are additionally important as FDG PET/CT is used to evaluate tumour response as well as for diagnosis, prognosis and staging. Therefore both the previous and these new guidelines specifically aim to achieve standardised uptake value harmonisation in multicentre settings.

*impactfactor:* 5.383

## **Dries W**

### **No prevention of radiotherapy-induced alopecia by scalp cooling**

van den Hurk C, de Beer F\*, Dries W\*, van de Sande I\*, Hermesen N\*, Breed W, van der Sangen M\*

Radiother Oncol. 2015 Oct;117(1):193-4

*Geen abstract beschikbaar*

*impactfactor:* 4.363

## **Haaren PM van**

### **A comprehensive evaluation of treatment accuracy, including end-to-end tests and clinical data, applied to intracranial stereotactic radiotherapy**

Seravalli E, van Haaren PM\*, van der Toorn PP\*, Hurkmans CW\*

Radiother Oncol. 2015 Jul;116(1):131-8

**BACKGROUND AND PURPOSE:** A methodology is presented to quantify the uncertainty associated with linear accelerator-based frameless intracranial stereotactic radiotherapy (SRT) combining end-to-end phantom tests and clinical data.

**METHODS AND MATERIALS:** The following steps of the SRT chain were analysed: planning computed tomography (CT) and magnetic resonance (MR) scans registration, target volume delineation, CT and cone beam CT (CBCT) registration and intrafraction-patient

displacement. The overall accuracy was established with an end-to-end test. The measured uncertainties were combined, deriving the total systematic (ST) and random (sT) error components, to estimate the GTV-PTV margin.

**RESULTS:** The uncertainty in the MR-CT registration was on average 0.40mm (averaged over AP, CC and LR directions). Rotational variations were smaller than 0.5° in all directions. Interobserver variation in GTV delineation was on average 0.29mm. The uncertainty in the CBCT-CT registration was on average 0.15mm. Again, rotational variations were smaller than 0.5° in all directions. The systematic and random intrafraction displacement errors were on average 0.55mm and 0.45mm, respectively. The systematic and random positional errors from the end-to-end test were on average 0.49mm and 0.53mm, respectively. Combining these uncertainties resulted in an average ST=0.9mm and sT=0.7mm and an average GTV-PTV margin of 2.8mm.

**CONCLUSION:** This comprehensive methodology including end-to-end tests enabled a GTV-PTV margin calculation considering all sources of uncertainties. This generic method can also be used for other treatment sites.

*impactfactor:* 4.363

### **Hurkmans CW**

#### **A comprehensive evaluation of treatment accuracy, including end-to-end tests and clinical data, applied to intracranial stereotactic radiotherapy**

Seravalli E, van Haaren PM\*, van der Toorn PP\*, Hurkmans CW\*

Radiother Oncol. 2015 Jul;116(1):131-8

*Voor abstract zie:* KFD - Haaren PM van

*impactfactor:* 4.363

### **Hurkmans CW**

#### **In Regard to Koshy et al**

Levy A, Guckenberger M, Hurkmans C\*, Nestle U, Belderbos J, De Ruyscher D, Faivre-Finn C, Le Pécoux C

Int J Radiat Oncol Biol Phys. 2015 Jul 15;92(4):945-6.

*geen abstract beschikbaar*

*impactfactor:* 4.258

### **Hurkmans CW**

#### **Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59

*Voor abstract zie:* Chirurgie - Koëter M

*impactfactor:* 2.546

**Hurkmans CW**

**Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials**

Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, Groen HJ, McRae SE, Widder J, Feng L, van den Borne BE\*, Munsell MF, Hurkmans C\*, Berry DA, van Werkhoven E, Kresl JJ, Dingemans AM, Dawood O, Haasbeek CJ, Carpenter LS, De Jaeger K\*, Komaki R, Slotman BJ, Smit EF, Roth JA  
Lancet Oncol. 2015 Jun;16(6):630-7. Epub 2015 May 13.

Voor abstract zie: Longgeneeskunde - Borne BE van den  
impactfactor: 24.690

**Hurkmans CW**

**SU-E-P-22: AAPM Task Group 263 Tackling Standardization of Nomenclature for Radiation Therapy**

Matuszak M, Moran J, Xiao Y, Mayo , Bosch W, Popple R, Marks L, Wu Q, Molineu A, Miller R, Yock T, McNutt T, Brown N, Purdie T, Yorke E, Santanam L, Gabriel P, Michalski J, Moore J, Richardson S, Siochi R, Napalitano M, Ulin K, Fitzgerald T, Feng M, Verbakel W, Siddiqui S, Morgas T, Martel M, Archambault Y, Ladra M, Lansing B, Ruo R, Fogliata-Cozzi A, Hurkmans C\*  
Med Phys. 2015 Jun;42(6):3231

**PURPOSE:** There is growing recognition of need for increased clarity and consistency in the nomenclatures used for body and organ structures, DVH metrics, toxicity, dose and volume units, etc. Standardization has multiple benefits; e.g. facilitating data collection for clinical trials, enabling the pooling of data between institutions, making transfers (i.e. hand-offs) between centers safer, and enabling vendors to define "default" settings. Towards this goal, the American Association of Physicists in Medicine (AAPM) formed a task group (TG263) in July of 2014, operating under the Work Group on Clinical Trials to develop consensus statements. Guiding principles derived from the investigation and example nomenclatures will be presented for public feedback.

**METHODS:** We formed a multi-institutional and multi-vendor collaborative group of 39 physicists, physicians and others involved in clinical use and electronic transfer of information. Members include individuals from IROC, NRG, IHE-RO, DICOM WG-7, ASTRO and EORTC groups with overlapping interests to maximize the quality of the consensus and increase the likelihood of adoption. Surveys of group and NRG members were used to define current nomenclatures and requirements. Technical requirements of vendor systems and the proposed DICOM standards were examined.

**RESULTS:** There is a marked degree of inter and intra institutional variation in current approaches, resulting from inter-vendor differences in capabilities, clinic specific conceptualizations and inconsistencies. Using a consensus approach, the group defined optimal formats for the naming of targets and normal structures. A formal objective assessment of 13 existing clinically-used software packages show that all had capabilities to accommodate these recommended nomenclatures.

**CONCLUSIONS:** A multi-stakeholder effort is making significant steps forward in developing a standard nomenclature that will work across platforms. Our current working list includes > 550 structures. Outreach efforts are ongoing to ensure broader participation in evaluating and testing the principles as they are developed by TG263.

impactfactor: 2.635



## **Lagerburg V**

### **Contact heat evoked potentials: Normal values and use in small fiber neuropathy**

Lagerburg V\*, Bakkers M, Bouwhuis A, Hoeijmakers JG, Smit AM, van den Berg SJ, Hordijk-de Boer I, Brouwer-van der Lee MD, Kranendonk D, Reulen JP, Faber CG, Merkies IS

Muscle Nerve. 2015 May;51(5):743-9

Introduction: Contact heat-evoked potentials (CHEPs) may be an objective, non-invasive diagnostic tool in small fiber neuropathy (SFN). This study provides CHEP normal values and examines its applicability in SFN patients. Methods: Standardized CHEPs (Medoc<sup>®</sup>, Ramat Yishai, Israel) were administered at the wrist and ankle. The N2 and P2 latencies and N2-P2-peak-peak-amplitude were recorded through EEG. Healthy subjects (97), stratified by age and gender, and SFN patients with abnormal intraepidermal nerve fiber density (42), were examined. CHEP reproducibility and inter-observer values were investigated. Results: CHEP normative values were determined. There was a 9-16% increase in latencies/cm height with increasing age. Amplitudes were higher in women than men, and decreased (17-71%) with aging. Test-retest reproducibility and interobserver values were >0.61 and > 0.96, respectively. In 73.8% of the patients, CHEPs were abnormal. Conclusion: This study provides normal values, reliability, and clinical applicability of CHEPs in SFN.

impactfactor: 2.283

## **Lagerburg V**

### **The organizational and clinical impact of integrating bedside equipment to an information system: A systematic literature review of patient data management systems (PDMS)**

Cheung A\*, van Velden FH, Lagerburg V\*, Minderman N\*

Int J Med Inform. 2015 Mar;84(3):155-165

Voor abstract zie: ICMT - Cheung A

impactfactor: 2.004

## **Schuring D**

### **Probabilistic evaluation of target dose deterioration in dose painting by numbers for stage II/III lung cancer**

Fontanarosa D, Witte M, Meijer G, Shakirin G, Steenhuijsen J, Schuring D\*, van Herk M, Lambin P

Pract Radiat Oncol. 2015 Jul-Aug;5(4):e375-82. Epub 2015 Feb 11

PURPOSE: Non-small cell lung cancer is typically irradiated with 60-66 Gy in 2-Gy fractions. Local control could be improved by increasing dose to the more radiation-resistant areas (eg, based on the standardized uptake values of a pretreatment [18F]fluoro-deoxyglucose positron emission tomography scan). Such dose painting approaches, however, are poorly suited for a conventional planning target volume margin expansion; therefore, typically no margins are used. This study investigates dose deterioration of a dose painting by numbers (DPBN) approach resulting from geometrical uncertainties.

METHODS AND MATERIALS: For 9 DPBN plans of stage II/III non-small cell lung cancer patients, the boost dose was escalated up to 130 Gy (in 33 fractions) or until a dose-limiting constraint was reached. Then, using Monte Carlo methods, a probabilistic evaluation of dose endpoints for 99%, 98%, and 2% of gross tumor volume at a 90% confidence level was performed considering 8 different combinations of systematic (?) and random (s) geometric error distributions.

RESULTS: Important underdosages, because of geometric uncertainties, of up to 38 Gy with minimal image guidance occur, reducing to 8 Gy with the highest level of image guidance, for a patient where a maximum dose of 119 Gy could be achieved. The evaluation showed that systematic errors had the largest influence. The effects of the uncertainties are most evident where the dose or its gradient is high.

CONCLUSIONS: Probabilistic evaluation showed that the geometric uncertainties have a large effect and should be evaluated before approving DPBN plans.

*impactfactor:* --

## **Schuring D**

### **Quality assurance for the EORTC 22071-26071 study: dummy run prospective analysis**

Fairchild A, Langendijk JA, Nuyts S, Scrase C, Tomsej M, Schuring D\*, Gulyban A, Ghosh S, Weber DC, Budach W

Radiat Oncol. 2014 Nov 26;9:248

PURPOSE: The phase III 22071-26071 trial was designed to evaluate the addition of panitumumab to adjuvant chemotherapy plus intensity modulated radiotherapy (IMRT) in locally advanced resected squamous cell head and neck cancer. We report the results of the dummy run (DR) performed to detect deviations from protocol guidelines.

METHODS AND MATERIALS: DR datasets consisting of target volumes, organs at risk (OAR) and treatment plans were digitally uploaded, then compared with reference contours and protocol guidelines by six central reviewers. Summary statistics and analyses of potential correlations between delineations and plan characteristics were performed.

RESULTS: Of 23 datasets, 20 (87.0%) GTVs were evaluated as acceptable/borderline, along with 13 (56.5%) CTVs and 10 (43.5%) PTVs. All PTV dose requirements were met by 73.9% of cases. Dose constraints were met for 65.2-100% of mandatory OARs. Statistically significant correlations were observed between the subjective acceptability of contours and the ability to meet dose constraints for all OARs ( $p \leq 0.01$ ) except for the parotids and spinal cord. Ipsilateral parotid doses correlated significantly with CTV and PTV volumes ( $p \leq 0.05$ ).

CONCLUSIONS: The observed wide variations in treatment planning, despite strict guidelines, confirms the complexity of development and quality assurance of IMRT-based multicentre studies for head and neck cancer.

*impactfactor:* 2.546

## **Vries A de**

### **Quantitative Spectral K-Edge Imaging in Preclinical Photon-Counting X-ray Computed Tomography**

de Vries A\*, Roessl E, Kneepkens E, Thran A, Brendel B, Martens G,

Proska R, Nicolay K, Gröll H.

Invest Radiol. 2015 Apr;50(4):297-304

OBJECTIVES: The objective of this study was to investigate the feasibility and the accuracy of spectral computed tomography (spectral CT) to determine the tissue concentrations and localization of high-attenuation, iodine-based contrast agents in mice. Iodine tissue concentrations determined with spectral CT are compared with concentrations measured with single-photon emission computed tomography (SPECT) and inductively coupled plasma mass spectrometry (ICP-MS).

MATERIALS AND METHODS: All animal procedures were performed according to the US National Institutes of Health principles of laboratory animal care and were approved by the ethical review committee of Maastricht, The Netherlands. Healthy Swiss mice ( $n = 4$ ) were injected with an iodinated emulsion radiolabeled with indium as multimodal contrast agent

for CT and SPECT. The CT and SPECT scans were acquired using a dedicated small-animal SPECT/CT system. Subsequently, scans were performed with a preclinical spectral CT scanner equipped with a photon-counting detector and 6 energy threshold levels. Quantitative data analysis of SPECT and spectral CT scans were obtained using 3-dimensional volumes-of-interest drawing methods. The ICP-MS on dissected organs was performed to determine iodine uptake per organ and was compared with the amounts determined from spectral CT and SPECT.

RESULTS: Iodine concentrations obtained with image-processed spectral CT data correlated well with data obtained either with noninvasive SPECT imaging (slope = 0.96,  $r = 0.75$ ) or with ICP-MS (slope = 0.99,  $r = 0.89$ ) in tissue samples.

CONCLUSIONS: This preclinical proof-of-concept study shows the in vivo quantification of iodine concentrations in tissues using spectral CT. Our multimodal imaging approach with spectral CT and SPECT using radiolabeled iodinated emulsions together with ICP-based quantification allows a direct comparison of all methods. Benchmarked against ICP-MS data, spectral CT in the present implementation shows a slight underestimation of organ iodine concentrations compared with SPECT but with a more narrow distribution. This slight deviation is most likely caused by experimental rather than technical issues.

*impactfactor:* 4.437

**Kwaliteit**

Schulz DN

### **Impact of Educational Level on Study Attrition and Evaluation of Web-Based Computer-Tailored Interventions: Results From Seven Randomized Controlled Trials**

Reinwand DA, Crutzen R, Elfeddali I, Schneider F, Schulz DN\*, Stanczyk NE, Tange H, Voncken-Brewster V, Walthouwer MJ, Hoving C, de Vries H

J Med Internet Res. 2015 Oct 7;17(10):e228

BACKGROUND: Web-based computer-tailored interventions have shown to be effective in improving health behavior; however, high dropout attrition is a major issue in these interventions.

OBJECTIVE: The aim of this study is to assess whether people with a lower educational level drop out from studies more frequently compared to people with a higher educational level and to what extent this depends on evaluation of these interventions.

METHODS: Data from 7 randomized controlled trials of Web-based computer-tailored interventions were used to investigate dropout rates among participants with different educational levels. To be able to compare higher and lower educated participants, intervention evaluation was assessed by pooling data from these studies. Logistic regression analysis was used to assess whether intervention evaluation predicted dropout at follow-up measurements.

RESULTS: In 3 studies, we found a higher study dropout attrition rate among participants with a lower educational level, whereas in 2 studies we found that middle educated participants had a higher dropout attrition rate compared to highly educated participants. In 4 studies, no such significant difference was found. Three of 7 studies showed that participants with a lower or middle educational level evaluated the interventions significantly better than highly educated participants ("Alcohol-Everything within the Limit":  $F_{2,376}=5.97$ ,  $P=.003$ ; "My Healthy Behavior":  $F_{2,359}=5.52$ ,  $P=.004$ ; "Master Your Breath":  $F_{2,317}=3.17$ ,  $P=.04$ ). One study found lower intervention evaluation by lower educated participants compared to participants with a middle educational level ("Weight in Balance":  $F_{2,37}=3.17$ ,  $P=.05$ ). Low evaluation of the interventions was not a significant predictor of dropout at a later follow-up measurement in any of the studies.

CONCLUSIONS: Dropout attrition rates were higher among participants with a lower or middle educational level compared with highly educated participants. Although lower educated participants evaluated the interventions better in approximately half of the studies, evaluation did not predict dropout attrition. Further research is needed to find other explanations for high dropout rates among lower educated participants.

*impactfactor:* 3.428

Schulz DN

### **Tailored eHealth Lifestyle Promotion: Which Behavioral Modules Do Users Prefer?**

Schulz DN\*, Kremers SP, De Vries H

J Health Commun. 2015;20(6):663-72

Health risk behaviors are widespread among adults and often co-occur. eHealth computer-tailored technology provides individuals with personalized feedback regarding multiple lifestyle behaviors. First, the authors investigated individuals' preferences for particular lifestyle modules and hypothesized that health preventive behavior modules would be preferred over addictive behavior modules. Second, characteristics associated with these choices were examined. A web-based questionnaire assessed demographics, health status, and five lifestyle behaviors (i.e., physical activity, fruit consumption, vegetable consumption, alcohol intake and tobacco use) among adults ( $N = 1,828$ ). Responses were translated into a health risk appraisal outlining whether respondents adhered to the national guidelines for

these behaviors. Next, respondents could select one of the lifestyle modules providing personalized advice. More than 60% of the participants failed to meet the guidelines for more than one lifestyle behavior. The physical activity module was the most popular, followed by the smoking and fruit modules. Young adults tended to prefer the physical activity and fruit modules, whereas the vegetable module was more popular among older adults. No consistent pattern was identified for the alcohol and smoking modules. The results support the authors' hypothesis that health preventive behaviors-in particular, physical activity-would be preferred. Although this could imply that physical activity could serve as a gateway behavior when aiming at multiple behavior changes, it is also conceivable that other mechanisms, such as the actual success of behavior change, or the fact that people can choose, may increase chances of multiple behavior change. Hence, mechanisms leading to multiple behavior change need to be further explored.

*impactfactor:* 1.617

## Schulz DN

### **Who Follows eHealth Interventions as Recommended? A Study of Participants' Personal Characteristics From the Experimental Arm of a Randomized Controlled Trial Reinwand DA, Schulz DN\*, Crutzen R, Kremers SP, de Vries H**

J Med Internet Res. 2015 May 11;17(5):e115

**BACKGROUND:** Computer-tailored eHealth interventions to improve health behavior have been demonstrated to be effective and cost-effective if they are used as recommended. However, different subgroups may use the Internet differently, which might also affect intervention use and effectiveness. To date, there is little research available depicting whether adherence to intervention recommendations differs according to personal characteristics.

**OBJECTIVE:** The aim was to assess which personal characteristics are associated with using an eHealth intervention as recommended.

**METHODS:** A randomized controlled trial was conducted among a sample of the adult Dutch population (N=1638) testing an intervention aimed at improving 5 healthy lifestyle behaviors: increasing fruit and vegetable consumption, increasing physical activity, reducing alcohol intake, and promoting smoking cessation. Participants were asked to participate in those specific online modules for which they did not meet the national guideline(s) for the respective behavior(s). Participants who started with fewer than the recommended number of modules of the intervention were defined as users who did not follow the intervention recommendation.

**RESULTS:** The fewer modules recommended to participants, the better participants adhered to the intervention modules. Following the intervention recommendation increased when participants were older ( $\chi^2(2)=39.8$ ,  $P<.001$ ), female ( $\chi^2(2)=15.8$ ,  $P<.001$ ), unemployed ( $\chi^2(2)=7.9$ ,  $P=.003$ ), ill ( $\chi^2(2)=4.5$ ,  $P=.02$ ), or in a relationship ( $\chi^2(2)=7.8$ ,  $P=.003$ ). No significant irrelevant differences were found between groups with different levels of education, incomes, or quality of life.

**CONCLUSION:** Our findings indicate that eHealth interventions were used differently by subgroups. The more frequent as-recommended intervention use by unemployed, older, and ill participants may be an indication that these eHealth interventions are attractive to people with a greater need for health care information. Further research is necessary to make intervention use more attractive for people with unhealthy lifestyle patterns.

*impactfactor:* 3.428

\* = Werkzaam in het Catharina Ziekenhuis

## Longgeneeskunde

**Borne BE van den**

**A randomized phase II study comparing paclitaxel-carboplatin-bevacizumab with or without nitroglycerin patches in patients with stage IV nonsquamous non-small-cell lung cancer: NVALT12 (NCT01171170)†**

Dingemans AC, Groen HJ, Herder GJ, Stigt JA, Smit EF, Bahce I, Burgers JA, van den Borne BE\*, Biesma B, Vincent A, van der Noort V, Aerts JG; NVALT study group

Ann Oncol. 2015 Nov;26(11):2286-93. Epub 2015 Sep

**BACKGROUND:** Nitroglycerin (NTG) increases tumor blood flow and oxygenation by inhibiting hypoxia-inducible-factor (HIF)-1. A randomized phase II study has shown improved outcome when NTG patches were added to vinorelbine/cisplatin in patients with advanced non-small-cell lung cancer (NSCLC). In addition, there is evidence that the combination of bevacizumab and HIF-1 inhibitors increases antitumor activity.

**PATIENTS AND METHODS:** In this randomized phase II trial, chemo-naïve patients with stage IV nonsquamous NSCLC were randomized to four cycles of carboplatin (area under the curve 6)-paclitaxel (200 mg/m<sup>2</sup>)-bevacizumab 15 mg/kg on day 1 every 3 weeks with or without NTG patches 15 mg (day -2 to +2) followed by bevacizumab with or without NTG until progression. Response was assessed every two cycles. Primary end point was progression-free survival (PFS). The study was powered (80%) to detect a decrease in the hazard of tumor progression of 33% at  $\alpha = 0.05$  with a two-sided log-rank test when 222 patients were enrolled and followed until 195 events were observed.

**RESULTS:** Between 1 January 2011 and 1 January 2013, a total of 223 patients were randomized; 112 control arm and 111 experimental arm; response rate was 54% in control arm and 38% in experimental arm. Median [95% confidence interval (CI)] PFS in control arm was 6.8 months (5.6-7.3) and 5.1 months (4.2-5.8) in experimental arm, hazard ratio (HR) 1.27 (95% CI 0.96-1.67). Overall survival (OS) was 11.6 months (8.8-13.6) in control arm and 9.4 months (7.8-11.3) in experimental arm, HR 1.02 (95% CI 0.71-1.46). In the experimental arm, no additional toxicity was observed except headache (6% versus 52% in patients treated with NTG).

**CONCLUSION:** Adding NTG to first-line carboplatin-paclitaxel-bevacizumab did not improve PFS and OS in patients with stage IV nonsquamous NSCLC.

*impactfactor: 7.040*

**Borne BE van den**

**Comorbidity in Patients With Small-Cell Lung Cancer: Trends and Prognostic Impact**

Aarts MJ, Aerts JG, van den Borne BE\*, Biesma B, Lemmens VE, Kloover JS

Clin Lung Cancer. 2015 Jul;16(4):282-91. Epub 2014 Dec 11

**INTRODUCTION:** We evaluated the trends in the prevalence of comorbidity and its prognostic impact in a cohort of unselected patients with small-cell lung cancer (SCLC).

**PATIENTS AND METHODS:** All patients ( $n = 4142$ ) diagnosed with SCLC from 1995 to 2012 were identified from the population-based Netherlands Cancer Registry in the Eindhoven region.

**RESULTS:** The prevalence of comorbidity increased from 55% in 1995 to 1998 to 76% in 2011 to 2012 and multimorbidity (ie,  $\geq 2$  concomitant diseases) from 23% to 51%. The prevalence of a comorbidity increased with age. Among the men, hypertension, cardiac disease, and diabetes, in particular, became more common (increased from 11% to 35%, from 19% to 36%, and from 7% to 18%, respectively). In the women, the rate of pulmonary disease, hypertension, and cardiac disease increased the most (increased from 18% to 30%, from 12% to 28%, and from 11% to 24%, respectively). Multimorbidity was associated with a slightly increased hazard of death, independent of treatment in those with limited-stage



SCLC (hazard ratio [HR] for = 2 comorbidities vs. no comorbidities, 1.2; 95% confidence interval [CI], 1.0-1.4). The prognostic effects of multimorbidity resulted from treatment in those with extensive-stage SCLC (HR for = 2 comorbidities vs. no comorbidities, final model, 1.2; 95% CI, 1.0-1.2). The prognostic impact of the specific comorbidities varied, with digestive disease reducing the hazard and cardiac disease increasing the hazard in those with limited-stage SCLC (HR for digestive disease vs. no digestive disease, 0.7 [95% CI, 0.5-0.9], and HR for cardiac vs. no cardiac disease, 1.2 [95% CI, 1.0-1.3]). Also, cardiac and cerebrovascular disease increased the hazard in those with extensive-stage SCLC (HR 1.2 [95% CI, 1.0-1.3] and HR 1.3 [95% CI, 1.1-1.6], respectively).

**CONCLUSION:** Comorbidity among patients with SCLC is very common and has been increasing. Multimorbidity was associated with a slightly increased hazard of death in those with limited-stage SCLC, independent of treatment. However, the prognostic effects in those with advanced-stage SCLC resulted from treatment. Digestive disease favorably affected survival and cardiac disease negatively affected the prognosis for those with limited-stage SCLC, and cardiac and cerebrovascular diseases had a negative prognostic effect for those with extensive-stage SCLC. With the burden of comorbidities in patients with SCLC increasing, more attention to individualized treatment approaches is needed.

*impactfactor:* 3.104

## **Borne BE van den**

### **Comparison of clinical outcome after first-line platinum-based chemotherapy in different types of KRAS mutated advanced non-small-cell lung cancer**

Mellema WW, Masen-Poos L, Smit EF, Hendriks LE, Aerts JG, Termeer A, Goosens MJ, Smit HJ, van den Heuvel MM, van der Wekken AJ, Herder GJ, Krouwels FH, Stigt JA, van den Borne BE\*, Haitjema TJ, Staal-Van den Brekel AJ, van Heemst RC, Pouw E, Dingemans AC

Lung Cancer. 2015 Nov;90(2):249-54. Epub 2015 Sep 15

**OBJECTIVES:** As suggested by in-vitro data, we hypothesize that subtypes of KRAS mutated non-small cell lung cancer (NSCLC) respond differently to chemotherapy regimens. **METHODS:** Patients with advanced NSCLC and known KRAS mutation, treated with first-line platinum-based chemotherapy, were retrieved from hospital databases. **PRIMARY OBJECTIVE:** to investigate overall response rate (ORR), progression free survival (PFS) and overall survival (OS) between different types of platinum-based chemotherapy per type of KRAS mutation.

**RESULTS:** 464 patients from 17 hospitals, treated between 2000 and 2013, were included. The majority of patients had stage IV disease (93%), had a history of smoking (98%) and known with an adenocarcinoma (91%). Most common types of KRAS mutation were G12C (46%), G12V (20%) and G12D (10%). Platinum was combined with pemetrexed (n=334), taxanes (n=68) or gemcitabine (n=62). Patients treated with taxanes had a significant improved ORR (50%) compared to pemetrexed (21%) or gemcitabine (25%; p<0.01). Patients treated with bevacizumab in addition to taxanes (n=38) had the highest ORR (62%). The PFS was significantly improved in patients treated with taxanes compared to pemetrexed (HR=0.72, p=0.02), but not OS (HR=0.87, p=0.41). In patients with G12V, significantly improved ORR (p<0.01) was observed for taxanes, but not PFS or OS. Patients with G12C or G12D mutation had comparable ORR, PFS and OS in all treatment groups. **CONCLUSION:** KRAS mutated NSCLC patients treated with taxane-based chemotherapy had best ORR. Response to chemotherapy regimens was different in types of KRAS mutation. Especially patients with G12V had better response to taxane treatment.

*impactfactor:* 3.958

**Borne BE van den**

### **Improvement in population-based survival of stage IV NSCLC due to increased use of chemotherapy**

Aarts MJ, van den Borne BE\*, Biesma B, Kloover JS, Aerts JG, Lemmens VE

Int J Cancer. 2015 Mar 1;136(5):E387-95

This study aimed to investigate which factors were associated with the administration of chemotherapy for patients with stage IV non-small cell lung cancer (NSCLC), and their relation to survival at a population-based level. All patients with NSCLC stage IV from 2001 to 2012 were identified in the Netherlands Cancer Registry in the Eindhoven area (n=75,428). Chemotherapy use and survival were evaluated by logistic and Cox regression analyses, respectively. The proportion of patients receiving chemotherapy increased from 30% in 2001 to 48% in 2012. Higher rates were found among younger patients [multivariable odds ratio (OR=64\_ vs . \_=75\_years) : 1.8 (95%CI 1.6-2.1)], high socioeconomic status [ORhigh\_ vs . \_low : 1.8 (95%CI 1.6-2.2)], no comorbidity [OR0\_ vs . \_=2 : 1.5 (95%CI 1.3-1.8)], diagnosed in recent years [OR2010-2012\_ vs . \_2001-2003 : 2.0 (95%CI 1.6-2.3)] and adenocarcinoma [ORsquamous\_ vs . \_adenocarcinoma : 0.8 (95%CI 0.6-0.9)]. Having liver metastasis was associated with reduced odds (ORliver\_ vs . \_brain : 0.8 (95%CI 0.7-1.0)). The variation between hospitals was large, up to OR 2.0 (95%CI 1.5-2.6). Median survival increased from 18 weeks in 2001-2003 to 21 weeks in 2010-2012 (log-rank p=0.007), and was 35 weeks in patients with and 10 weeks without chemotherapy. The multivariable hazard of death reduced significantly over time [HR2001-2003\_ vs . \_2010-2012 : 1.1 (95%CI 1.0-1.2), HR2004-2005\_ vs . \_2010-2012 : 1.2 (95%CI 1.1-1.3)] and only remained significant for 2004-2006 after additional adjustment for chemotherapy [final multivariable model, HR2004-2006\_ vs . \_2010-2012 : 1.1 (95%CI 1.0-1.2)]. Besides, prognostic factors were having chemotherapy [final multivariable model: HR 0.4 (95%CI 0.4-0.4)], female sex [HRmale\_ vs . \_female : 1.1 (95%CI 1.0-1.1)], socioeconomic status [HRintermediate\_and\_high\_ vs . \_low both 0.9 (95%CI 0.9-1.0)], comorbidity [HRunknown\_ vs . \_=2 : 1.3 (95%CI 1.2-1.5)], histology [HRother\_ vs . \_adenocarcinoma : 1.1 (95%CI 1.1-1.2)], and location of metastasis [range: 1.2 (HRlymph\_nodes\_ vs . \_brain) - 1.6 (HRliver\_ vs . \_brain)]. In conclusion, population-based survival increased due to increasing administration rates of chemotherapy. The administration of chemotherapy was affected by hospital of diagnosis and both patient and tumour characteristics. Identifying patients who benefit from chemotherapy should become a key issue.

*impactfactor:* 5.085

**Borne BE van den**

### **Patient reported outcomes following stereotactic ablative radiotherapy or surgery for stage IA non-small-cell lung cancer: Results from the ROSEL multicenter randomized trial**

Louie AV, van Werkhoven E, Chen H, Smit E, Paul MA, Widder J, Groen HJ, van den Borne BE\*, De Jaeger K\*, Slotman BJ, Senan S

Radiother Oncol. 2015 Oct;117(1):44-8

We report quality of life and indirect costs from patient reported outcomes from the ROSEL randomized control trial comparing stereotactic ablative radiotherapy (SABR, also known as stereotactic body radiotherapy or SBRT) versus surgical resection for medically operable stage IA non-small cell lung cancer.

ROSEL closed prematurely after accruing and randomizing 22 patients. This exploratory analysis found the global health related quality of life and indirect costs to be significantly favorable and cheaper, with SABR.

*impactfactor:* 4.363

## **Borne BE van den**

### **Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials.**

Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, Groen HJ, McRae SE, Widder J, Feng L, van den Borne BE\*, Munsell MF, Hurkmans C\*, Berry DA, van Werkhoven E, Kresl JJ, Dingemans AM, Dawood O, Haasbeek CJ, Carpenter LS, De Jaeger K\*, Komaki R, Slotman BJ, Smit EF, Roth JA

Lancet Oncol. 2015 Jun;16(6):630-7. Epub 2015 May 13

**BACKGROUND:** The standard of care for operable, stage I, non-small-cell lung cancer (NSCLC) is lobectomy with mediastinal lymph node dissection or sampling. Stereotactic ablative radiotherapy (SABR) for inoperable stage I NSCLC has shown promising results, but two independent, randomised, phase 3 trials of SABR in patients with operable stage I NSCLC (STARS and ROSEL) closed early due to slow accrual. We aimed to assess overall survival for SABR versus surgery by pooling data from these trials. **METHODS:** Eligible patients in the STARS and ROSEL studies were those with clinical T1-2a (<4 cm), N0M0, operable NSCLC. Patients were randomly assigned in a 1:1 ratio to SABR or lobectomy with mediastinal lymph node dissection or sampling. We did a pooled analysis in the intention-to-treat population using overall survival as the primary endpoint. Both trials are registered with ClinicalTrials.gov (STARS: NCT00840749; ROSEL: NCT00687986). **FINDINGS:** 58 patients were enrolled and randomly assigned (31 to SABR and 27 to surgery). Median follow-up was 40.2 months (IQR 23.0-47.3) for the SABR group and 35.4 months (18.9-40.7) for the surgery group. Six patients in the surgery group died compared with one patient in the SABR group. Estimated overall survival at 3 years was 95% (95% CI 85-100) in the SABR group compared with 79% (64-97) in the surgery group (hazard ratio [HR] 0.14 [95% CI 0.017-1.190], log-rank p=0.037). Recurrence-free survival at 3 years was 86% (95% CI 74-100) in the SABR group and 80% (65-97) in the surgery group (HR 0.69 [95% CI 0.21-2.29], log-rank p=0.54). In the surgery group, one patient had regional nodal recurrence and two had distant metastases; in the SABR group, one patient had local recurrence, four had regional nodal recurrence, and one had distant metastases. Three (10%) patients in the SABR group had grade 3 treatment-related adverse events (three [10%] chest wall pain, two [6%] dyspnoea or cough, and one [3%] fatigue and rib fracture). No patients given SABR had grade 4 events or treatment-related death. In the surgery group, one (4%) patient died of surgical complications and 12 (44%) patients had grade 3-4 treatment-related adverse events. Grade 3 events occurring in more than one patient in the surgery group were dyspnoea (four [15%] patients), chest pain (four [15%] patients), and lung infections (two [7%]). **INTERPRETATION:** SABR could be an option for treating operable stage I NSCLC. Because of the small patient sample size and short follow-up, additional randomised studies comparing SABR with surgery in operable patients are warranted.

*impactfactor:* 24.690

**Borne BE van den**

**Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials**

Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, Groen HJ, McRae SE, Widder J, Feng L, van den Borne BE\*, Munsell MF, Hurkmans C\*, Berry DA, van Werkhoven E, Kresl JJ, Dingemans AM, Dawood O, Haasbeek CJ, Carpenter LS, De Jaeger K\*, Komaki R, Slotman BJ, Smit EF, Roth JA

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**METHODS:** Eligible patients in the STARS and ROSEL studies were those with clinical T1-2a (<4 cm), N0M0, operable NSCLC. Patients were randomly assigned in a 1:1 ratio to SABR or lobectomy with mediastinal lymph node dissection or sampling. We did a pooled analysis in the intention-to-treat population using overall survival as the primary endpoint. Both trials are registered with ClinicalTrials.gov (STARS: NCT00840749; ROSEL: NCT00687986).

**FINDINGS:** 58 patients were enrolled and randomly assigned (31 to SABR and 27 to surgery). Median follow-up was 40.2 months (IQR 23.0-47.3) for the SABR group and 35.4 months (18.9-40.7) for the surgery group. Six patients in the surgery group died compared with one patient in the SABR group. Estimated overall survival at 3 years was 95% (95% CI 85-100) in the SABR group compared with 79% (64-97) in the surgery group (hazard ratio [HR] 0.14 [95% CI 0.017-1.190], log-rank  $p=0.037$ ). Recurrence-free survival at 3 years was 86% (95% CI 74-100) in the SABR group and 80% (65-97) in the surgery group (HR 0.69 [95% CI 0.21-2.29], log-rank  $p=0.54$ ). In the surgery group, one patient had regional nodal recurrence and two had distant metastases; in the SABR group, one patient had local recurrence, four had regional nodal recurrence, and one had distant metastases. Three (10%) patients in the SABR group had grade 3 treatment-related adverse events (three [10%] chest wall pain, two [6%] dyspnoea or cough, and one [3%] fatigue and rib fracture). No patients given SABR had grade 4 events or treatment-related death. In the surgery group, one (4%) patient died of surgical complications and 12 (44%) patients had grade 3-4 treatment-related adverse events. Grade 3 events occurring in more than one patient in the surgery group were dyspnoea (four [15%] patients), chest pain (four [15%] patients), and lung infections (two [7%]).

**INTERPRETATION:** SABR could be an option for treating operable stage I NSCLC. Because of the small patient sample size and short follow-up, additional randomised studies comparing SABR with surgery in operable patients are warranted.

*impactfactor:* 24.690

**Romme EA**

**Fracture prevention in COPD patients; a clinical 5-step approach**

Romme EA, Geusens P, Lems WF, Rutten EP, Smeenk FW\*, van den Bergh JP, van Hal PT, Wouters EF

Respir Res. 2015 Mar 7;16:32

Although osteoporosis and its related fractures are common in patients with COPD, patients at high risk of fracture are poorly identified, and consequently, undertreated. Since there are no fracture prevention guidelines available that focus on COPD patients, we developed a

clinical approach to improve the identification and treatment of COPD patients at high risk of fracture. We organised a round-table discussion with 8 clinical experts in the field of COPD and fracture prevention in the Netherlands in December 2013. The clinical experts presented a review of the literature on COPD, osteoporosis and fracture prevention. Based on the Dutch fracture prevention guideline, they developed a 5-step clinical approach for fracture prevention in COPD. Thereby, they took into account both classical risk factors for fracture (low body mass index, older age, personal and family history of fracture, immobility, smoking, alcohol intake, use of glucocorticoids and increased fall risk) and COPD-specific risk factors for fracture (severe airflow obstruction, pulmonary exacerbations and oxygen therapy). Severe COPD (defined as postbronchodilator FEV1 < 50% predicted) was added as COPD-specific risk factor to the list of classical risk factors for fracture. The 5-step clinical approach starts with case finding using clinical risk factors, followed by risk evaluation (dual energy X-ray absorptiometry and imaging of the spine), differential diagnosis, treatment and follow-up. This systematic clinical approach, which is evidence-based and easy-to-use in daily practice by pulmonologists, should contribute to optimise fracture prevention in COPD patients at high risk of fracture.

*impactfactor:* 3.093

## **Smeenk FW**

### **Differential response to pulmonary rehabilitation in COPD: multidimensional profiling**

Spruit MA, Augustin IM, Vanfleteren L, Janssen DJ, Gaffron S, Pennings HJ, Smeenk F\*, Pieters W, van den Bergh JJ, Michels AJ, Groenen MT, Rutten EP, Wouters EF, Franssen FM; CIRO+ Rehabilitation Network

Eur Respir J. 2015 Dec;46(6):1625-35

The aim of the present study was to profile a multidimensional response to pulmonary rehabilitation in patients with chronic obstructive pulmonary disease (COPD). Dyspnoea, exercise performance, health status, mood status and problematic activities of daily life were assessed before and after a 40-session pulmonary rehabilitation programme in 2068 patients with COPD (mean forced expiratory volume in 1 s of 49% predicted). Patients were ordered by their overall similarity concerning their multidimensional response profile, which comprises the overall response on MRC dyspnoea grade, 6MWD, cycle endurance time, Canadian Occupational Performance Measure performance and satisfaction scores, Hospital Anxiety and Depression Scale anxiety and depression, and St George's Respiratory Questionnaire total score, using a novel non-parametric regression technique. Patients were clustered into four groups with distinct multidimensional response profiles: n=378 (18.3%; "very good responder"), n=742 (35.9%; "good responder"), n=731 (35.4%; "moderate responder"), and n=217 (10.5%; "poor responder"). Patients in the "very good responder" cluster had higher symptoms of dyspnoea, number of hospitalisations <12 months, worse exercise performance, worse performance and satisfaction scores for problematic activities of daily life, more symptoms of anxiety and depression, worse health status, and a higher proportion of patients following an inpatient PR programme compared to the other three clusters. A multidimensional response outcome needs to be considered to study the efficacy of pulmonary rehabilitation services in patients with COPD, as responses to regular outcomes are differential within patients with COPD.

*impactfactor:* 7.636

**Smeenk FW**

**Effects of bariatric surgery on inspiratory muscle strength**

Pouwels S\*, Kools-Aarts M\*, Said M\*, Teijink JA\*, Smeenk FW\*, Nienhuijs SW\*  
Springerplus. 2015 Jul 7;4:322

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: --

**Smeenk FW**

**Fracture prevention in COPD patients; a clinical 5-step approach**

Romme EA, Geusens P, Lems WF, Rutten EP, Smeenk FW\*, van den Bergh JP, van Hal PT, Wouters EF Respir Res. 2015 Mar 7;16:32

Voor abstract zie: *Longgeneeskunde - Romme EA*

impactfactor: 3.093

**Smeenk FW**

**Identifying Physical Activity Profiles in COPD Patients Using Topic Models**

Spina G, Casale P, Albert PS, Alison J, Garcia-Aymerich J, Costello RW, Hernandez NA, van Gestel AJ, Leuppi JD, Mesquita R, Singh SJ, Smeenk FW\*, Tal-Singer R, Wouters EF, Spruit MA, den Brinker AC

IEEE J Biomed Health Inform. 2015 Sep;19(5):1567-76

With the growing amount of physical activity (PA) measures, the need for methods and algorithms that automatically analyze and interpret unannotated data increases. In this paper, PA is seen as a combination of multimodal constructs that can cooccur in different ways and proportions during the day. The design of a methodology able to integrate and analyze them is discussed, and its operation is illustrated by applying it to a dataset comprising data from COPD patients and healthy subjects acquired in daily life. The method encompasses different stages. The first stage is a completely automated method of labeling low-level multimodal PA measures. The information contained in the PA labels are further structured using topic modeling techniques, a machine learning method from the text processing community. The topic modeling discovers the main themes that pervade a large set of data. In our case, topic models discover PA routines that are active in the assessed days of the subjects under study. Applying the designed algorithm to our data provides new learnings and insights. As expected, the algorithm discovers that PA routines for COPD patients and healthy subjects are substantially different regarding their composition and moments in time in which transitions occur. Furthermore, it shows consistent trends relating to disease severity as measured by standard clinical practice.

impactfactor: 1.440

**Smeenk FW**

**Preoperative exercise therapy in lung surgery patients: A systematic review**

Pouwels S\*, Fiddelaers J, Teijink JA\*, Woorst JF\*, Siebenga J, Smeenk FW\*  
Respir Med. 2015 Dec;109(12):1495-504. Epub 2015 Aug 15

Voor abstract zie: *Chirurgie - Pouwels S*

impactfactor: 3.086

**Smeenk FW**

**Six-minute walk distance in patients with chronic obstructive pulmonary disease: Which reference equations should we use?**

Andrianopoulos V, Holland AE, Singh SJ, Franssen FM, Pennings HJ5, Michels AJ, Smeenk FW\*, Vogiatzis I, Wouters EF, Spruit MA

Chron Respir Dis. 2015 May;12(2):111-9

The use of different 6-min walk distance (6MWD) reference equations probably results in different predicted 6MWD reference values. We wished to investigate the impact of several 6MWD reference equations for adults in patients with chronic obstructive pulmonary disease (COPD) and factors accountable for different 6MWD% predicted values. Twenty-two 6MWD reference equations were applied to a data set of 2757 patients with COPD. The predicted 6MWD reference value of Troosters and colleagues was used as the point of reference. Four out of 21 remaining equations resulted in comparable 6MWD% predicted, 16 equations resulted in significantly higher 6MWD% predicted and 1 equation resulted in a significantly lower 6MWD% predicted. Similar differences in 6MWD% predicted were observed after stratification by sex. Body mass index and global initiative for chronic obstructive lung disease (GOLD) stage classification demonstrated varying results within and between the groups; 9 out of 21 equations resulted in comparable 6MWD% predicted in underweight patients but only 1 equation demonstrated comparable result in obese. Eight equations in GOLD I, whilst 5 out of 21 equations in GOLD IV resulted in comparable 6MWD% predicted. Existing 6MWD reference equations will give varying results. The choice of 6MWD reference equation should consider the consistency of 6-min walk test operating procedures and at least be specific for the country/region of origin.

impactfactor: 2.694

**Wielders PL**

**Population Pharmacokinetics and Pharmacodynamics of GSK961081 (Batefenterol), a Muscarinic Antagonist and  $\beta_2$ -Agonist, in Moderate-to-Severe COPD Patients: Substudy of a Randomized Trial**

Ambery CL, Wielders P\*, Ludwig-Sengpiel A, Chan R, Riley JH

Drugs R D. 2015 Sep;15(3):281-91

GSK961081 (batefenterol) is a novel bifunctional molecule composed of a muscarinic antagonist and a  $\beta_2$ -agonist. The aims of this substudy were (1) to characterize the population pharmacokinetics (PK) and pharmacodynamics (PD) of GSK961081 in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD); and (2) to investigate the relationship between systemic exposure to GSK961081 and key cardiac-related safety parameters. Three once-daily doses (100, 400, and 800  $\mu$ g) and three twice-daily doses (100, 200, and 400  $\mu$ g) of GSK961081 DISKUS were investigated. A two-compartment disposition PK model with first-order absorption adequately described the plasma GSK961081 concentration–time data. An empirical maximum-effects PD model adequately described the forced expiratory volume in 1 s (FEV1) response relationship with the covariate baseline FEV1 on day 1. No clear relationships between GSK961081 plasma drug levels and cardiac-related safety parameters were apparent. The PK and PD models will be used to guide the dose selection and development of GSK961081 in patients with COPD.

impactfactor: --

\* = Werkzaam in het Catharina Ziekenhuis

## **Maag-, Darm- en Leverziekten**



## Curvers WL

### **Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel.**

Duits LC, Phoa KN, Curvers WL<sup>∞</sup>, Ten Kate FJ, Meijer GA, Seldenrijk CA, Offerhaus GJ, Visser M, Meijer SL, Krishnadath KK, Tijssen JG, Mallant-Hent RC, Bergman JJ

Gut. 2015 May;64(5):700-6

**OBJECTIVE:** Reported malignant progression rates for low-grade dysplasia (LGD) in Barrett's oesophagus (BO) vary widely. Expert histological review of LGD is advised, but limited data are available on its clinical value. This retrospective cohort study aimed to determine the value of an expert pathology panel organised in the Dutch Barrett's Advisory Committee (BAC) by investigating the incidence rates of high-grade dysplasia (HGD) and oesophageal adenocarcinoma (OAC) after expert histological review of LGD.

**DESIGN:** We included all BO cases referred to the BAC for histological review of LGD diagnosed between 2000 and 2011. The diagnosis of the expert panel was related to the histological outcome during endoscopic follow-up. Primary endpoint was development of HGD or OAC. **RESULTS:** 293 LGD patients (76% men; mean 63 years±11.9) were included. Following histological review, 73% was downstaged to non-dysplastic BO (NDBO) or indefinite for dysplasia (IND). In 27% the initial LGD diagnosis was confirmed. Endoscopic follow-up was performed in 264 patients (90%) with a median follow-up of 39 months (IQR 16-72). For confirmed LGD, the risk of HGD/OAC was 9.1% per patient-year. Patients downstaged to NDBO or IND had a malignant progression risk of 0.6% and 0.9% per patient-year, respectively. **CONCLUSIONS:** Confirmed LGD in BO has a markedly increased risk of malignant progression. However, the vast majority of patients with community LGD will be downstaged after expert review and have a low progression risk. Therefore, all BO patients with LGD should undergo expert histological review of the diagnosis for adequate risk stratification.

<sup>∞</sup> = Ten tijde van publicatie werkzaam bij: Department of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

impactfactor: 14.66

## Curvers WL

### **Diagnosis by endoscopy and advanced imaging**

Swager A, Curvers WL<sup>∞</sup>, Bergman JJ

Best Pract Res Clin Gastroenterol. 2015 Feb;29(1):97-111

Evaluation of patients with Barrett's oesophagus (BO) using dye-based chromoendoscopy, optical chromoendoscopy, autofluorescence imaging, or confocal laser endomicroscopy does not significantly increase the number of patients with a diagnosis of early neoplasia compared with high-definition white light endoscopy (HD-WLE) with random biopsy analysis. These newer imaging techniques are not more effective in standard surveillance of patients with BO because the prevalence of early neoplasia is low and HD-WLE with random biopsy analysis detects most cases of neoplasia. The evaluation and treatment of patients with BO and early-stage neoplasia should be centralized in tertiary referral centers, where procedures are performed under optimal conditions, by expert endoscopists. Lesions that require resection are almost always detected by HD-WLE, although advanced imaging techniques can detect additional flat lesions. However, these are of limited clinical significance because they are effectively eradicated by ablation therapy. No endoscopic imaging technique can reliably assess submucosal or lymphangio-invasion. Endoscopic resection of early-stage neoplasia in patients with BO is important for staging and

management. Optical chromoendoscopy can also be used to evaluate lesions before endoscopic resection and in follow-up after successful ablation therapy.

∞ = Ten tijde van publicatie werkzaam bij: Department of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

impactfactor: 3.478

## Curvers WL

### Fluorescence spectroscopy incorporated in an Optical Biopsy System for the detection of early neoplasia in Barrett's esophagus

Boerwinkel DF, Holz JA, Hawkins DM, Curvers WL<sup>∞</sup>, Aalders MC, Weusten BL, Visser M, Meijer SL, Bergman JJ

Dis Esophagus. 2015 May-Jun;28(4):345-51

Endoscopic surveillance is recommended for patients with Barrett's esophagus (BE) to detect high-grade intraepithelial neoplasia (HGIN) or early cancer (EC). Early neoplasia is difficult to detect with white light endoscopy and random biopsies are associated with sampling error. Fluorescence spectroscopy has been studied to distinguish non-dysplastic Barrett's epithelium (NDBE) from early neoplasia. The Optical Biopsy System (OBS) uses an optical fiber integrated in a regular biopsy forceps. This allows real-time spectroscopy and ensures spot-on correlation between the spectral signature and corresponding physical biopsy. The OBS may provide an easy-to-use endoscopic tool during BE surveillance. We aimed to develop a tissue-differentiating algorithm and correlate the discriminating properties of the OBS with the constructed algorithm to the endoscopist's assessment of the Barrett's esophagus. In BE patients undergoing endoscopy, areas suspicious for neoplasia and endoscopically non-suspicious areas were investigated with the OBS, followed by a correlating physical biopsy with the optical biopsy forceps. Spectra were correlated to histology and an algorithm was constructed to discriminate between HGIN/EC and NDBE using smoothed linear discriminant analysis. The constructed classifier was internally cross-validated and correlated to the endoscopist's assessment of the BE segment. A total of 47 patients were included (39 males, age 66 years): 35 BE patients were referred with early neoplasia and 12 patients with NDBE. A total of 245 areas were investigated with following histology: 43 HGIN/EC, 66 low-grade intraepithelial neoplasia, 108 NDBE, 28 gastric or squamous mucosa. Areas with low-grade intraepithelial neoplasia and gastric/squamous mucosa were excluded. The area under the receiver operating characteristic curve of the constructed classifier was 0.78. Sensitivity and specificity for the discrimination between NDBE and HGIN/EC of OBS alone were 81% and 58% respectively. When OBS was combined with the endoscopist's assessment, sensitivity was 91% and specificity 50%. If this protocol would have guided the decision to obtain biopsies, half of the biopsies would have been avoided, yet 4/43 areas containing HGIN/EC (9%) would have been inadvertently classified as unsuspicious. In this study, the OBS was used to construct an algorithm to discriminate neoplastic from non-neoplastic BE. Moreover, the feasibility of OBS with the constructed algorithm as an adjunctive tool to the endoscopist's assessment during endoscopic BE surveillance was demonstrated. These results should be validated in future studies. In addition, other probe-based spectroscopy techniques may be integrated in this optical biopsy forceps system.

∞ = Ten tijde van publicatie werkzaam bij: Department of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam, The Netherlands

impactfactor: 1.782

## Curvers WL

### **PPI-responsive esophageal eosinophilia cannot be distinguished from eosinophilic esophagitis by endoscopic signs**

Warners MJ, van Rhijn BD, Curvers WL<sup>∞</sup>, Smout AJ, Bredenoord AJ

Eur J Gastroenterol Hepatol. 2015 May;27(5):506-11

**BACKGROUND:** Eosinophilic esophagitis (EoE) is a chronic antigen-mediated disease histologically characterized by eosinophil-predominant inflammation. One-third of patients respond to proton pump inhibitor (PPI) treatment; this group is identified as having PPI-responsive esophageal eosinophilia (PPI-REE). If we could predict the response to PPIs on the basis of endoscopic signs, futile treatment efforts and additional endoscopies to assess treatment response can be prevented.

**OBJECTIVE:** To determine whether endoscopic signs can distinguish PPI-REE from EoE.

**METHODS:** Endoscopic images of 30 EoE and 30 PPI-REE patients were included. Baseline characteristics were compared between groups. Complete clinical remission after a PPI trial for at least 8 weeks was classified as PPI-REE. Per patient, at least three depersonalized images were incorporated into a slideshow. These images were scored by two experienced endoscopists according to a validated classification system.

**RESULTS:** Characteristics were highly comparable between EoE and PPI-REE patients. Endoscopic signs were similar and did not enable differentiation between EoE and PPI-REE [presence of: rings (P=0.893), white exudates (P=0.209), furrows (P=0.371), edema (P=0.554), crepe paper esophagus (P=1.000), and strictures (P=0.071)].

**CONCLUSION:** Endoscopic signs at baseline endoscopy cannot distinguish EoE from PPI-REE before a PPI trial; the demographic and clinical characteristics in both groups are similar. Endoscopic features do not enable differentiation between PPI-REE and EoE.

<sup>∞</sup> = Ten tijde van publicatie werkzaam bij: Department of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Amsterdam, The Netherlands.

impactfactor: 2.253

## Gilissen LP

### **A Rare Cause of Haematemesis; a Primary Aorto-Esophageal Fistula: Case Report and Review of Literature**

Denise Strijbos\*, Johanna W M Holtkamp, Marc R H M Van Sambeek\*, Simon W Nienhuijs\*, Arnold Stronkhorst\* and Lennard P L Gilissen\*

Gastro Open Access, 2015; 3(1): 118

Impactfactor: --

## Gilissen LP

### **Costs of Leaks and Bleeding After Sleeve Gastrectomies**

Bransen J\*, Gilissen LP\*, van Rutte PW, Nienhuijs SW\*

Obes Surg. 2015 Oct;25(10):1767-71

Voor abstract zie: Chirurgie - Bransen J

impactfactor: 3.747

## Gilissen LP

### **Identification of Patients With Variants in TPMT and Dose Reduction Reduces Hematologic Events During Thiopurine Treatment of Inflammatory Bowel Disease**

Coenen MJ, de Jong DJ, van Marrewijk CJ, Derijks LJ, Vermeulen SH, Wong DR, Klungel OH, Verbeek AL, Hooymans PM, Peters WH, te Morsche RH, Newman WG, Scheffer H,

Guchelaar HJ, Franke B; TOPIC Recruitment Team. Collaborators: Stronkhorst A\*, Gilissen LP\*, Schoon EJ\*

Gastroenterology. 2015 Oct;149(4):907-17.e7

Voor abstract zie: *Maag-darm-leverziekten - Stronkhorst A*

impactfactor: 16.716

## Schoon EJ

### Identification of Patients With Variants in TPMT and Dose Reduction Reduces Hematologic Events During Thiopurine Treatment of Inflammatory Bowel Disease

Coenen MJ, de Jong DJ, van Marrewijk CJ, Derijks LJ, Vermeulen SH, Wong DR, Klungel OH, Verbeek AL, Hooymans PM, Peters WH, te Morsche RH, Newman WG, Scheffer H, Guchelaar HJ, Franke B; TOPIC Recruitment Team. Collaborators: Stronkhorst A\*, Gilissen LP\*, Schoon EJ\*

Gastroenterology. 2015 Oct;149(4):907-17.e7

**BACKGROUND & AIMS:** More than 20% of patients with inflammatory bowel disease (IBD) discontinue thiopurine therapy because of severe adverse drug reactions (ADRs); leukopenia is one of the most serious ADRs. Variants in the gene encoding thiopurine S-methyltransferase (TPMT) alter its enzymatic activity, resulting in higher levels of thiopurine metabolites, which can cause leukopenia. We performed a prospective study to determine whether genotype analysis of TPMT before thiopurine treatment, and dose selection based on the results, affects the outcomes of patients with IBD.

**METHODS:** In a study performed at 30 Dutch hospitals, patients were assigned randomly to groups that received standard treatment (control) or pretreatment screening (intervention) for 3 common variants of TPMT (TPMT\*2, TPMT\*3A, and TPMT\*3C). Patients in the intervention group found to be heterozygous carriers of a variant received 50% of the standard dose of thiopurine (azathioprine or 6-mercaptopurine), and patients homozygous for a variant received 0%-10% of the standard dose. We compared, in an intention-to-treat analysis, outcomes of the intervention (n = 405) and control groups (n = 378) after 20 weeks of treatment. Primary outcomes were the occurrence of hematologic ADRs (leukocyte count < 3.0\*10(9)/L or reduced platelet count < 100\*10(9)/L) and disease activity (based on the Harvey-Bradshaw Index for Crohn's disease [n = 356] or the partial Mayo score for ulcerative colitis [n = 253]).

**RESULTS:** Similar proportions of patients in the intervention and control groups developed a hematologic ADR (7.4% vs 7.9%; relative risk, 0.93; 95% confidence interval, 0.57-1.52) in the 20 weeks of follow-up evaluation; the groups also had similar mean levels of disease activity (P = .18 for Crohn's disease and P = .14 for ulcerative colitis). However, a significantly smaller proportion of carriers of the TPMT variants in the intervention group (2.6%) developed hematologic ADRs compared with patients in the control group (22.9%) (relative risk, 0.11; 95% confidence interval, 0.01-0.85).

**CONCLUSIONS:** Screening for variants in TPMT did not reduce the proportions of patients with hematologic ADRs during thiopurine treatment for IBD. However, there was a 10-fold reduction in hematologic ADRs among variant carriers who were identified and received a dose reduction, compared with variant carriers who did not, without differences in treatment efficacy.

Voor abstract zie: *Maag-darm-leverziekten - Stronkhorst A*

impactfactor: 16.716

## **Schoon EJ**

### **Learning endoscopic resection in the esophagus.**

van Vilsteren FG, Pouw RE, Alvarez Herrero L, Bisschops R, Houben M, Peters FT, Schenk BE, Weusten BL, Schoon EJ\*, Bergman JJ

Endoscopy. 2015 Nov;47(11):972-9. Epub 2015 Sep 11

Background: Endoscopic resection is the cornerstone of endoscopic management of esophageal early neoplasia. However, endoscopic resection is a complex technique requiring knowledge and expertise. Our aims were to identify the most important learning points in performing endoscopic resection in a training setting and to provide information on how to improve endoscopic resection technique.

Methods: Six gastroenterologists at centers with multidisciplinary expertise in upper gastrointestinal oncology participated in a structured endoscopic resection training program, consisting of four training days with lectures and hands-on training on live pigs, further one-to-one hands-on training days, and written feedback (by an expert) on videos of unsupervised endoscopic resection procedures. The first 20 endoscopic resections of each participant were prospectively registered. Ninety learning points were independently identified by participants using a standardized questionnaire and by an expert providing written feedback on 33 unsupervised endoscopic resection videos. Three expert endoscopists selected and ranked the most important learning points in a consensus meeting.

Results: The top 10 tips (illustrated by unique videos of three perforations) were: (1) allow time for inspection and use a high-definition endoscope; (2) create a preprocedural plan by placing electrocoagulation markings; (3) know the management of bleeding; (4) optimize the endoscopic view by repeatedly cleaning out stomach and target area; (5) use a therapeutic endoscope during resection; (6) always perform a test suction; (7) keep instruments close to the tip; (8) lift edges in piecemeal endoscopic cap resections; (9) know the management of perforation; (10) pin specimens down.

Conclusions: This study summarized the most important learning points for performing endoscopic resection encountered during a structured endoscopic resection training program.

*impactfactor:* 5.053

## **Schoon EJ**

### **Metal or plastic stents for preoperative biliary drainage in resectable pancreatic cancer**

Tol JA, van Hooft JE, Timmer R, Kubben FJ, van der Harst E, de Hingh IH\*, Vleggaar FP, Molenaar IQ, Keulemans YC, Boerma D, Bruno MJ, Schoon EJ\*, van der Gaag NA, Besselink MG, Fockens P, van Gulik TM, Rauws EA, Busch OR, Gouma DJ

Gut. 2015 Aug 25. pii: gutjnl-2014-308762

*Voor abstract zie: Maag-darm-leverziekten - Hingh IH de*

*impactfactor:* 14.66

## **Schoon EJ**

### **Simplified protocol for focal radiofrequency ablation using the HALO90 device: short-term efficacy and safety in patients with dysplastic Barrett's esophagus**

Künzli HT, Schölvinck DW, Phoa KN, Schoon EJ\*, Houben MH, Bergman JJ, Weusten BL

Endoscopy. 2015 Jul;47(7):592-7. Epub 2015 Feb 12

**BACKGROUND AND STUDY AIMS:** The standard protocol for focal radiofrequency ablation (RFA) of Barrett's esophagus comprises two applications of radiofrequency energy, cleaning of the ablated areas and catheter, and two further applications ( $2 \times 15 \text{ J/cm}^2$ )-cleaning ( $2 \times 15 \text{ J/cm}^2$ ). A simplified protocol ( $3 \times 15 \text{ J/cm}^2$ , no cleaning) proved noninferior to standard protocol for individual islands of Barrett's esophagus, but may be associated with higher stenosis rates when applied circumferentially and sequentially over time. We evaluated the efficacy and safety of the above mentioned simplified protocol.

**PATIENTS AND METHODS:** Barrett's esophagus patients undergoing focal RFA using the simplified protocol in four tertiary referral centers were retrospectively included. During each focal ablation, the gastroesophageal junction (GEJ) was ablated circumferentially in addition to Barrett's esophagus islands or tongues. Sessions continued at 8 to 12-week intervals until complete resolution of Barrett's esophagus. Primary outcome parameters comprised complete remission of dysplasia and of intestinal metaplasia, and stenosis requiring dilation.

**RESULTS:** 83 patients with dysplastic Barrett's esophagus (median Prague classification C1M3) were enrolled; 66/83 (80%) had endoscopic resection of a visible lesion before RFA. Intention-to-treat analysis showed complete remission of dysplasia in 78/83 (94%) and of intestinal metaplasia in 72/83 (87%). Stenosis requiring dilation developed in 9/83 (11%), necessitating a median 2 dilation sessions (range 1-9), with  $\geq 8$  sessions in three patients.

**CONCLUSION:** A treatment algorithm incorporating the simplified protocol of  $3 \times 15 \text{ J/cm}^2$ , with no cleaning, for all focal RFA sessions, appears effective. The associated number and severity of stenoses, however, raises safety concerns.

*impactfactor: 5.053*

## **Schoon EJ**

### **Simulated colonoscopy training leads to improved performance during patient-based assessment**

Koch AD, Ekkelenkamp VE, Haringsma J, Schoon EJ\*, de Man RA, Kuipers EJ

Gastrointest Endosc. 2015 Mar;81(3):630-6. Epub 2014 Dec 2

**BACKGROUND:** Virtual reality (VR) endoscopy simulators are increasingly being used in the training of novice endoscopists. There are, however, insufficient data regarding the effect of simulator training on the early learning curve of novice endoscopists.

**OBJECTIVE:** The aim of this study was to assess the clinical performance of novice endoscopists during colonoscopy after intensive and prolonged training on a VR endoscopy simulator.

**DESIGN:** Prospective study.

**SETTING:** Single university medical center.

**PATIENTS:** Patient-based assessment (PBA) of performance was carried out on patients routinely scheduled for colonoscopy.

**INTERVENTIONS:** Eighteen trainees without any endoscopic experience were included in the study. They were divided into 2 groups. The simulator-training program consisted of either 50 (group I) or 100 (group II) VR colonoscopies. After 10, 30, and 50 (group I) and after 20, 60, and 100 (group II) VR colonoscopies, trainees underwent both simulator-based assessment and PBA.

**MAIN OUTCOME MEASUREMENTS:** Cecal intubation time, colonic insertion depth, and cecal intubation rate.

**RESULTS:** Eighteen novices participated in the study. All completed VR training and assessments. The mean cecal intubation time on the SBA decreased from a baseline of 9.50 minutes to 2.20 minutes at completion of the training ( $P = .002$ ). Colonic insertion depth

during PBA improved from 29.4 cm to 63.7 cm ( $P < .001$ ). The learning effect of simulator training ceased after 60 colonoscopies.

LIMITATIONS: Single-center study, no formal sample size calculation.

CONCLUSIONS: VR training by using a colonoscopy simulator leads to a significant improvement in performance with the simulator itself and, more importantly, to significantly improved performances during patient-based colonoscopy. This study demonstrates the rationale for intensive simulator training in the early learning curve of novices performing colonoscopy.

*impactfactor:* 5.210

## **Strijbos D**

### **A Rare Cause of Haematemesis; a Primary Aorto-Esophageal Fistula: Case Report and Review of Literature**

Denise Strijbos\*, Johanna W M Holtkamp, Marc R H M Van Sambeek\*, Simon W Nienhuijs\*, Arnold Stronkhorst\* and Lennard P L Gilissen\*

Gastro Open Access, 2015; 3(1): 118

Aorto-Esophageal fistula is a rare condition, causes excessive bleeding from the upper gastrointestinal tract and is associated with a high mortality. This case report demonstrates the presentation of a 63-year old female with a primary aorto-esophageal fistula, due to a ruptured thoracic aneurysm. She first presented with a sentinel haemorrhage, followed by a new bleeding several hours later. An earlier performed upper gastrointestinal endoscopy elsewhere, because of dysphasia, already mentioned an impression from a non pulsing compressive swelling. No further analysis was performed. At current presentation, she was hemodynamically instable, with mild haematemesis. After stabilising she was admitted to the Intensive Care unit; however, haematemesis worsened. An immediate Computed Tomography (CT) scan showed an Aorto-Esophageal Fistula (AEF), due to a ruptured thoracic aortic aneurysm. Emergent surgical treatment consisted of endovascular stent-graft of the thoracic aorta and a total thoracic esophagectomy combined with immediate esophago-gastrostomy. Unfortunately, the subsequent multi-organ failure was fatal. A critical view to the surgical approach is given, combined with a review of diagnostic and therapeutic options in aorto-esophageal fistulae.

*Impactfactor* --

## **Stronkhorst A**

### **A Rare Cause of Haematemesis; a Primary Aorto-Esophageal Fistula: Case Report and Review of Literature**

Denise Strijbos\*, Johanna W M Holtkamp, Marc R H M Van Sambeek\*, Simon W Nienhuijs\*, Arnold Stronkhorst\* and Lennard P L Gilissen\*

Gastro Open Access, 2015; 3(1): 118

*Impactfactor* --

## **Stronkhorst A**

### **Identification of Patients With Variants in TPMT and Dose Reduction Reduces Hematologic Events During Thiopurine Treatment of Inflammatory Bowel Disease**

Coenen MJ, de Jong DJ, van Marrewijk CJ, Derijks LJ, Vermeulen SH, Wong DR, Klungel OH, Verbeek AL, Hooymans PM, Peters WH, te Morsche RH, Newman WG, Scheffer H, Guchelaar HJ, Franke B; TOPIC Recruitment Team. Collaborators: Stronkhorst A\*, Gilissen LP\*, Schoon EJ\*

Gastroenterology. 2015 Oct;149(4):907-17.e7

**BACKGROUND & AIMS:** More than 20% of patients with inflammatory bowel disease (IBD) discontinue thiopurine therapy because of severe adverse drug reactions (ADRs); leukopenia is one of the most serious ADRs. Variants in the gene encoding thiopurine S-methyltransferase (TPMT) alter its enzymatic activity, resulting in higher levels of thiopurine metabolites, which can cause leukopenia. We performed a prospective study to determine whether genotype analysis of TPMT before thiopurine treatment, and dose selection based on the results, affects the outcomes of patients with IBD.

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*impactfactor:* 16.716

## **Stronkhorst A**

### **Randomized Comparison of Surveillance Intervals in Familial Colorectal Cancer**

Hennink SD, van der Meulen-de Jong AE, Wolterbeek R, Crobach AS, Becx MC, Crobach WF, van Haastert M, Ten Hove WR, Kleibeuker JH, Meijssen MA, Nagengast FM, Rijk MC, Salemans JM, Stronkhorst A, Tuynman HA, Vecht J, Verhulst ML, de Vos Tot Nederveen Cappel WH, Walinga H, Weinhardt OK, Westerveld D, Witte AM, Wolters HJ, Cats A, Veenendaal RA, Morreau H, Vasen HFJ

Clin Oncol. 2015 Dec 10;33(35):4188-93. Epub 2015 Nov 2



**PURPOSE:** Colonoscopic surveillance is recommended for individuals with familial colorectal cancer (CRC). However, the appropriate screening interval has not yet been determined. The aim of this randomized trial was to compare a 3-year with a 6-year screening interval.

**PATIENTS AND METHODS:** Individuals between ages 45 and 65 years with one first-degree relative with CRC age < 50 years or two first-degree relatives with CRC were selected. Patients with zero to two adenomas at baseline were randomly assigned to one of two groups: group A (colonoscopy at 6 years) or group B (colonoscopy at 3 and 6 years). The primary outcome measure was advanced adenomatous polyps (AAPs). Risk factors studied included sex, age, type of family history, and baseline endoscopic findings.

**RESULTS:** A total of 528 patients were randomly assigned (group A, n = 262; group B, n = 266). Intention-to-treat analysis showed no significant difference in the proportion of patients with AAPs at the first follow-up examination at 6 years in group A (6.9%) versus 3 years in group B (3.5%). Also, the proportion of patients with AAPs at the final follow-up examination at 6 years in group A (6.9%) versus 6 years in group B (3.4%) was not significantly different. Only AAPs at baseline was a significant predictor for the presence of AAPs at first follow-up. After correction for the difference in AAPs at baseline, differences between the groups in the rate of AAPs at first follow-up and at the final examination were statistically significant.

**CONCLUSION:** In view of the relatively low rate of AAPs at 6 years and the absence of CRC in group A, we consider a 6-year surveillance interval appropriate. A surveillance interval of 3 years might be considered in patients with AAPs and patients with = three adenomas.

*impactfactor:* 18.428

\* = Werkzaam in het Catharina Ziekenhuis

## **Medische Psychologie**

**Hout GC van**

**You Deserve a Ribbon**

van Hout G\*

Obes Surg. 2015 Jul;25(7):1251

*Geen abstract beschikbaar*

*impactfactor: 3.747*

**Nusselein BA**

**Can the Montreal Cognitive Assessment Predict Discharge Destination in a Stroke Population in the Hospital?**

Geubbels HJ, Nusselein BA\*, van Heugten CM, Valentijn SA\*, Rasquin SM

J Stroke Cerebrovasc Dis. 2015 May;24(5):1094-9. Epub 2015 Mar 25

**BACKGROUND:** To decide on an appropriate discharge destination for stroke survivors from hospital, factors such as activities of daily living and age are often taken into account as predictors. Cognition has been found to support the decision whether to send a patient home or to a dependent living situation. The Montreal Cognitive Assessment (MOCA) has been proven to be a suitable cognitive screening instrument in the acute phase after stroke. However, its predictive value in the determination of discharge destination is unknown. The aim of the present study was to examine whether cognitive functioning, as measured with the MOCA, in the acute phase after stroke could predict discharge destination.

**METHODS:** The study involved 211 patients with a first-ever cerebral stroke within the first week after stroke. Demographic and stroke-specific data, cognitive functioning (MOCA), and level of functional disability (Barthel Index [BI]) were collected. Multivariate logistic regression analyses were used to predict discharge destination (dependent versus independent living situation).

**RESULTS:** Both age ( $B = -.05$ ;  $P < .01$ ) and BI score ( $B = .33$ ;  $P < .001$ ) were found to be significantly related to discharge destination with explained variance of 43%. Adding MOCA score as a predictor variable to the model resulted in a nonsignificant improvement of the model, explaining 44% of the variance.

**CONCLUSIONS:** Cognitive functioning, as measured by a single screening instrument such as the MOCA, in the acute phase after stroke is not predictive for discharge destination.

*impactfactor: 1.669*

**Schiffer AA**

**Mindfulness and eating behaviour styles in morbidly obese males and females**

Ouwens MA, Schiffer AA\*, Visser LI, Raeijmaekers NJ, Nyklíček I

Appetite. 2015 Apr;87:62-7

**BACKGROUND:** Morbid obesity is a highly prevalent condition that is associated with a high risk of various diseases and high health care costs. Understanding determinants of eating behaviours that are characteristic of many morbidly obese persons is important for the development of new interventions aimed at changing eating behaviour after bariatric surgery. Dispositional mindfulness seems promising as one such potential determinant. Therefore, the association between mindfulness and eating behaviour was examined in females and males with morbid obesity.

**METHODS:** Outpatients with morbid obesity who were candidates for bariatric surgery ( $N = 2335$ ; 78.8% female) completed the Dutch Eating Behaviour Questionnaire (DEBQ), the Freiburg Mindfulness Inventory (FMI) and the Hospital Anxiety and Depression Scale (HADS), in addition to the collection of relevant demographic and medical data.

RESULTS: Three separate multiple regression analyses with three eating behaviour styles (restrained, emotional, external) as dependent variables showed that mindfulness was positively associated with restrained eating behaviour (Beta=.28,  $p=.001$ ), and negatively associated with emotional (Beta=-.22,  $p=.001$ ) and external (Beta=-.32,  $p=.001$ ) eating behaviours, independent of sex, age, educational level, Body Mass Index and affective symptoms.

CONCLUSION: Dispositional mindfulness was associated with more restrained, and less emotional and external eating behaviour in morbidly obese outpatients, above and beyond affective symptoms. Future studies, establishing the causal direction of the associations, are needed.

impactfactor: 2.691

### **Valentijn SA**

#### **Can the Montreal Cognitive Assessment Predict Discharge Destination in a Stroke Population in the Hospital?**

Geubbels HJ, Nusselein BA\*, van Heugten CM, Valentijn SA\*, Rasquin SM

J Stroke Cerebrovasc Dis. 2015 May;24(5):1094-9. Epub 2015 Mar 25

Voor abstract zie: Medische psychologie - Nusselein BA

impactfactor: 1.669

\* = Werkzaam in het Catharina Ziekenhuis

## **Mondziekten en Kaakchirurgie**

**Pijpe J**

**Systemic diseases and the risk of developing salivary stones: a case control study**

Kraaij S, Karagozolu KH, Kenter YA, Pijpe J\*, Gilijsse M, Brand HS

Oral Surg Oral Med Oral Pathol Oral Radiol. 2015 May;119(5):539-43

**OBJECTIVE:** To investigate the possible relationship between the presence of salivary stones and systemic diseases, medication, smoking, and alcohol consumption.

**STUDY DESIGN:** A retrospective, case control study. Medical records of patients with salivary stones and those of control patients without salivary stones were retrospectively reviewed. Data regarding the affected salivary gland, the presence of systemic disease, and the use of medication, tobacco, and alcohol were recorded. Statistical analysis was performed using the Fisher Exact tests.

**RESULTS:** Medical records of 208 patients with salivary stones and those of 208 control patients were reviewed. Of the patients diagnosed with salivary stones, the submandibular gland was affected in 85.6% of the patients, the parotid gland in 9.6%, and the sublingual gland in 2.4% of the patients. None of the recorded systemic diseases was more prevalent in patients with salivary stones. Patients with salivary stones used significantly more antibiotics compared with the control group ( $P = .037$ ). No significant differences were observed for other types of medication. There was no correlation between salivary stone formation, smoking, and alcohol consumption.

**CONCLUSIONS:** The present study suggested that systemic diseases, medication, smoking, and alcohol consumption play no or only a limited role in the onset of salivary stones.

*impactfactor: 1.261*

\* = Werkzaam in het Catharina Ziekenhuis

## Neurologie

## Hanse MC

### **Prognostic value and kinetics of circulating endothelial cells in patients with recurrent glioblastoma randomised to bevacizumab plus lomustine, bevacizumab single agent or lomustine single agent. A report from the Dutch Neuro-Oncology Group BELOB trial**

Beije N, Kraan J, Taal W, van der Holt B, Oosterkamp HM, Walenkamp AM, Beerepoot L, Hanse M\*, van Linde ME, Otten A, Vernhout R, de Vos FY, Gratama JW, Sleijfer S, van den Bent MJ

Br J Cancer. 2015 Jul 14;113(2):226-31

**BACKGROUND:** Angiogenesis is crucial for glioblastoma growth, and anti-vascular endothelial growth factor agents are widely used in recurrent glioblastoma patients. The number of circulating endothelial cells (CECs) is a surrogate marker for endothelial damage. We assessed their kinetics and explored their prognostic value in patients with recurrent glioblastoma.

**METHODS:** In this side study of the BELOB trial, 141 patients with recurrent glioblastoma were randomised to receive single-agent bevacizumab or lomustine, or bevacizumab plus lomustine. Before treatment, after 4 weeks and after 6 weeks of treatment, CECs were enumerated.

**RESULTS:** The number of CECs increased during treatment with bevacizumab plus lomustine, but not during treatment in the single-agent arms. In patients treated with lomustine single agent, higher absolute CEC numbers after 4 weeks (log10CEC hazard ratio (HR) 0.41, 95% CI 0.18-0.91) and 6 weeks (log10CEC HR 0.16, 95% CI 0.05-0.56) of treatment were associated with improved overall survival (OS). Absolute CEC numbers in patients receiving bevacizumab plus lomustine or bevacizumab single agent were not associated with OS.

**CONCLUSION:** CEC numbers increased during treatment with bevacizumab plus lomustine but not during treatment with either agent alone, suggesting that this combination induced the greatest vascular damage. Although the absolute number of CECs was not associated with OS in patients treated with bevacizumab either alone or in combination, they could serve as a marker in glioblastoma patients receiving lomustine single agent.

*impactfactor:* 4.836

## Hanse MC

### **The impact of bevacizumab on health-related quality of life in patients treated for recurrent glioblastoma: results of the randomised controlled phase 2 BELOB trial**

Dirven L, van den Bent MJ, Bottomley A, van der Meer N, van der Holt B, Vos MJ, Walenkamp AM, Beerepoot LV, Hanse MC\*, Reijneveld JC, Otten A, de Vos FY, Smits M, Bromberg JE, Taal W, Taphoorn MJ; Dutch Neuro-Oncology Group (LWNO)

Eur J Cancer. 2015 Jul;51(10):1321-30

**BACKGROUND:** The BELOB study, a randomised controlled phase 2 trial comparing lomustine, bevacizumab and combined lomustine and bevacizumab in patients with recurrent glioblastoma, showed that the 9-month overall survival rate was most promising in the combination arm. Here we report the health-related quality of life (HRQoL) results, a secondary trial end-point.

**METHODS:** HRQoL was measured at baseline and every 6 weeks until progression using the European Organisation for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ-C30) and brain module (QLQ-BN20). HRQoL was assessed over time for five preselected scales (global health (GH), physical (PF) and social



functioning (SF), motor dysfunction (MD) and communication deficit (CD)). Moreover, mean changes in HRQoL from baseline until progression were determined.

RESULTS: 138/148 patients with at least a baseline HRQoL assessment were analysed. Over time, HRQoL remained relatively stable in all treatment arms for all five scales, at least during the first three treatment cycles. More than half (54-61%) of the patients showed stable (<10 point change) or improved (≥10 point change) HRQoL during their progression-free time, except for SF (43%), irrespective of treatment arm. Deterioration of mean HRQoL was most profound at disease progression for all scales except SF, which deteriorated earlier in disease course. Compared to baseline, 40% of patients had clinically relevant (≥10 points) worse GH, PF and SF, while 44% and 31% had increased MD and CD at disease progression, irrespective of treatment arm.

CONCLUSIONS: Bevacizumab, whether or not in combination with lomustine, did not negatively affect HRQoL in patients treated for recurrent glioblastoma in this randomised study.

*impactfactor:* 5.417

## Keizer K

### The Prognostic Value of CT Angiography and CT Perfusion in Acute Ischemic Stroke

van Seeters T, Biessels GJ, Kappelle LJ, van der Schaaf IC, Dankbaar JW, Horsch AD, Niesten JM, Luitse MJ, Majoie CB, Vos JA, Schonewille WJ, van Walderveen MA, Wermer MJ, Duijm LE\*, Keizer K, Bot JC, Visser MC, van der Lugt A, Dippel DW, Kesselring FO, Hofmeijer J, Lycklama À Nijeholt GJ, Boiten J, van Rooij WJ, de Kort PL, Roos YB, van Dijk EJ, Pleiter CC, Mali WP, van der Graaf Y, Velthuis BK; Dutch acute stroke study (DUST) investigators

Cerebrovasc Dis. 2015 Nov;40(5-6):258-69

BACKGROUND: CT angiography (CTA) and CT perfusion (CTP) are important diagnostic tools in acute ischemic stroke. We investigated the prognostic value of CTA and CTP for clinical outcome and determined whether they have additional prognostic value over patient characteristics and non-contrast CT (NCCT).

METHODS: We included 1,374 patients with suspected acute ischemic stroke in the prospective multicenter Dutch acute stroke study. Sixty percent of the cohort was used for deriving the predictors and the remaining 40% for validating them. We calculated the predictive values of CTA and CTP predictors for poor clinical outcome (modified Rankin Scale score 3-6). Associations between CTA and CTP predictors and poor clinical outcome were assessed with odds ratios (OR). Multivariable logistic regression models were developed based on patient characteristics and NCCT predictors, and subsequently CTA and CTP predictors were added. The increase in area under the curve (AUC) value was determined to assess the additional prognostic value of CTA and CTP. Model validation was performed by assessing discrimination and calibration.

RESULTS: Poor outcome occurred in 501 patients (36.5%). Each of the evaluated CTA measures strongly predicted outcome in univariable analyses: the positive predictive value (PPV) was 59% for Alberta Stroke Program Early CT Score (ASPECTS) =7 on CTA source images (OR 3.3; 95% CI 2.3-4.8), 63% for presence of a proximal intracranial occlusion (OR 5.1; 95% CI 3.7-7.1), 66% for poor leptomeningeal collaterals (OR 4.3; 95% CI 2.8-6.6), and 58% for a >70% carotid or vertebrobasilar stenosis/occlusion (OR 3.2; 95% CI 2.2-4.6). The

same applied to the CTP measures, as the PPVs were 65% for ASPECTS =7 on cerebral blood volume maps (OR 5.1; 95% CI 3.7-7.2) and 53% for ASPECTS =7 on mean transit time maps (OR 3.9; 95% CI 2.9-5.3). The prognostic model based on patient characteristics and NCCT measures was highly predictive for poor clinical outcome (AUC 0.84; 95% CI 0.81-0.86). Adding CTA and CTP predictors to this model did not improve the predictive value (AUC 0.85; 95% CI 0.83-0.88). In the validation cohort, the AUC values were 0.78 (95% CI 0.73-0.82) and 0.79 (95% CI 0.75-0.83), respectively. Calibration of the models was satisfactory.

**CONCLUSIONS:** In patients with suspected acute ischemic stroke, admission CTA and CTP parameters are strong predictors of poor outcome and can be used to predict long-term clinical outcome. In multivariable prediction models, however, their additional prognostic value over patient characteristics and NCCT is limited in an unselected stroke population.

*impactfactor:* 3.754

## **Keizer K**

### **Transient anti-NMDAR encephalitis in a newborn infant due to transplacental transmission**

Hilderink M\*, Titulaer MJ, Schreurs MW, Keizer K\*, Bunt JE\*

Neurol Neuroimmunol Neuroinflamm. 2015 Jun 18;2(4):e126 eCollection 2015

*Geen Abstract beschikbaar*

*impactfactor:* --

## **Keizer K**

### **Value of Computed Tomographic Perfusion–Based Patient Selection for Intra-Arterial Acute Ischemic Stroke Treatment**

Borst J, Berkhemer OA, Roos YB, van Bavel E, van Zwam WH, van Oostenbrugge RJ, van Walderveen MA, Lingsma HF, van der Lugt A, Dippel DW, Yoo AJ, Marquering HA, Majoie CB; MR CLEAN investigators; MR CLEAN Investigators and Affiliations. Collaborators: Keizer K, Tielbeek AV

Stroke. 2015 Dec;46(12):3375-82. Epub 2015 Nov 5

**BACKGROUND AND PURPOSE:** The utility of computed tomographic perfusion (CTP)-based patient selection for intra-arterial treatment of acute ischemic stroke has not been proven in randomized trials and requires further study in a cohort that was not selected based on CTP. Our objective was to study the relationship between CTP-derived parameters and outcome and treatment effect in patients with acute ischemic stroke because of a proximal intracranial arterial occlusion.

**METHODS:** We included 175 patients who underwent CTP in the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in The Netherlands (MR CLEAN). Association of CTP-derived parameters (ischemic-core volume, penumbra volume, and percentage ischemic core) with outcome was estimated with multivariable ordinal logistic regression as an adjusted odds ratio for a shift in the direction of a better outcome on the modified Rankin Scale. Interaction between CTP-derived parameters and treatment effect was determined using multivariable ordinal logistic regression. Interaction with treatment effect was also tested for mismatch (core <70 mL; penumbra core >1.2; penumbra core >10 mL).

**RESULTS:** The adjusted odds ratio for improved functional outcome for ischemic core, percentage ischemic core, and penumbra were 0.79 per 10 mL (95% confidence interval: 0.71-0.89; P<0.001), 0.82 per 10% (95% confidence interval: 0.66-0.90; P=0.002), and 0.97 per 10 mL (96% confidence interval: 0.92-1.01; P=0.15), respectively. No significant

interaction between any of the CTP-derived parameters and treatment effect was observed. We observed no significant interaction between mismatch and treatment effect.

CONCLUSIONS: CTP seems useful for predicting functional outcome, but cannot reliably identify patients who will not benefit from intra-arterial therapy.

*impactfactor:* 5.723

## **Nuenen BF van**

### **Reorganization of corticostriatal circuits in healthy G2019S LRRK2 carriers.**

Helmich RC, Thaler A, van Nuenen BF\*, Gurevich T, Mirelman A, Marder KS, Bressman S, Orr-Urtreger A, Giladi N, Bloem BR, Toni I; On behalf of the LRRK Ashkenazi Jewish Consortium

Neurology. 2015 Jan 27;84(4):399-406. Epub 2014 Dec 24

OBJECTIVE: We investigated system-level corticostriatal changes in a human model of premotor Parkinson disease (PD), i.e., healthy carriers of the G2019S LRRK2 mutation that is associated with a markedly increased, age-dependent risk of developing PD.

METHODS: We compared 37 asymptomatic LRRK2 G2019S mutation carriers (age range 30-78 years) with 32 matched, asymptomatic nonmutation carriers (age range 30-74 years). Using fMRI, we tested the hypothesis that corticostriatal connectivity in premotor PD shifts from severely affected to less affected striatal subregions, as shown previously in symptomatic PD. Specifically, we predicted that in premotor PD, the shift in corticostriatal connectivity would follow the same gradient of striatal dopamine depletion known from overt PD, with the dorsoposterior putamen being more affected than the ventroanterior putamen.

RESULTS: The known parallel topology of corticostriatal loops was preserved in each group, but the topography of putamen connectivity shifted. In LRRK2 G2019S mutation carriers, the right inferior parietal cortex had reduced functional connectivity with the dorsoposterior putamen but increased connectivity with the ventroanterior putamen, as compared with noncarriers. This shift in functional connectivity increased with age in LRRK2 G2019S mutation carriers.

CONCLUSIONS: Asymptomatic LRRK2 G2019S mutation carriers show a reorganization of corticostriatal circuits that mirrors findings in idiopathic PD. These changes may reflect premotor basal ganglia dysfunction or circuit-level compensatory changes.

*impactfactor:* 8.25

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## **Nucleaire Geneeskunde**

**Edelbroek M**

**Association Between Postprandial Symptoms and Gastric Emptying After Sleeve Gastrectomy**

Burgerhart JS, van Rutte PW\*, Edelbroek MA\*, Wyndaele DN\*, Smulders JF\*, van de Meeberg PC, Siersema PD, Smout AJ

Obes Surg. 2015 Feb;25(2):209-14

Voor abstract zie: *Chirurgie - Rutte PW van*

impactfactor: 3.747

**Roef MJ**

**[The quality of patient information brochures can be improved: a discussion using radium-223 therapy as an example] - De kwaliteit van patiëntenfolders kan beter: een beschouwing aan de hand van Radium-223-Therapie**

Vogel WV, Lam MG, Vegt E, Prompers L, Roef MJ\*

Ned Tijdschr Geneeskd. 2015;159:A8948

Patients and their peers need to be adequately informed to ensure proper treatment selection, and to facilitate optimal realisation and outcome of treatment. Written patient information can contribute, but only when brochures are of sufficient quality. An evaluation of patient brochures for radium-223 therapy in the Netherlands revealed significant differences in the information provided, as well as discrepancies between the brochures and national guidelines and product documentation. This potentially leads to confusion, false expectations, wrong treatment decisions, suboptimal realisation and outcome of treatment, and unnecessary toxicity and in radiation hygiene risks. Here we discuss the option of national patient information brochures that can be used by all centres in order to circumvent such issues. This would require collaboration between all medical professions, patient organisations and other groups involved, and responsibilities for medical information, distribution and updates must be properly defined. A national patient information brochure of this kind is currently under development for radium-223 therapy.

impactfactor: --

**Wyndaele D**

**Association Between Postprandial Symptoms and Gastric Emptying After Sleeve Gastrectomy**

Burgerhart JS, van Rutte PW\*, Edelbroek MA\*, Wyndaele DN\*, Smulders JF\*, van de Meeberg PC, Siersema PD, Smout AJ

Obes Surg. 2015 Feb;25(2):209-14

Voor abstract zie: *Chirurgie - Rutte PW van*

impactfactor: 3.747

**Wyndaele D**

**Improving the Success Rate of Repeat Sentinel Node Biopsy in Recurrent Breast Cancer**

Vugts G\*, Maaskant-Braat AJ\*, Voogd AC, van Riet YE\*, Roumen RM, Luiten EJ, Rutgers EJ, Wyndaele D\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Ann Surg Oncol. 2015 Dec;22 Suppl 3:529-35.Epub 2015 Aug 11

Voor abstract zie: *Chirurgie - Vugts G*

impactfactor: 3.930

**Wyndaele D**

**Radium-223 Dichloride (Ra-223) for the Treatment of Metastatic Castration-resistant Prostate Cancer: Optimizing Clinical Practice in Nuclear Medicine Centers**

Oyen, Wim; Sundram, Francis; Haug, Alexander R.; Kairemo, Kalevi; Lewington, Valerie; Mäenpää, Hanna; Mortensen, Jann; Mottaghy, Felix; Virgolini, Irene; O'Sullivan, Joe M.; Wyndaele, Dirk

The Journal of OncoPathology, Volume 3, Number 1, February 2015, pp. 1-25(25)

Options for the treatment of metastatic castration-resistant prostate cancer (mCRPC) have expanded significantly during the last decade, with six new agents receiving regulatory approval in Europe and the United States. One of these treatments is radium-223 dichloride (Ra-223), the first radiopharmaceutical to offer significant clinical benefits in patients with mCRPC, including prolonging overall survival. The availability of Ra-223 for treating mCRPC marks a paradigm shift in the role of therapeutic nuclear medicine from one of bone pain palliation into one of frontline treatment. As experience in the use of Ra-223 expands, it has become clear that it is vital for nuclear medicine specialists to understand the clinical profile of Ra-223 and where it fits in the treatment algorithm in order to optimize use of the treatment in clinical practice. Participation in the multidisciplinary team responsible for the management of mCRPC patients is essential to ensure appropriate selection of patients and the delivery of safe and effective care. Effective interaction with radiation safety authorities is also required to ensure that local policies reflect the low-risk profile of this life-prolonging treatment. This paper aims to encourage an exchange of best practice between nuclear medicine centers around the world, assisting centers as they initiate or expand their therapeutic services.

*impactfactor:* --

**Wyndaele D**

**Results Of A Dutch Cost-Effectiveness Model Of Radium-223 In Comparison To Cabazitaxel, Abiraterone, And Enzalutamide In Patients With Metastatic Castration Resistant Prostate Cancer Previously Treated With Docetax**

Gaultney J, Baka A, Leliveld-Kors A, Noordzij W, Wyndaele D\*, De Meyer C

Value Health. 2015 Nov;18(7):A459

*Geen abstract beschikbaar*

*impactfactor:* 3.279

\* = Werkzaam in het Catharina Ziekenhuis

## Onderwijs & Onderzoek

**Houterman S**

**Agreements and discrepancies between the estimated walking distance, nongraded and graded treadmill testing, and outside walking in patients with intermittent claudication**

Fokkenrood HJ\*, van den Houten MM\*, Houterman S\*, Breek JC, Scheltinga MR, Teijink JA\*

Ann Vasc Surg. 2015 Aug;29(6):1218-24

Voor abstract zie: *Chirurgie - Fokkenrood HJ*

impactfactor: 1.170

**Houterman S**

**Are Carbohydrate-Deficient Transferrin Assays Useful for the Detection of Recurrent 'Binge Drinking' in Children with an Alcohol Intoxication in the Emergency Department?**

Stokbroekx MA\*, Houterman S\*, Coolen SA, van der Lely N, Pelleboer RA\*

Alcohol Alcohol. 2014 Nov;49(6):635-8. Epub 2014 Sep 15

Voor abstract zie: *Stokbroekx, MA – Kindergeneeskunde*

impactfactor: 2.889

**Houterman S**

**Beslisondersteuning is meer dan een algoritme: heparinepomp-protocol op de Intensive Care**

Boer AK\*, Kreeftenberg H\*, Bindels A\*, Roos A\*, Houterman S\*, Korsten E\*, van Dijk-van Berkel M\*

Ned Tijdschr Klin Chem Labgeneesk 2015; 40(3): 211-2

Geen abstract beschikbaar

impactfactor: --

**Houterman S**

**Crew Resource Management in the Intensive Care Unit: a prospective 3-year cohort study**

Haerkens MH, Kox M, Lemson J, Houterman S\*, van der Hoeven JG, Pickkers P

Acta Anaesthesiol Scand. 2015 Nov;59(10):1319-29. Epub 2015 Jun 16

**BACKGROUND:** Human factors account for the majority of adverse events in both aviation and medicine. Human factors awareness training entitled "Crew Resource Management (CRM)" is associated with improved aviation safety. We determined whether implementation of CRM impacts outcome in critically ill patients.

**METHODS:** We performed a prospective 3-year cohort study in a 32-bed ICU, admitting 2500-3000 patients yearly. At the end of the baseline year, all personnel received CRM training, followed by 1 year of implementation. The third year was defined as the clinical effect year. All 7271 patients admitted to the ICU in the study period were included. The primary outcome measure was ICU complication rate. Secondary outcome measures were ICU and hospital length of stay, and standardized mortality ratio.

**RESULTS:** Occurrence of serious complications was 67.1/1000 patients and 66.4/1000 patients during the baseline and implementation year respectively, decreasing to 50.9/1000 patients in the post-implementation year ( $P = 0.03$ ). Adjusted odds ratios for occurrence of complications were 0.92 (95% CI 0.71-1.19,  $P = 0.52$ ) and 0.66 (95% CI 0.51-0.87,  $P = 0.003$ )



in the implementation and post-implementation year. The incidence of cardiac arrests was 9.2/1000 patients and 8.3/1000 patients during the baseline and implementation year, decreasing to 3.5/1000 patients ( $P = 0.04$ ) in the post-implementation year, while cardiopulmonary resuscitation success rate increased from 19% to 55% and 67% ( $P = 0.02$ ). Standardized mortality ratio decreased from 0.72 (95% CI 0.63-0.81) in the baseline year to 0.60 (95% CI 0.53-0.67) in the post-implementation year ( $P = 0.04$ ).

**CONCLUSION:** Our data indicate an association between CRM implementation and reduction in serious complications and lower mortality in critically ill patients.

*impactfactor:* 2.322

## Houterman S

### **Femoral Mechanical-Anatomical Angle Measurements in Total Knee Arthroplasty: Analog versus Digital**

van Groningen B, den Teuling JW, Houterman S\*, Janssen RP

J Knee Surg. 2015 Aug;28(4):315-9. Epub 2014 Jun 26

Preoperative planning in total knee arthroplasty with intramedullary guiding systems requires the measurement of the femoral mechanical-anatomical angle (FMAA) for optimal alignment correction. The main goal of this study was to assess the agreement between two digital FMAA measurements and the analog FMAA measurement. Overall 41 anteroposterior weight-bearing hip-to-ankle radiographs of patients undergoing total knee arthroplasty were used for the measurements of the FMAA. The analog method (gold standard, GS) was compared with two new digital methods (DIG1 and DIG2) using intraclass correlation (ICC) and Bland-Altman plots, measured by three blinded raters. The ICC for measurements of the FMAA comparing the GS and DIG1 was 0.48 (95% confidence interval [CI] 0.20-0.68), and 0.53 (95% CI 0.26-0.73) for comparing GS and DIG2. The ICC between raters for DIG1 was 0.79 (95% CI 0.68-0.88) and 0.88 (95% CI 0.80-0.93) for DIG2. Bland-Altman plots showed a mean difference between the GS and DIG1 of -0.44 degrees, with 95% limits of agreement from 1.21 to -2.09 degrees. The mean difference between the GS and DIG2 was -0.68 degrees with 95% limits of agreement from 0.99 to -2.35 degrees. It was concluded that the digital FMAA measurement is less reliable than analog measurement in total knee arthroplasty.

*impactfactor:* --

## Houterman S

### **Laparoscopische refertilisatie : Onderzoek naar zwangerschapsresultaten en prognostische factoren**

drs. J.A.H. van Seeters, prof. dr. B.W. Mol , dr. M.A.H.M. Wiegerinck , dr. S. Houterman\* , dr. C.A.M. Koks Nederlands Tijdschrift voor Obstetrie & Gynaecologie, 2015; 128(mei):126-30

Sterilisatie bij vrouwen is een veel voorkomende vorm van anticonceptie. Een kleine groep ontwikkelt echter spijt en ontwikkelt een nieuwe kinderwens.

Behandelingsopties hierbij zijn een IVF-behandeling of een refertilisatie. Wij evalueerden de factoren die het zwangerschapspercentage na een laparoscopischerefertilisatie sterilisatie beïnvloeden.

Een retrospectief cohortonderzoek is verricht, waarbij vrouwen zijn geïncludeerd die een refertilisatie hebben ondergaan van 1997 tot mei 2012.

Er is sprake van een follow-up van ten minste 12 maanden. Primaire uitkomstmaten zijn de tijd tot het optreden van een zwangerschap, al dan niet doorgaand, en van een extra-uteriene graviditeit.

Voor secundaire uitkomstmaten is gekeken naar mogelijke prognostische factoren als leeftijd, BMI, intoxicaties en methode en duur van de sterilisatie.

Er werd een zwangerschapspercentage van 60% bereikt, met een doorgaand zwangerschapspercentage van 44%.

Bij 6 patiënten trad een EUG op. De leeftijd van de patiënt bleek de enige prognostische factor te zijn.

Female sterilization is a widely used contraceptive method. In a small group of women however, poststerilization regret occurs.

These women have the option to choose between a surgical re-anastomosis and IVF-treatment.

We evaluated the factors that affect pregnancy rates after a tubal re-anastomosis for post-sterilization regret.

We performed a retrospective cohort study, which included women who underwent a laparoscopic refertilization between 1997 and march 2012.

Women were followed for at least 12 months. Primary outcomes are the time to a clinical pregnancy, ongoing pregnancy rate and the occurrence of ectopic pregnancies. For secondary outcomes we examined whether clinical characteristics like BMI, intoxications and method and length of sterilization could influence the chance of getting pregnant.

A pregnancy rate of 60% was seen, with an ongoing pregnancy rate of 44%. Six patients had an ectopic pregnancy. Women's age appeared to be the only clinical important prognostic factor.

*impactfactor:*      --

\* = Werkzaam in het Catharina Ziekenhuis

## **Operatiekamers**

**Braam L**

**Hysteroscopische operaties onder sedatie op de polikliniek**

Van Vliet HA\*, Kuijsters N\*, Braam L\*, Schoot BC\*

NTOG 2015; 128: 412-7

*Geen abstract beschikbaar.*

*impactfactor:* --

\* = Werkzaam in het Catharina Ziekenhuis

## Orthopedie

**Besselaar AT**

**Interpositie van dermis graft bij de behandeling van distale tibiofibulaire synostose**

Letsch MT\*, Besselaar A\*, de Boer HL\*, Hoogbergen MM\*

Ned. Tijdschr Traum 2015 nr 6, 128-131

Voor abstract zie: *Plastische Chirurgie - Letsch MT*

impactfactor: --

**Hove RP van**

**Titanium-Nitride Coating of Orthopaedic Implants: A Review of the Literature**

van Hove RP\*, Sierevelt IN, van Royen BJ, Nolte PA

Biomed Res Int. 015;2015:485975

Surfaces of medical implants can be enhanced with the favorable properties of titanium-nitride (TiN). In a review of English medical literature, the effects of TiN-coating on orthopaedic implant material in preclinical studies were identified and the influence of these effects on the clinical outcome of TiN-coated orthopaedic implants was explored. The TiN-coating has a positive effect on the biocompatibility and tribological properties of implant surfaces; however, there are several reports of third body wear due to delamination, increased ultrahigh molecular weight polyethylene wear, and cohesive failure of the TiN-coating. This might be due to the coating process. The TiN-coating process should be optimized and standardized for titanium alloy articulating surfaces. The clinical benefit of TiN-coating of CoCrMo knee implant surfaces should be further investigated.

impactfactor: 1.579

**Kempen R van**

**The long-term prognosis of Legg-Calvé-Perthes disease: a historical prospective study with a median follow-up of forty one years**

Heesakkers N, van Kempen R\*, Feith R, Hendriks J, Schreurs W

Int Orthop. 2015 May;39(5):859-63. Epub 2014 Nov 19

**PURPOSE:** The purpose of this study is predicting the clinical and radiological long-term outcome and identifying prognostic factors of Legg-Calvé-Perthes disease (LCPD) in Catterall 2 and 3 hips.

**METHODS:** Sixty hips (59 patients) were diagnosed with LCPD between 1959 to 1974 and were followed prospectively. Forty-two of these 60 hips were classified as Catterall 2 or 3. In 2002, 33 hips (32 patients) with Catterall type 2 or 3 were evaluated clinically and radiographically. In 2010, 27 hips (26 patients) were re-evaluated.

**RESULTS:** In 2002, 15 hips had Catterall 2 type LCPD and 18 hips Catterall 3. Twelve of the 33 hips (36 %) had signs of osteoarthritis. In 2010, 14 hips were classified as Catterall 2 and 13 hips as Catterall 3. Catterall 2 hips had a significantly better Harris Hip Score (HHS) ( $p=0.001$ ). There were 15 hips (55 %) with signs of osteoarthritis.

**CONCLUSION:** The long-term prognosis of LCPD Catterall type 2 and 3 is relatively benign. However, more than 50 % of the patients will develop signs of osteoarthritis between the 4th and 5th decades. At the latest follow-up a strong increase in the number of cases with osteoarthritis was seen. Sphericity of the femoral head is an important predicting factor in the development of osteoarthritis.

impactfactor: 2.025

**Steen MC van der**

**Individual differences in temporal anticipation and adaptation during sensorimotor synchronization**

Mills PF, van der Steen MC<sup>∞</sup>, Schultz BG, Keller PE

Timing & Time Perception 2015;3(1-2):13-31. Interpersonal coordination during musical joint action (e.g., ensemble performance) requires individuals to anticipate and adapt to each other's action timing. Individuals differ in their ability to both anticipate and adapt, however, little is known about the relationship between these skills. The present study used paced finger tapping tasks to examine the relationship between anticipatory skill and adaptive (error correction) processes. Based on a computational model, it was hypothesized that temporal anticipation and adaptation will act together to facilitate synchronization accuracy and precision. Adaptive ability was measured as the degree of temporal error correction that participants (N= 52) engaged in when synchronizing with a 'virtual partner', that is, an auditory pacing signal that modulated its timing based on the participant's performance. Anticipation was measured through a prediction index that reflected the degree to which participants' inter-tap intervals led or lagged behind inter-onset intervals in tempo-changing sequences. A correlational analysis revealed a significant positive relationship between the prediction index and temporal error correction estimates, suggesting that anticipation and adaptation interact to facilitate synchronization performance. Hierarchical regression analyses revealed that adaptation was the best predictor of synchronization accuracy, whereas both adaptation and anticipation predicted synchronization precision. Together these results demonstrate a relationship between anticipatory and adaptive mechanisms, and indicate that individual differences in these two abilities are predictive of synchronization performance.

<sup>∞</sup> ten tijde van publicatie werkzaam bij Max Planck Institute for Human Cognitive and Brain Sciences

Impactfactor: --

**Steen MC van der**

**Modeling effects of cerebellar and basal ganglia lesions on adaptation and anticipation during sensorimotor synchronization**

Steen MC van der <sup>∞</sup>, Schwartze M, Kotz SA, Keller PE

Ann N Y Acad Sci. 2015 Mar;1337:101-10

This study addressed the role of subcortical brain structures in temporal adaptation and anticipation during sensorimotor synchronization. The performance of patients with cerebellar or basal ganglia lesions was compared with that of healthy control participants on tasks requiring the synchronization of drum strokes with adaptive and tempo-changing auditory pacing sequences. The precision of sensorimotor synchronization was generally lower in patients relative to controls (i.e., variability of asynchronies was higher in patients), although synchronization accuracy (mean asynchrony) was commensurate. A computational model of adaptation and anticipation (ADAM) was used to examine potential sources of individual differences in precision by estimating participants' use of error correction, temporal prediction, and the amount of variability associated with central timekeeping and peripheral motor processes. Parameter estimates based on ADAM indicate that impaired precision was attributable to increased variability of timekeeper and motor processes as well as to reduced temporal prediction in both patient groups. Adaptive processes related to continuously applied error correction were, by contrast, intact in patients.

These findings highlight the importance of investigating how subcortical structures, including the cerebellum and basal ganglia, interact with a broader network of cortical regions to support temporal adaptation and anticipation during sensorimotor synchronization.

∞ = Ten tijde van publicatie werkzaam bij Max Planck Institute for Human Cognitive and Brain Sciences.  
impactfactor: 4.383

## **Steen MC van der**

### **Sensorimotor synchronization with tempo-changing auditory sequences:**

#### **Modeling temporal adaptation and anticipation**

Steen MC van der ∞, Jacoby N, Fairhurst MT, Keller PE

Brain Res. 2015 Nov 11;1626:66-87

The current study investigated the human ability to synchronize movements with event sequences containing continuous tempo changes. This capacity is evident, for example, in ensemble musicians who maintain precise interpersonal coordination while modulating the performance tempo for expressive purposes. Here we tested an ADaptation and Anticipation Model (ADAM) that was developed to account for such behavior by combining error correction processes (adaptation) with a predictive temporal extrapolation process (anticipation). While previous computational models of synchronization incorporate error correction, they do not account for prediction during tempo-changing behavior. The fit between behavioral data and computer simulations based on four versions of ADAM was assessed. These versions included a model with adaptation only, one in which adaptation and anticipation act in combination (error correction is applied on the basis of predicted tempo changes), and two models in which adaptation and anticipation were linked in a joint module that corrects for predicted discrepancies between the outcomes of adaptive and anticipatory processes. The behavioral experiment required participants to tap their finger in time with three auditory pacing sequences containing tempo changes that differed in the rate of change and the number of turning points. Behavioral results indicated that sensorimotor synchronization accuracy and precision, while generally high, decreased with increases in the rate of tempo change and number of turning points. Simulations and model-based parameter estimates showed that adaptation mechanisms alone could not fully explain the observed precision of sensorimotor synchronization. Including anticipation in the model increased the precision of simulated sensorimotor synchronization and improved the fit of model to behavioral data, especially when adaptation and anticipation mechanisms were linked via a joint module based on the notion of joint internal models. Overall results suggest that adaptation and anticipation mechanisms both play an important role during sensorimotor synchronization with tempo-changing sequences. This article is part of a Special Issue entitled SI: Prediction and Attention.

∞ = Ten tijde van publicatie werkzaam bij Max Planck Institute for Human Cognitive and Brain Sciences.  
impactfactor: 3.028

\* = Werkzaam in het Catharina Ziekenhuis



**Pamm**

**Brands AV****Charcot-Leyden crystals in acute myeloid leukemia**

van de Kerkhof D\*, Scharnhorst V\*, Huysentruyt CJ\*, Brands-Nijenhuis AV\*, Ermens AA  
Int J Lab Hematol. 2015 Aug;37(4):e100-2

*Geen abstract beschikbaar*

*impactfactor: 1.819*

**Demeyere TB****Thinking beyond the mass: ANCA-associated vasculitis mimicking a pancreatic malignancy**

De Bie AJ\*, Dekker MJ\*, Vermeulen Windsant IC\*, Nikkessen S, Demeyere TB\*, Konings CJ\*, de Hingh IH\*, Franssen CF, Creemers GJ\*

Neth J Med. 2015 Aug;73(7):341-4

*Voor abstract zie: Inwendige geneeskunde - Bie AJ de*

*impactfactor: 1.969*

**Huysentruyt CJ****Charcot-Leyden crystals in acute myeloid leukemia**

van de Kerkhof D\*, Scharnhorst V\*, Huysentruyt CJ\*, Brands-Nijenhuis AV\*, Ermens AA  
Int J Lab Hematol. 2015 Aug;37(4):e100-2

*Geen abstract beschikbaar.*

*impactfactor: 1.819*

**Jansz AR****Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie: AKL - Geerts N*

*impactfactor: 2.824*

**Klinkhamer PJ****Pipelle Prospective ENDometrial carcinoma (PIPENDO) study, pre-operative recognition of high risk endometrial carcinoma: a multicentre prospective cohort study**

Visser NC, Bulten J, van der Wurff AA, Boss EA, Bronkhorst CM, Feijen HW, Haartsen JE, van Herk HA, de Kievit IM, Klinkhamer PJ\*, Pijlman BM, Snijders MP, Vandenput I\*, Vos MC, de Wit PE, van de Poll-Franse LV,, Massuger LF, Pijnenborg JM

BMC Cancer. 2015 Jun 30;15:487

BACKGROUND: Endometrial carcinoma is the most common gynaecologic malignancy in industrialised countries and the incidence is still rising. Primary treatment is based on preoperative risk classification and consists in most cases of hysterectomy with bilateral salpingo-oophorectomy. In patients with serous and clear cell histology a complete surgical staging is mandatory. However, in routine clinical practice final histology regularly does not correspond with the preoperative histological diagnosis. This results in both over and under treatment.

**METHODS/DESIGN:** The aim of this multicentre, prospective cohort study is to select a panel of prognostic biomarkers to improve preoperative diagnosis of endometrial carcinoma in order to identify those patients that need extended surgery and/or additional treatment. Additionally, we will determine whether incorporation of cervical cytology and comorbidity could improve this preoperative risk classification. All patients treated for endometrial carcinoma in the participating hospitals from September 2011 till December 2013 are included. Patient characteristics, as well as comorbidity are registered. Patients without preoperative histology, history of hysterectomy and/or endometrial carcinoma or no surgical treatment including hysterectomy are excluded. The preoperative histology and final pathology will be reviewed and compared by expert pathologists. Additional immunohistochemical analysis of IMP3, p53, ER, PR, MLH1, PTEN, beta-catenin, p16, Ki-67, stathmin, ARID1A and L1CAM will be performed. Preoperative histology will be compared with the final pathology results. Follow-up will be at least 24 months to determine risk factors for recurrence and outcome.

**DISCUSSION:** This study is designed to improve surgical treatment of endometrial carcinoma patients. A total of 432 endometrial carcinoma patients were enrolled between 2011 and 2013. Follow-up will be completed in 2015. Preoperative histology will be evaluated systematically and background endometrium will be classified. This is the first study incorporating immunohistochemistry, cervical cytology and comorbidity to define the optimal panel of prognostic biomarkers that contribute in clinical decision making in the management of endometrial carcinoma.

*impactfactor:* 3.362

## **Klinkhamer PJ**

### **Spontaneous regression and recurrence of stage III Merkel cell carcinoma**

Jansen SC, Groeneveld-Haenen CP, Klinkhamer PJ\*, Roumen RM

BMJ Case Rep. 2015 Feb 25;2015. pii: bcr2014208344.

Merkel cell carcinoma (MCC) is a malignant neuroendocrine carcinoma originating in the skin. It is typically aggressive with a tendency to recur locally and metastasise. There have been several case reports about spontaneous regression of MCC over the past years, but to the best of our knowledge this is the first case of a regional lymph node metastasised MCC with complete spontaneous regression and recurrence. In addition, the primary tumour has an unusual localisation on the foot.

*impactfactor:* --

## **Lijnschoten G van**

### **Variation in circumferential resection margin: Reporting and involvement in the South-Netherlands**

Homan J, Bökkerink GM, Aarts MJ, Lemmens VE, van Lijnschoten G\*, Rutten HJ\*, Wijsman JH, Nagtegaal ID, de Wilt JH

Eur J Surg Oncol. 2015 Nov;41(11):1485-92

**BACKGROUND:** Since the introduction of total mesorectal surgery the outcome of rectal cancer patients has improved significantly. Involvement of the circumferential resection margin (CRM) is an important predictor of increased local recurrence, distant metastases and decreased overall survival. Abdomino perineal excision (APE) is associated with increased risk of CRM involvement. Aim of this study was to analyze reporting of CRM and to identify predictive factors for CRM involvement.

**METHODS:** A population-based dataset was used selecting 2153 patients diagnosed between 2008 and 2013 with primary rectal cancer undergoing surgery. Variation in CRM reporting

was assessed and predictive factors for CRM involvement were calculated and used in multivariate analyses.

**RESULTS:** Large variation in CRM reporting was found between pathology departments, with missing cases varying from 6% to 30%. CRM reporting increased from 77% in 2008 to 90% in 2012 ( $p < 0.001$ ). CRM involvement significantly decreased from 12% to 6% over the years ( $p < 0.001$ ). In multivariate analysis type of operation, low anterior resection or APE, did not influence the risk of CRM involvement. Clinical T4-stage [odds ratio (OR) = 3.51; 95% confidence interval (CI) = 1.85-6.65] was associated with increased risk of CRM involvement, whereas neoadjuvant treatment ( $5 \times 5$  gray radiotherapy [OR 0.39; CI 0.25-0.62] or chemoradiation therapy [OR 0.30; CI 0.17-0.53]) were associated with significant decreased risk of CRM involvement.

**CONCLUSION:** Although significant improvements are made during the last years there still is variation in reporting of CRM involvement in the Southern Netherlands. In multivariate analysis APE was no longer associated with increased risk of CRM involvement.

*impactfactor:* 3.009

### **Wegdam-Blans MC**

#### **Chronic Q Fever Diagnosis— Consensus Guideline versus Expert Opinion.**

Kampschreur LM, Wegdam-Blans MC, Wever PC, Renders NH, Delsing CE, Sprong T, van Kasteren ME, Bijlmer H, Notermans D, Oosterheert JJ, Stals FS, Nabuurs-Franssen MH, Bleeker-Rovers CP; Dutch Q Fever Consensus Group

Emerg Infect Dis. 2015 Jul;21(7):1183-8

Chronic Q fever, caused by *Coxiella burnetii*, has high mortality and morbidity rates if left untreated. Controversy about the diagnosis of this complex disease has emerged recently. We applied the guideline from the Dutch Q Fever Consensus Group and a set of diagnostic criteria proposed by Didier Raoult to all 284 chronic Q fever patients included in the Dutch National Chronic Q Fever Database during 2006–2012. Of the patients who had proven cases of chronic Q fever by the Dutch guideline, 46 (30.5%) would not have received a diagnosis by the alternative criteria designed by Raoult, and 14 (4.9%) would have been considered to have possible chronic Q fever. Six patients with proven chronic Q fever died of related causes. Until results from future studies are available, by which current guidelines can be modified, we believe that the Dutch literature-based consensus guideline is more sensitive and easier to use in clinical practice.

*impactfactor:* 6.75

### **Wegdam-Blans MC**

#### **Coxiellaburnetii Infectivity Lower in Children than Adults Following Community Exposure: Overlooked Cause of Infrequent Q-Fever Reporting in the Young**

Hackert VH, Dukers-Muijters NH, van Loo IH, Wegdam-Blans M\*, Somers C, Hoebe CJ

Pediatr Infect Dis J. 2015 Dec;34(12):1283-8

**BACKGROUND:** Q fever is rarely reported in children/adolescents. While lower reporting rates are commonly attributed to milder disease and subsequent underdiagnosis in infected children/adolescents, pertinent evidence is scarce. We present data from a large, well-defined single-point source outbreak of Q fever to fill this gap.

**METHODS:** We compared A) Q-fever testing and notification rates in children/adolescents who were 0-19 years versus adults 20+ years of age in 2009/10; B) serological attack rates (SAR) of acute Q fever in children/adolescents versus adults following on-source exposure on the outbreak farm's premises; C) incidence of Q-fever infection in children/adolescents versus adults following off-source exposure in the municipality located closest to the farm.

RESULTS: A) Children/adolescents represented 19.3%(59404/307348) of the study area population, 12.1%(149/1217) of all subjects tested in 2009/10, and 4.3%(11/253) of notified laboratory-confirmed community cases. B) SAR of acute Q fever in children with on-source exposure was 71%(12/17), similar to adults (68%(40/59)). C) Incidence of infection in children/adolescents following community (off-source) exposure was 4.5%(13/287) versus 11.0%(12/109) in adults (adjusted OR=0.36,95%CI=0.16-0.84,P=0.02). No children/adolescents reported clinical symptoms. Proportion of notified infections was significantly lower in children/adolescents (2.5%) than adults (10.4%) (RR=0.26,95%CI=0.08-0.80,P=0.02).

CONCLUSION: Notified Q fever was less frequent in children/adolescents than adults. While underrecognition contributed to this phenomenon, lower infectivity in children following community exposure played an unexpected major role. On-source (presumed high-dose) exposure, by contrast, was associated with high serologic and clinical attack rates not only in adults, but also in children/adolescents. Our findings allow for improved age-specific clinical and public health risk assessment in Q-fever outbreaks.

*impactfactor:* 2.723

## Wegdam-Blans MC

### Genetic Variation in Pattern Recognition Receptors and Adaptor Proteins Associated With Development of Chronic Q Fever

Schoffelen T, Ammerdorffer A, Hagenaars JC, Bleeker-Rovers CP, Wegdam-Blans MC\*, Wever PC, Joosten LA, van der Meer JW, Sprong T, Netea MG, van Deuren M, van de Vosse E

J Infect Dis. 2015 Sep 1;212(5):818-29

BACKGROUND: Q fever is an infection caused by *Coxiella burnetii*. Persistent infection (chronic Q fever) develops in 1%-5% of patients. We hypothesize that inefficient recognition of *C. burnetii* and/or activation of host-defense in individuals carrying genetic variants in pattern recognition receptors or adaptors would result in an increased likelihood to develop chronic Q fever.

METHODS: Twenty-four single-nucleotide polymorphisms in genes encoding Toll-like receptors, nucleotide-binding oligomerization domain-like receptor-2, av $\beta$ 3 integrin, CR3, and adaptors myeloid differentiation primary response protein 88 (MyD88), and Toll interleukin 1 receptor domain-containing adaptor protein (TIRAP) were genotyped in 139 patients with chronic Q fever and in 220 controls with cardiovascular risk-factors and previous exposure to *C. burnetii*. Associations between these single-nucleotide polymorphisms and chronic Q fever were assessed by means of univariate logistic regression models. Cytokine production in whole-blood stimulation assays was correlated with relevant genotypes.

RESULTS: Polymorphisms in TLR1 (R80T), NOD2 (1007fsX1), and MYD88 (-938C>A) were associated with chronic Q fever. No association was observed for polymorphisms in TLR2, TLR4, TLR6, TLR8, ITGAV, ITGB3, ITGAM, and TIRAP. No correction for multiple testing was performed because only genes with a known role in initial recognition of *C. burnetii* were included. In the whole-blood assays, individuals carrying the TLR1 80R-allele showed increased interleukin 10 production with *C. burnetii* exposure.

CONCLUSIONS: Polymorphisms in TLR1 (R80T), NOD2 (L1007fsX1), and MYD88 (-938C>A) are associated with predisposition to development of chronic Q fever. For TLR1, increased interleukin 10 responses to *C. burnetii* in individuals carrying the risk allele may contribute to the increased risk of chronic Q fever.

*impactfactor:* 5.997

### **Wegdam-Blans MC**

**Specific in vitro interferon-gamma and IL-2 production as biomarkers during treatment of chronic Q fever** Schoffelen T, Wegdam-Blans MC\*, Ammerdorffer A, Pronk MJ\*, Soethoudt YE, Netea MG, van der Meer JW, Bleeker-Rovers CP, van Deuren M

Front Microbiol. 2015 Feb 12;6:93. eCollection 2015

**BACKGROUND:** Antibiotic treatment of chronic Q fever is cumbersome and of long duration. To monitor treatment, there is a need for alternative biomarkers. *Coxiella burnetii*-specific interferon (IFN)- $\gamma$  and interleukin (IL)-2 production reflect the type of effector and memory T-cell response. In chronic Q fever, *C. burnetii*-specific IFN- $\gamma$  production is higher and IL-2 production is lower than in individuals with past Q fever. Here we explore whether *C. burnetii*-specific IFN- $\gamma$  and IL-2 production correlate to treatment response.

**METHODS:** We studied the longitudinal *C. burnetii*-specific IFN- $\gamma$ /IL-2 ratio in fifteen proven chronic Q fever patients. All patients were followed for at least 18 months during antibiotic treatment. Treatment was considered successful when clinical recovery was observed, a positive PCR for *C. burnetii* DNA in blood became persistently negative, anti-phase I IgG showed a fourfold decrease or more, and imaging techniques showed disappearance of infectious foci.

**RESULTS:** Overall, the IFN- $\gamma$ /IL-2 ratio declined when patients experienced a successful treatment outcome. When treatment failed, IFN- $\gamma$ /IL-2 ratios did not significantly decrease. The median ( $\pm$ IQR) slope of the longitudinal IFN- $\gamma$ /IL-2 ratio with successful treatment was -2.10 (-7.02 to -0.06), and -0.15 (-1.13 to 0.25) with unsuccessful treatment ( $P = 0.19$ ). Q fever endocarditis patients had higher IFN- $\gamma$ /IL-2 ratios than patients with endovascular infections.

**CONCLUSION:** We propose that the IFN- $\gamma$ /IL-2 ratio can be used as an additional biomarker for monitoring chronic Q fever treatment, with declining ratios being indicative of successful treatment.

*impactfactor:* 3.989

### **Wegdam-Blans MC**

**Vascular complications and surgical interventions after world's largest Q fever outbreak**

Broos PP\*, Hagens JC, Kampschreur LM, Wever PC, Bleeker-Rovers CP, Koning OH, Teijink JA\*, Wegdam-Blans MC\*

J Vasc Surg. 2015 Nov;62(5):1273-80. Epub 2015 Sep 10

Voor abstract zie: Chirurgie - Broos PP

*impactfactor:* 3.021

\* = Werkzaam in het Catharina Ziekenhuis

## **Plastische Chirurgie**

**Boer H de**

**Interpositie van dermis graft bij de behandeling van distale tibiofibulaire synostose**

Letsch MT\*, Besselaar A\*, de Boer HL\*, Hoogbergen MM\*

Ned. Tijdschr Traum 2015 nr 6, 128-131

Voor abstract zie: *Plastische Chirurgie - Letsch MT*

impactfactor: --

**Boer H de**

**Treatment of mallet fingers in Dutch hospitals: a nationwide survey of practice**

Haagsma A\*, de Boer HL\*, Quintus AC\*, Strikkeling NJ, Zeebregts CJ, Smit JM\*

Eur J Emerg Med. 2015 Jun;22(3):211-4. Epub 1 Mar 2014

Voor abstract zie: *Plastische Chirurgie - Haagsma A*

impactfactor: 1.583

**Haagsma A**

**Treatment of mallet fingers in Dutch hospitals: a nationwide survey of practice**

Haagsma A\*, de Boer HL\*, Quintus AC\*, Strikkeling NJ, Zeebregts CJ, Smit JM\*

Eur J Emerg Med. 2015 Jun;22(3):211-4. Epub 1 Mar 2014

OBJECTIVE: The aim of this study was to create an overview of the treatment of mallet fingers in Dutch hospitals.

METHODS: A national online questionnaire was used to determine the treatment of mallet fingers in Dutch emergency units.

RESULTS: Data were received from 58 units (response rate 97%). All the emergency units treated an uncomplicated mallet finger with a splint. The treatment of complicated mallet fingers was less uniform. The departments of general, orthopaedic and plastic surgery were involved in the treatment and their involvement varied according to the type of mallet finger and showed variations in the follow-up treatment.

CONCLUSION: There is a general consensus on the treatment of uncomplicated mallet fingers. The follow-up treatment of uncomplicated lesions as well as the treatment of complicated mallet fingers should be fields of future research.

impactfactor: 1.583

**Hoogbergen MM**

**Interpositie van dermis graft bij de behandeling van distale tibiofibulaire synostose**

Letsch MT\*, Besselaar A\*, de Boer HL\*, Hoogbergen MM\*

Ned. Tijdschr Traum 2015 nr 6, 128-131

Voor abstract zie: *Plastische Chirurgie - Letsch MT*

impactfactor: --

**Kerver AL**

**The anatomical relationship of the superficial radial nerve and the lateral antebrachial cutaneous nerve: A possible factor in persistent neuropathic pain**

Poublon AR, Walbeehm ET, Duraku LS, Eilers PH, Kerver AL<sup>∞</sup>, Kleinrensink GJ, Coert JH  
J Plast Reconstr Aesthet Surg. 2015 Feb;68(2):237-42. Epub 2014 Oct 16

The superficial branch of the radial nerve (SBRN) is known for developing neuropathic pain syndromes after trauma. These pain syndromes can be hard to treat due to the involvement of other nerves in the forearm. When a nerve is cut, the Schwann cells, and also other cells in the distal segment of the transected nerve, produce the nerve growth factor (NGF) in the



entire distal segment. If two nerves overlap anatomically, similar to the lateral antebrachial cutaneous nerve (LACN) and SBRN, the increase in secretion of NGF, which is mediated by the injured nerve, results in binding to the high-affinity NGF receptor, tyrosine kinase A (TrkA). This in turn leads to possible sprouting and morphological changes of uninjured fibers, which ultimately causes neuropathic pain. The aim of this study was to map the level of overlap between the SBRN and LACN. Twenty arms (five left and 15 right) were thoroughly dissected. Using a new analysis tool called CASAM (Computer Assisted Surgical Anatomy Mapping), the course of the SBRN and LACN could be compared visually. The distance between both nerves was measured at 5-mm increments, and the number of times they intersected was documented. In 81% of measurements, the distance between the nerves was >10 mm, and in 49% the distance was even <5 mm. In 95% of the dissected arms, the SBRN and LACN intersected. On average, they intersected 2.25 times. The close (anatomical) relationship between the LACN and the SBRN can be seen as a factor in the explanation of persistent neuropathic pain in patients with traumatic or iatrogenic lesion of the SBRN or the LACN.

∞ = Ten tijde van publicatie werkzaam bij: Department of Neuroscience and Anatomy, Erasmus MC, Rotterdam, The Netherlands  
*impactfactor:* 1.421

## **Letsch MT**

### **Interpositie van dermis graft bij de behandeling van distale tibiofibulaire synostose**

Letsch MT\*, Besselaar A\*, de Boer HL\*, Hoogbergen MM\*

Ned. Tijdschr Traum 2015 nr 6, 128-131

Een distale tibiofibulaire synostose kan optreden na een operatieve behandeling of traumatisch letsel ter plaatse van het distale tibiofibulaire gewricht. Er bestaat onvoldoende consensus over de meest optimale behandeling en recidivering is een regelmatig optredende complicatie.

In dit artikel beschrijven wij drie casus met een distale tibiofibulaire synostose door verschillende oorzaken, waarbij resectie van de synostose plaatsvond.

Toepassing van een dermisgraft uit de lies ter interpositie laat goede resultaten zien in het voorkomen van een recidief.

*impactfactor:* --

## **Smit JM**

### **Treatment of mallet fingers in Dutch hospitals: a nationwide survey of practice**

Haagsma A\*, de Boer HL\*, Quintus AC\*, Strikkeling NJ, Zeebregts CJ, Smit JM\*

Eur J Emerg Med. 2015 Jun;22(3):211-4. Epub 1 Mar 2014

Voor abstract zie: Plastische Chirurgie - Haagsma A

*impactfactor:* 1.583

\* = Werkzaam in het Catharina Ziekenhuis

## Radiologie

**Bosch HC van den**

**Automatic indicator dilution curve extraction in dynamic-contrast enhanced imaging using spectral clustering**

Saporito S, Herold IH\*, Houthuizen P\*, van den Bosch HC\*, Korsten HH\*, van Assen HC, Mischi M

Phys Med Biol. 2015 Jul 7;60(13):5225-40

Voor abstract zie: *Anesthesiologie - Herold IH*

impactfactor: 2.761

**Bosch HC van den**

**Site-specific association between distal aortic pulse wave velocity and peripheral arterial stenosis severity: a prospective cardiovascular magnetic resonance study**

van den Bosch HC\*, Westenberg JJ, Setz-Pels W\*, Wondergem J, Wolterbeek R, Duijm LE, Teijink JA\*, de Roos A\*

J Cardiovasc Magn Reson. 2015 Jan 20;17(1):2

**BACKGROUND:** Vascular disease expression in one location may not be representative for disease severity in other vascular territories, however, strong correlation between disease expression and severity within the same vascular segment may be expected. Therefore, we hypothesized that aortic stiffening is more strongly associated with disease expression in a vascular territory directly linked to that aortic segment rather than in a more remote segment. We prospectively compared the association between aortic wall stiffness, expressed by pulse wave velocity (PWV), sampled in the distal aorta, with the severity of peripheral arterial occlusive disease (PAOD) as compared to atherosclerotic markers sampled in remote vascular territories such as PWV in the proximal aorta and the normalized wall index (NWI), representing the vessel wall thickness, of the left common carotid artery. **METHODS:** Forty-two patients (23 men; mean age  $64 \pm 10$  years) underwent velocity-encoded cardiovascular magnetic resonance (CMR) in the proximal and distal aorta, whole-body contrast-enhanced MR angiography (CE-MRA) and carotid vessel wall imaging with black-blood CMR in the work-up for PAOD. Strength of associations between aortic stiffness, carotid NWI and peripheral vascular stenosis grade were assessed and evaluated with multiple linear regression.

**RESULTS:** Stenosis severity correlated well with PWV in the distal aorta (Pearson  $rP=0.64$ ,  $p<0.001$ , Spearman  $rS=0.65$ ,  $p<0.001$ ) but to a lesser extent with PWV in the proximal aorta ( $rP=0.48$ ,  $p=0.002$ ,  $rS=0.22$ ,  $p=0.18$ ). Carotid NWI was not associated with peripheral stenosis severity ( $rP=0.17$ ,  $p=0.28$ ,  $rS=0.14$ ,  $p=0.37$ ) nor with PWV in the proximal aorta ( $rP=0.22$ ,  $p=0.17$ ) nor in the distal aorta ( $rP=0.21$ ,  $p=0.18$ ). Correlation between stenosis severity and distal aortic PWV remained statistically significant after correction for age and gender.

**CONCLUSIONS:** Distal aortic wall stiffness is more directly related to peripheral arterial stenosis severity than markers from more remote vascular territories such as proximal aortic wall stiffness or carotid arterial wall thickness. Site-specific evaluation of vascular disease may be required for full vascular risk estimation.

impactfactor: 4.556

**Duijm LE**

**Site-specific association between distal aortic pulse wave velocity and peripheral arterial stenosis severity: a prospective cardiovascular magnetic resonance study**

van den Bosch HC\*, Westenberg JJ, Setz-Pels W\*, Wondergem J\*, Wolterbeek R, Duijm LE\*, Teijink JA\*, de Roos A\*

J Cardiovasc Magn Reson. 2015 Jan 20;17(1):2

Voor abstract zie: *Radiologie - Bosch HC van den*

*impactfactor: 4.556*

**Duijm LE**

**The Prognostic Value of CT Angiography and CT Perfusion in Acute Ischemic Stroke**

van Seeters T, Biessels GJ, Kappelle LJ, van der Schaaf IC, Dankbaar JW, Horsch AD, Niesten JM, Luitse MJ, Majoie CB, Vos JA, Schonewille WJ, van Walderveen MA, Wermer MJ, Duijm LE\*, Keizer K, Bot JC, Visser MC, van der Lugt A, Dippel DW, Kesselring FO, Hofmeijer J, Lycklama À Nijeholt GJ, Boiten J, van Rooij WJ, de Kort PL, Roos YB, van Dijk EJ, Pleiter CC, Mali WP, van der Graaf Y, Velthuis BK; Dutch acute stroke study (DUST)

investigators.Cerebrovasc Dis. 2015 Nov;40(5-6):258-69

**BACKGROUND:** CT angiography (CTA) and CT perfusion (CTP) are important diagnostic tools in acute ischemic stroke. We investigated the prognostic value of CTA and CTP for clinical outcome and determined whether they have additional prognostic value over patient characteristics and non-contrast CT (NCCT).

**METHODS:** We included 1,374 patients with suspected acute ischemic stroke in the prospective multicenter Dutch acute stroke study. Sixty percent of the cohort was used for deriving the predictors and the remaining 40% for validating them. We calculated the predictive values of CTA and CTP predictors for poor clinical outcome (modified Rankin Scale score 3-6). Associations between CTA and CTP predictors and poor clinical outcome were assessed with odds ratios (OR). Multivariable logistic regression models were developed based on patient characteristics and NCCT predictors, and subsequently CTA and CTP predictors were added. The increase in area under the curve (AUC) value was determined to assess the additional prognostic value of CTA and CTP. Model validation was performed by assessing discrimination and calibration.

**RESULTS:** Poor outcome occurred in 501 patients (36.5%). Each of the evaluated CTA measures strongly predicted outcome in univariable analyses: the positive predictive value (PPV) was 59% for Alberta Stroke Program Early CT Score (ASPECTS) =7 on CTA source images (OR 3.3; 95% CI 2.3-4.8), 63% for presence of a proximal intracranial occlusion (OR 5.1; 95% CI 3.7-7.1), 66% for poor leptomeningeal collaterals (OR 4.3; 95% CI 2.8-6.6), and 58% for a >70% carotid or vertebrobasilar stenosis/occlusion (OR 3.2; 95% CI 2.2-4.6). The same applied to the CTP measures, as the PPVs were 65% for ASPECTS =7 on cerebral blood volume maps (OR 5.1; 95% CI 3.7-7.2) and 53% for ASPECTS =7 on mean transit time maps (OR 3.9; 95% CI 2.9-5.3). The prognostic model based on patient characteristics and NCCT measures was highly predictive for poor clinical outcome (AUC 0.84; 95% CI 0.81-0.86). Adding CTA and CTP predictors to this model did not improve the predictive value (AUC 0.85; 95% CI 0.83-0.88). In the validation cohort, the AUC values were 0.78 (95% CI 0.73-0.82) and 0.79 (95% CI 0.75-0.83), respectively. Calibration of the models was satisfactory.

**CONCLUSIONS:** In patients with suspected acute ischemic stroke, admission CTA and CTP parameters are strong predictors of poor outcome and can be used to predict long-term

clinical outcome. In multivariable prediction models, however, their additional prognostic value over patient characteristics and NCCT is limited in an unselected stroke population.  
*impactfactor:* 3.754

## **Klompénhouwer E**

### **Arbitration of discrepant BI-RADS 0 recalls by a third reader at screening mammography lowers recall rate but not the cancer detection rate and sensitivity at blinded and non-blinded double reading**

Klompénhouwer EG\*, Weber RJ\*, Voogd AC, den Heeten GJ, Strobbe LJ, Broeders MJ, Tjan-Heijnen VC, Duijm LE

Breast. 2015 Oct;24(5):601-7. Epub 2015 Jun 24

**PURPOSE:** To evaluate the characteristics of low suspicion lesions (BI-RADS 0) at blinded and non-blinded double reading of screening mammograms and to determine the potential effect of arbitration of discrepant BI-RADS 0 recalls by a third reader on screening outcome.

**METHODS:** We included a series of 84,927 consecutive digital screening mammograms, double read in a blinded (43,184 screens) or non-blinded (41,743 screens) fashion, between July 2009 and July 2011. Discrepant readings were routinely recalled for further evaluation. During 2 years of follow-up, radiology, surgical and pathology reports were collected of all recalled women. Arbitration of discrepant BI-RADS 0 recalls (only one radiologist assigning a BI-RADS 0 score) was retrospectively performed by a third screening radiologist.

**RESULTS:** At blinded and non-blinded double reading, 32.0% and 32.5% of recalls were assigned BI-RADS 0 with a positive predictive value (PPV) of 7.2% and 6.8%, respectively. Compared to non-blinded double reading, BI-RADS 0 recalls at blinded double reading showed a higher discrepancy rate (9.0 versus 4.3 per 1000 screens,  $p < 0.001$ ) and false positive recall rate (10.1 versus 8.4 per 1000 screens,  $p = 0.012$ ). Arbitration of discrepant BI-RADS 0 recalls would have significantly lowered recall rate (from 3.4% to 2.8% at blinded double reading,  $p < 0.001$ , and from 2.8% to 2.5% at non-blinded double reading,  $p = 0.008$ ), without a decrease in cancer detection rate (from 7.5% to 7.3%,  $p = 0.751$ , and from 6.6% to 6.5%,  $p = 0.832$ , respectively) and program sensitivity (from 83.2% to 81.2%,  $p = 0.453$ , and from 76.0% to 74.6%,  $p = 0.667$ , respectively). Arbitration would have significantly increased the PPV at blinded double reading (from 22.3% to 26.3%,  $p = 0.015$ ).

**CONCLUSION:** We advise arbitration of discrepant BI-RADS 0 recalls, at (non-)blinded double reading of screening mammograms, to reduce recall rates and improve the PPV of recall at blinded double reading.

*impactfactor:* 2.381

## **Klompénhouwer E**

### **Axillary reverse mapping (ARM) in clinically node positive breast cancer patients.**

Beek MA, Gobardhan PD, Klompénhouwer EG, Rutten HJ, Voogd AC, Luiten EJ  
Eur J Surg Oncol. 2015 Jan;41(1):59-63.

**BACKGROUND:** Axillary reverse mapping (ARM) is a technique to map and preserve upper extremity lymphatic drainage during axillary lymph node dissection (ALND) in breast cancer patients. We prospectively evaluated the metastatic involvement of ARM-nodes in patients who underwent an ALND for clinically node positive disease following (neo)adjuvant chemotherapy (NAC) in comparison to patients in whom primary ALND was performed without NAC.

**PATIENTS AND METHODS:** Patients with clinically node positive invasive breast cancer, confirmed by fine needle aspiration cytology and scheduled for primary ALND were enrolled in the study. Patients were separated into two groups: one group treated with NAC (NAC+

group) and one group not treated with NAC (NAC- group). ARM was performed in all patients by injecting blue dye into the ipsilateral upper extremity. During ALND, ARM-nodes were first identified and removed separately, followed by a standard ALND.

RESULTS: 91 patients were included in the NAC+ and 21 patients in the NAC- group. There was no difference in the ARM visualization rate between the two groups (86.8% for NAC+ group versus 90.5% for NAC- group,  $P = 0.647$ ). In the NAC+ group 16.5% of the patients had metastatic involvement of the ARM-nodes versus 36.8% of the patients in the NAC- group ( $P = 0.048$ ).

CONCLUSION: The risk of metastatic involvement of ARM-nodes in clinically node positive breast cancer patients is significantly lower in patients who have received NAC.

*impactfactor:* 3.009

## **Klompenshouwer E**

### **Blinded double reading yields a higher programme sensitivity than non-blinded double reading at digital screening mammography: A prospect population based study in the south of The Netherlands**

Klompenshouwer EG\*, Voogd AC, den Heeten GJ, Strobbe LJ, de Haan AF, Wauters CA, Broeders MJ, Duijm LE

Eur J Cancer. 2015 Feb;51(3):391-9

PURPOSE: To prospectively determine the screening mammography outcome at blinded and non-blinded double reading in a biennial population based screening programme in the south of the Netherlands.

METHODS: We included a consecutive series of 87,487 digital screening mammograms, obtained between July 2009 and July 2011. Screening mammograms were double read in either a blinded (2nd reader was not informed about the 1st reader's decision) or non-blinded fashion (2nd reader was informed about the 1st reader's decision). This reading strategy was alternated on a monthly basis. Women with discrepant readings between the two radiologists were always referred for further analysis. During 2years follow-up, we collected the radiology reports, surgical correspondence and pathology reports of all referred women and interval breast cancers.

RESULTS: Respectively 44,491 and 42,996 screens had been read either in a blinded or non-blinded fashion. Referral rate (3.3% versus 2.8%,  $p < 0.001$ ) and false positive rate (2.6% versus 2.2%,  $p = 0.002$ ) were significantly higher at blinded double reading whereas the cancer detection rate per 1000 screens (7.4 versus 6.5,  $p = 0.14$ ) and positive predictive value of referral (22% versus 23%,  $p = 0.51$ ) were comparable. Blinded double reading resulted in a significantly higher programme sensitivity (83% versus 76%,  $p = 0.01$ ). Per 1000 screened women, blinded double reading would yield 0.9 more screen detected cancers and 0.6 less interval cancers than non-blinded double reading, at the expense of 4.4 more recalls.

CONCLUSION: We advocate the use of blinded double reading in order to achieve a better programme sensitivity, at the expense of an increased referral rate and false positive referral rate.

*impactfactor:* 5.417

## **Klompenghouwer E**

### **Comparison of the diagnostic workup of women referred at non-blinded or blinded double reading in a population-based screening mammography programme in the south of the Netherlands**

Weber RJ\*, Klompenghouwer EG\*, Voogd AC, Strobbe LJ, Broeders MJ, Duijm LE  
Br J Cancer. 2015 Sep 29;113(7):1094-8.

Voor abstract zie: *Radiologie - Weber RJ*

impactfactor: 4.836

## **Klompenghouwer E**

### **Discrepant screening mammography assessments at blinded and non-blinded double reading: impact of arbitration by a third reader on screening outcome**

Klompenghouwer EG\*, Voogd AC, den Heeten GJ, Strobbe LJ, Tjan-Heijnen VC, Broeders MJ, Duijm LE

Eur Radiol. 2015 Oct;25(10):2821-9

OBJECTIVES: To determine the value of adding a third reader for arbitration of discrepant screening mammography assessments.

METHODS: We included a consecutive series of 84,927 digital screening mammograms, double read in a blinded or non-blinded fashion. Arbitration was retrospectively performed by a third screening radiologist. Two years' follow-up was performed.

RESULTS: Discrepant readings comprised 57.2% (830/1452) and 29.1% (346/1188) of recalls at blinded and non-blinded double readings, respectively. At blinded double reading, arbitration would have decreased recall rate (3.4 to 2.2%,  $p < 0.001$ ) and programme sensitivity (83.2 to 76.0%,  $p = 0.013$ ), would not have influenced the cancer detection rate (CDR; 7.5 to 6.8 per 1,000 screens,  $p = 0.258$ ) and would have increased the positive predictive value of recall (PPV; 22.3 to 31.2%,  $p < 0.001$ ). At non-blinded double reading, arbitration would have decreased recall rate (2.8 to 2.3%,  $p < 0.001$ ) and increased PPV (23.2 to 27.5%,  $p = 0.021$ ), but would not have affected CDR (6.6 to 6.3 per 1,000 screens,  $p = 0.604$ ) and programme sensitivity (76.0 to 72.7%,  $p = 0.308$ ).

CONCLUSION: Arbitration of discrepant screening mammography assessments is a good tool to improve recall rate and PPV, but is not desirable as it reduces the programme sensitivity at blinded double reading.

impactfactor: 4.014

## **Klompenghouwer E**

### **Two decades of axillary management in breast cancer**

Beek MA, Verheuve NC, Luiten EJ, Klompenghouwer EG\*, Rutten HJ\*, Roumen RM, Gobardhan PD, Voogd AC

Br J Surg. 2015 Dec;102(13):1658-64

BACKGROUND: Axillary lymph node dissection (ALND) in patients with breast cancer provides prognostic information. For many years, positive nodes were the most important indication for adjuvant systemic therapy. It was also believed that regional control could not be achieved without axillary clearance in a positive axilla. However, during the past 20 years the treatment and staging of the axilla has undergone many changes. This large population-based study was conducted in the south-east of the Netherlands to evaluate the changing patterns of care regarding the axilla, including the introduction of sentinel lymph node biopsy (SLNB) in the late 1990s, implementation of the results of the American College of

Surgeons Oncology Group Z0011 study, and the initial effects of the European Organization for Research and Treatment of Cancer AMAROS study.

**METHODS:** Data from the population-based Eindhoven Cancer Registry of all women diagnosed with invasive breast cancer in the south of the Netherlands between January 1993 and July 2014 were used.

**RESULTS:** The proportion of 347037 women staged by SLNB without completion ALND increased from 0 per cent in 1993-1994 to 69.0 per cent in 2013-2014. In the same period the proportion undergoing ALND decreased from 88.8 to 18.7 per cent. Among women with one to three positive lymph nodes, the proportion undergoing SLNB alone increased from 10.6 per cent in 2011-2012 to 37.6 per cent in 2013-2014.

**CONCLUSION:** This population-based study demonstrated the radical transformation in management of the axilla since the introduction of SLNB and following the recent publication of trials on management of the axilla with a low metastatic burden.

*impactfactor:* 5.542

### **Lambrecht M**

#### **In Reply to Dahele, Tekatli and Senan: Stereotactic Body Radiotherapy for Central Lung Tumours**

Adebahr S, Collette S, Shash E, Lambrecht M\*, Le Pechoux C, Faivre-Finn C, De Ruyscher D, Peulen H, Belderbos J, Dziadziuszko R, Fink C, Guckenberger M, Hurkmans C, Nestle U

Br J Radiol. 2015 Sep;88(1053):20150532. Epub 2015 Jul 7

*Geen abstract beschikbaar*

*impactfactor:* --

### **Lambrecht M**

#### **LungTech, an EORTC Phase II trial of stereotactic body radiotherapy for centrally located lung tumours: a clinical perspective**

Adebahr S, Collette S, Shash E, Lambrecht M\*, Le Pechoux C, Faivre-Finn C, De Ruyscher D, Peulen H, Belderbos J, Dziadziuszko R, Fink C, Guckenberger M, Hurkmans C, Nestle U

Br J Radiol. 2015 Jul;88(1051):20150036

Evidence supports stereotactic body radiotherapy (SBRT) as a curative treatment option for inoperable early stage non-small-cell lung cancer (NSCLC) resulting in high rates of tumour control and low risk of toxicity. However, promising results are mainly derived from SBRT of peripheral pulmonary lesions, whereas SBRT for the central tumours can lead to severe radiation sequelae owing to the spatial proximity to the serial organs at risk. Robust data on the tolerance of mediastinal structures to high-dose hypofractionated radiation are limited; furthermore, there are many open questions regarding the efficiency, safety and response assessment of SBRT in inoperable, centrally located early stage NSCLC, which are addressed in a prospective multicentre study [sponsored by the European Organization for Research and Treatment of Cancer (EORTC 22113-08113-LungTech)]. In this review, we summarize the current status regarding SBRT for centrally located early stage NSCLC that leads to the rationale of the LungTech trial. Outline and some essential features of the study with focus on a summary of current experiences in dose/fraction-toxicity coherences after SBRT to the mediastinal structures that lead to LungTech normal tissue constraints are provided.

*impactfactor:* 2.026



## **Nederend J**

### **Screening outcome and surgical treatment during and after the transition from screen-film to digital screening mammography in the south of The Netherlands**

Weber RJ\*, Nederend J\*, Voogd AC, Strobbe LJ, Duijm LE

Int J Cancer. 2015 Jul 1;137(1):135-43. Epub 2014 Dec 10

Voor abstract zie: *Radiologie - Weber R*

impactfactor: *5.085*

## **Setz-Pels W**

### **Site-specific association between distal aortic pulse wave velocity and peripheral arterial stenosis severity: a prospective cardiovascular magnetic resonance study**

van den Bosch HC\*, Westenberg JJ, Setz-Pels W\*, Wondergem J\*, Wolterbeek R, Duijm LE\*, Teijink JA\*, de Roos A\*

J Cardiovasc Magn Reson. 2015 Jan 20;17(1):2

Voor abstract zie: *Radiologie - Bosch HC van den*

impactfactor: *4.556*

## **Tielbeek AV**

### **A randomized trial of intraarterial treatment for acute ischemic stroke**

Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, van Walderveen MA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama à Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PL, van Rooij WJ, van den Berg JS, van Hasselt BA, Aerden LA, Dallinga RJ, Visser MC, Bot JC, Vroomen PC, Eshghi O, Schreuder TH, Heijboer RJ, Keizer K, Tielbeek AV\*, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers ME, Jenniskens SF, Beenen LF, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Majoie CB, Dippel DW; MR CLEAN Investigators

N Engl J Med. 2015 Jan;372(1):11-20

**BACKGROUND:** In patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion, intraarterial treatment is highly effective for emergency revascularization. However, proof of a beneficial effect on functional outcome is lacking.

**METHODS:** We randomly assigned eligible patients to either intraarterial treatment plus usual care or usual care alone. Eligible patients had a proximal arterial occlusion in the anterior cerebral circulation that was confirmed on vessel imaging and that could be treated intraarterially within 6 hours after symptom onset. The primary outcome was the modified Rankin scale score at 90 days; this categorical scale measures functional outcome, with scores ranging from 0 (no symptoms) to 6 (death). The treatment effect was estimated with ordinal logistic regression as a common odds ratio, adjusted for prespecified prognostic factors. The adjusted common odds ratio measured the likelihood that intraarterial treatment would lead to lower modified Rankin scores, as compared with usual care alone (shift analysis).

**RESULTS:** We enrolled 500 patients at 16 medical centers in The Netherlands (233 assigned to intraarterial treatment and 267 to usual care alone). The mean age was 65 years (range, 23 to 96), and 445 patients (89.0%) were treated with intravenous alteplase before randomization. Retrievable stents were used in 190 of the 233 patients (81.5%) assigned to

intraarterial treatment. The adjusted common odds ratio was 1.67 (95% confidence interval [CI], 1.21 to 2.30). There was an absolute difference of 13.5 percentage points (95% CI, 5.9 to 21.2) in the rate of functional independence (modified Rankin score, 0 to 2) in favor of the intervention (32.6% vs. 19.1%). There were no significant differences in mortality or the occurrence of symptomatic intracerebral hemorrhage.

**CONCLUSIONS:** In patients with acute ischemic stroke caused by a proximal intracranial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe. (Funded by the Dutch Heart Foundation and others; MR CLEAN Netherlands Trial Registry number, NTR1804, and Current Controlled Trials number, ISRCTN10888758.).

Comment in *Interventional thrombectomy for major stroke--a step in the right direction.* [N Engl J Med. 2015]

*impactfactor:* 55.873

### **Tielbeek AV**

#### **Value of Computed Tomographic Perfusion–Based Patient Selection for Intra-Arterial Acute Ischemic Stroke Treatment**

Borst J, Berkhemer OA, Roos YB, van Bavel E, van Zwam WH, van Oostenbrugge RJ, van Walderveen MA, Lingsma HF, van der Lugt A, Dippel DW, Yoo AJ, Marquering HA, Majoie CB; MR CLEAN investigators; MR CLEAN Investigators and Affiliations.

Collaborators: Keizer K, Tielbeek AV

Stroke. 2015 Dec;46(12):3375-82. Epub 2015 Nov 5

Voor abstract zie: Neurologie - Keizer, K

*impactfactor:* 5.723

### **Weber RJ**

#### **Screening outcome and surgical treatment during and after the transition from screen-film to digital screening mammography in the south of The Netherlands**

Weber RJ\*, Nederend J\*, Voogd AC, Strobbe LJ, Duijm LE

Int J Cancer. 2015 Jul 1;137(1):135-43. Epub 2014 Dec 10

We determined screening outcome of subsequent screens during and after the transition from screen-film mammography (SFM) to full-field digital mammography (FFDM). A consecutive series of 102,863 subsequent (SFM screens with a prior SFM screen (SFM-SFM cohort), 91,941 FFDM screens with a prior SFM screen (FFDM-SFM cohort) and 90,407 FFDM screens with a prior FFDM screen (FFDM-FFDM cohort) were obtained between January 2006 and July 2013. The referral rate and cancer detection rate (CDR) per 1,000 screens were higher at FFDM-SFM than at SFM-SFM (2.7% vs. 1.2% ( $p < 0.001$ ) and 7.0 vs. 4.9,  $p < 0.001$ ), at the expense of a lower positive predictive value (PPV) of referral (25.8% vs. 39.6%,  $p < 0.001$ ). These parameters were comparable for FFDM-SFM and FFDM-FFDM. Ductal carcinoma in situ (DCIS) and invasive cancer rates increased during transition and remained stable after transition. The rate of DCIS of intermediate grade increased during the transition from 0.2 per 1,000 screened women at SFM-SFM to 0.6 at FFDM-SFM ( $p < 0.001$ ) and 0.5 at FFDM-FFDM ( $p = 0.001$ ). Compared to SFM-SFM, a significantly higher rate of invasive cancers were stage T1a-b at FFDM-SFM ( $p < 0.001$ ) and FFDM-FFDM ( $p < 0.001$ ). Breast conserving surgery rates increased during transition ( $p < 0.001$ ) and remained stable afterwards. The CDR and referral rate remained significantly higher at FFDM than at SFM, at the expense of a decreased PPV of referral. During transition, DCIS was more often of intermediate grade and invasive cancers were of smaller size.

*impactfactor:* 5.085

**Weber RJ**

**Arbitration of discrepant BI-RADS 0 recalls by a third reader at screening mammography lowers recall rate but not the cancer detection rate and sensitivity at blinded and non-blinded double reading**

Klompenshouwer EG\*, Weber RJ\*, Voogd AC, den Heeten GJ, Strobbe LJ, Broeders MJ, Tjan-Heijnen VC, Duijm LE

Breast. 2015 Oct;24(5):601-7. Epub 2015 Jun 24

Voor abstract zie: *Radiologie - Klompenshouwer E*

impactfactor: 2.381

**Weber RJ**

**Comparison of the diagnostic workup of women referred at non-blinded or blinded double reading in a population-based screening mammography programme in the south of the Netherlands**

Weber RJ\*, Klompenshouwer EG\*, Voogd AC, Strobbe LJ, Broeders MJ, Duijm LE

Br J Cancer. 2015 Sep 29;113(7):1094-8

BACKGROUND: To determine whether referred women experience differences in diagnostic workup at non-blinded or blinded double reading of screening mammograms.

METHODS: We included a consecutive series of respectively 42.996 and 44.491 screens, double read either in a non-blinded or blinded manner between 2009 and 2011. This reading strategy was alternated on a monthly basis.

RESULTS: The overall ultrasound-guided core needle biopsy (CNB) rate and stereotactic CNB (SCNB) rate per 1000 screens were higher at blinded than at non-blinded reading (7.5 vs 6.0,  $P=0.008$  and 8.1 vs 6.6,  $P=0.009$ ). Among women with benign workup, these rates were higher at blinded reading (2.6 vs 1.4,  $P<0.001$  and 5.9 vs 4.7,  $P=0.013$ ). The benign biopsy rates were higher at blinded double reading ( $P<0.001$ ), whereas the positive predictive value of biopsy did not differ ( $P=0.103$ ).

CONCLUSIONS: Blinded double-reading results in higher overall CNB and SCNB rates than non-blinded double reading, as well as a higher benign biopsy rate.

impactfactor: 4.836

**Wondergem JH**

**Site-specific association between distal aortic pulse wave velocity and peripheral arterial stenosis severity: a prospective cardiovascular magnetic resonance study**

van den Bosch HC\*, Westenbergh JJ, Setz-Pels W\*, Wondergem J\*, Wolterbeek R, Duijm LE\*, Teijink JA\*, de Roos A\*

J Cardiovasc Magn Reson. 2015 Jan 20;17(1):2

Voor abstract zie: *Radiologie - Bosch HC van den*

impactfactor: 4.556

\* = Werkzaam in het Catharina Ziekenhuis

## Radiotherapie

**Beer F de**

**No prevention of radiotherapy-induced alopecia by scalp cooling**

van den Hurk C, de Beer F\*, Dries W\*, van de Sande I\*, Hermesen N\*, Breed W, van der Sangen M\*

Radiother Oncol. 2015 Oct;117(1):193-4

*Geen abstract beschikbaar*

*impactfactor:* 4.363

**Berg HA van den**

**[Breast-conserving surgery and radiotherapy as a one-day procedure] - Borstsparende ingreep en bestraling in dagbehandeling**

Koper PC, Marinelli AW, van den Berg HA\*, van Riet YE\*, van der Sijp JR, Struikmans H  
Ned Tijdschr Geneesk. 2015;159:A8195

A single dose of irradiation to the lumpectomy cavity alone after breast-conserving surgery in breast cancer patients has been available in the Netherlands since 2011. This new treatment modality is used in the Haaglanden Medical Centre in The Hague and in the Catharina Hospital in Eindhoven. The goal of intraoperative radiation therapy is to limit the patient burden caused by whole breast irradiation, while maintaining excellent local tumour control. The technique is used only in patients with a low probability of recurrent disease in the breast. Approximately 150 patients receive intraoperative radiation therapy each year. In the Netherlands, an estimated 4,000 breast cancer patients were eligible in 2013 for this new treatment technique or another method of partial breast irradiation. In both hospitals the results are closely monitored. Only 15 of the first 200 patients experienced a side effect within a period of 3 months after intraoperative radiation therapy. These side effects were successfully treated either with antibiotics or with surgery.

*impactfactor:* --

**Berg HA van den**

**Effect of adjuvant chemotherapy on recurrence-free survival varies by neo-adjuvant treatment in patients with stage III rectal cancer**

van Erning FN, Rutten HJ\*, van den Berg HA\*, Lemmens VE, van Halteren HK

Eur J Surg Oncol. 2015 Dec;41(12):1630-5

**INTRODUCTION:** Adjuvant chemotherapy still is a controversial therapy for rectal cancer patients. The aim of this study was to analyze the effect of adjuvant chemotherapy on recurrence-free survival (RFS) for patients with stage III rectal cancer treated in clinical practice, taking into account which neo-adjuvant treatment patients received. **METHODS:** Patients from regions in the Netherlands diagnosed between 1996 and 2013 with pathological stage III rectal cancer who received short-course radiotherapy, chemoradiation or no neo-adjuvant treatment and who underwent surgery were included. After stratification by neo-adjuvant treatment, 5-year RFS according to adjuvant chemotherapy receipt was calculated using Kaplan-Meier curves. Cox regression was used to discriminate the independent effect of adjuvant chemotherapy on the risk of recurrence/death.

**RESULTS:** The study population consisted of 829 patients, of whom 537 (65%) patients received short-course radiotherapy, 128 (15%) patients received chemoradiation and 164 (20%) patients received no neo-adjuvant treatment. Adjuvant chemotherapy was administered to 152 (18%) patients. Adjuvant chemotherapy was associated with improved 5-year RFS for patients who received short-course radiotherapy (61% vs. 46%,  $p = 0.005$ ) and

for patients who did not receive any neo-adjuvant treatment (70% vs. 28%,  $p < 0.0001$ ). In multivariable analyses, adjuvant chemotherapy was associated with a reduced risk of recurrence/death for patients treated with short-course radiotherapy (HR 0.65, 95% CI 0.46-0.93) and for patients without neo-adjuvant treatment (HR 0.35, 95% CI 0.18-0.71), but not for patients treated with chemoradiation (HR 1.11, 95% CI 0.51-2.41).  
**CONCLUSION:** Among patients with stage III rectal cancer, the effect of adjuvant chemotherapy on RFS seems to vary by neo-adjuvant treatment.

*impactfactor:* 3.009

### **Berg HA van den**

#### **Effect of preoperative treatment strategies on the outcome of patients with clinical T3, non-metastasized rectal cancer: A comparison between Dutch and Canadian expert centers**

Breugom AJ, Vermeer TA\*, van den Broek CB, Vuong T, Bastiaannet E, Azoulay L, Dekkers OM, Niazi T, van den Berg HA\*, Rutten HJ\*, van de Velde CJ

Eur J Surg Oncol. 2015 Aug;41(8):1039-44

Voor abstract zie: Chirurgie - Vermeer TA

*impactfactor:* 3.009

### **Budiharto TC**

#### **Final analysis of a prospective trial on functional imaging for nodal staging in patients with prostate cancer at high risk for lymph node involvement**

Van den Bergh L, Lerut E, Haustermans K, Deroose CM, Oyen R, Isebaert S, Budiharto T\*, Ameye F, Mottaghy FM, Bogaerts K, Van Poppel H, Joniau S

Urol Oncol. 2015 Mar;33(3):109.e23-31. Epub 2015 Feb 2

**PURPOSE:** Accurate staging modalities to diagnose lymph node involvement in patients with prostate cancer (PCa) are lacking. We wanted to prospectively assess sensitivity, specificity, and positive predictive value (PPV) and negative predictive value of 11C-choline positron emission tomography (PET)-computed tomography (CT) and diffusion-weighted (DW) magnetic resonance imaging (MRI) for nodal staging in patients with PCa at high risk for lymph node involvement.

**MATERIAL AND METHODS:** In total, 75 patients with a risk=10% but<35% for lymph node (LN) metastases (Partin tables) who had NO lesions based on the findings of contrast-enhanced CT scans were included. Patients underwent 11C-choline PET-CT and DW MRI before surgery, which consisted of a superextended lymph node dissection followed by radical prostatectomy. LNs were serially sectioned and histopathologically examined after pankeratin staining. These results were used as the gold standard to compare with the imaging results.

**RESULTS:** Of 1,665 resected LNs (median = 21, range: 7-49), 106 affected LNs (median = 2, range: 1-10) were found in 37 of 75 patients (49%). On a region-based analysis, we found a low sensitivity of 8.2% and 9.5% and a PPV of 50.0% and 40.0% for 11C-choline PET-CT and DW MRI, respectively. The patient-based analysis showed a sensitivity of 18.9% and 36.1% for and a PPV of 63.6% and 86.7% 11C-choline PET-CT and DW MRI, respectively. Even when both imaging modalities were combined, sensitivity values remained too low to be clinically useful.

**CONCLUSIONS:** Because of the low sensitivity, there is no indication for routine clinical use of either 11C-choline PET-CT or DW MRI for LN staging in patients with PCa, in whom CT scan findings were normal.

*impactfactor:* 2.768

**Hermesen N**

**No prevention of radiotherapy-induced alopecia by scalp cooling**

van den Hurk C, de Beer F\*, Dries W\*, van de Sande I\*, Hermesen N\*, Breed W, van der Sangen M\*

Radiother Oncol. 2015 Oct;117(1):193-4

*Geen abstract beschikbaar*

*impactfactor:* 4.363

**Jaeger K de**

**Patient reported outcomes following stereotactic ablative radiotherapy or surgery for stage IA non-small-cell lung cancer: Results from the ROSEL multicenter randomized trial**

Louie AV, van Werkhoven E, Chen H, Smit E, Paul MA, Widder J, Groen HJ, van den Borne BE\*, De Jaeger K\*, Slotman BJ, Senan S

Radiother Oncol. 2015 Oct;117(1):44-8

*Voor abstract zie: Longgeneeskunde - van den Borne BE*

*impactfactor:* 4.363

**Jaeger K de**

**Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials**

Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, Groen HJ, McRae SE, Widder J, Feng L, van den Borne BE\*, Munsell MF, Hurkmans C\*, Berry DA, van Werkhoven E, Kresl JJ, Dingemans AM, Dawood O, Haasbeek CJ, Carpenter LS, De Jaeger K\*, Komaki R, Slotman BJ, Smit EF, Roth JA

Lancet Oncol. 2015 Jun;16(6):630-7. Epub 2015 May 13

*Voor abstract zie: Longgeneeskunde - Borne BE van den*

*impactfactor:* 24.690

**Lybeert ML**

**Second Cancer Risk Up to 40 Years after Treatment for Hodgkin's Lymphoma**

Schaapveld M, Aleman BM, van Eggermond AM, Janus CP, Krol AD, van der Maazen RW, Roesink J, Raemaekers JM, de Boer JP, Zijlstra JM, van Imhoff GW, Petersen EJ, Poortmans PM, Beijert M, Lybeert ML\*, Mulder I, Visser O, Louwman MW, Krul IM, Lugtenburg PJ, van Leeuwen FE

N Engl J Med. 2015 Dec 24;373(26):2499-511

**BACKGROUND:** Survivors of Hodgkin's lymphoma are at increased risk for treatment-related subsequent malignant neoplasms. The effect of less toxic treatments, introduced in the late 1980s, on the long-term risk of a second cancer remains unknown.

**METHODS:** We enrolled 3905 persons in the Netherlands who had survived for at least 5 years after the initiation of treatment for Hodgkin's lymphoma. Patients had received treatment between 1965 and 2000, when they were 15 to 50 years of age. We compared the risk of a second cancer among these patients with the risk that was expected on the basis of cancer incidence in the general population. Treatment-specific risks were compared within the cohort.

**RESULTS:** With a median follow-up of 19.1 years, 1055 second cancers were diagnosed in 908 patients, resulting in a standardized incidence ratio (SIR) of 4.6 (95% confidence

interval [CI], 4.3 to 4.9) in the study cohort as compared with the general population. The risk was still elevated 35 years or more after treatment (SIR, 3.9; 95% CI, 2.8 to 5.4), and the cumulative incidence of a second cancer in the study cohort at 40 years was 48.5% (95% CI, 45.4 to 51.5). The cumulative incidence of second solid cancers did not differ according to study period (1965-1976, 1977-1988, or 1989-2000) ( $P=0.71$  for heterogeneity). Although the risk of breast cancer was lower among patients who were treated with supradiaphragmatic-field radiotherapy not including the axilla than among those who were exposed to mantle-field irradiation (hazard ratio, 0.37; 95% CI, 0.19 to 0.72), the risk of breast cancer was not lower among patients treated in the 1989-2000 study period than among those treated in the two earlier periods. A cumulative procarbazine dose of 4.3 g or more per square meter of body-surface area (which has been associated with premature menopause) was associated with a significantly lower risk of breast cancer (hazard ratio for the comparison with no chemotherapy, 0.57; 95% CI, 0.39 to 0.84) but a higher risk of gastrointestinal cancer (hazard ratio, 2.70; 95% CI, 1.69 to 4.30).

**CONCLUSIONS:** The risk of second solid cancers did not appear to be lower among patients treated in the most recent calendar period studied (1989-2000) than among those treated in earlier periods. The awareness of an increased risk of second cancer remains crucial for survivors of Hodgkin's lymphoma. (Funded by the Dutch Cancer Society.).

*Comment in:* Second Cancers after Treatment for Hodgkin's Lymphoma--Continuing Cause for Concern. [N Engl J Med. 2015]

*impactfactor:* 55.873

## **Martijn H**

### **Adjuvant chemotherapy for rectal cancer patients treated with preoperative (chemo)radiotherapy and total mesorectal excision: a Dutch Colorectal Cancer Group (DCCG) randomized phase III trial†**

Breugom AJ, van Gijn W, Muller EW, Berglund Å, van den Broek CB, Fokstuen T, Gelderblom H, Kapiteijn E, Leer JW, Marijnen CA, Martijn H\*, Meershoek-Klein Kranenbarg E, Nagtegaal ID, Pålman L, Punt CJ, Putter H, Roodvoets AG, Rutten HJ\*, Steup WH, Glimelius B, van de Velde CJ; Cooperative Investigators of the Dutch Colorectal Cancer Group and the Nordic Gastrointestinal Tumour Adjuvant Therapy Group

Ann Oncol. 2015 Apr;26(4):696-701

**BACKGROUND:** The discussion on the role of adjuvant chemotherapy for rectal cancer patients treated according to current guidelines is still ongoing. A multicentre, randomized phase III trial, PROCTOR-SCRIPT, was conducted to compare adjuvant chemotherapy with observation for rectal cancer patients treated with preoperative (chemo)radiotherapy and total mesorectal excision (TME).

**PATIENTS AND METHODS:** The PROCTOR-SCRIPT trial recruited patients from 52 hospitals. Patients with histologically proven stage II or III rectal adenocarcinoma were randomly assigned (1:1) to observation or adjuvant chemotherapy after preoperative (chemo)radiotherapy and TME. Radiotherapy consisted of 5 × 5 Gy. Chemoradiotherapy consisted of 25 × 1.8-2 Gy combined with 5-FU-based chemotherapy. Adjuvant chemotherapy consisted of 5-FU/LV (PROCTOR) or eight courses capecitabine (SCRIPT). Randomization was based on permuted blocks of six, stratified according to centre, residual tumour, time between last irradiation and surgery, and preoperative treatment. The primary end point was overall survival.



RESULTS: Of 470 enrolled patients, 437 were eligible. The trial closed prematurely because of slow patient accrual. Patients were randomly assigned to observation (n = 221) or adjuvant chemotherapy (n = 216). After a median follow-up of 5.0 years, 5-year overall survival was 79.2% in the observation group and 80.4% in the chemotherapy group [hazard ratio (HR) 0.93, 95% confidence interval (CI) 0.62-1.39; P = 0.73]. The HR for disease-free survival was 0.80 (95% CI 0.60-1.07; P = 0.13). Five-year cumulative incidence for locoregional recurrences was 7.8% in both groups. Five-year cumulative incidence for distant recurrences was 38.5% and 34.7%, respectively (P = 0.39).

CONCLUSION: The PROCTOR-SCRIPT trial could not demonstrate a significant benefit of adjuvant chemotherapy with fluoropyrimidine monotherapy after preoperative (chemo)radiotherapy and TME on overall survival, disease-free survival, and recurrence rate. However, this trial did not complete planned accrual.

impactfactor: 7.040

### **Sande I van de**

#### **No prevention of radiotherapy-induced alopecia by scalp cooling**

van den Hurk C, de Beer F\*, Dries W\*, van de Sande I\*, Hermesen N\*, Breed W, van der Sangen M\*

Radiother Oncol. 2015 Oct;117(1):193-4

*Geen abstract beschikbaar*

impactfactor: 4.363

### **Sangen MJ van der**

#### **[Axillary treatment in breast cancer: surgery, radiotherapy, or none of these?] - Okselbehandeling bij borstkanker: opereren, bestralen of achterwegelaten?**

Boersma LJ, van der Sangen MJ\*

Ned Tijdschr Geneeskd. 2015;159(0):A9510

The AMAROS trial showed that substituting axillary lymph node dissection by radiotherapy of the axillary and periclavicular nodes (ART) in patients with sentinel node (SN) metastases results in less lymphoedema, without a significant difference in the 5-year axillary recurrence rate (ARR). Three surgical studies showed no increase in ARR after omitting axillary treatment in cases of limited SN metastases, provided that adjuvant systemic therapy and tangential breast radiotherapy were applied. On the other hand, several recent radiotherapy trials, including a meta-analysis by the Early Breast Cancer Trialists' Collaborative Group, showed that regional radiotherapy improves disease-free survival where there are positive axillary nodes. In view of the low ARR and good overall survival with contemporary breast cancer treatments, limiting axillary treatment and its associated morbidity is a logical development. However, it is too early to omit axillary treatment in all SN-positive patients. ART is a safe next step in reducing axillary treatment.

Impactfactor: --

**Sangen MJ van der**

**Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial**

Shapiro J, van Lanschot JJ, Hulshof MC, van Hagen P, van Berge Henegouwen MJ, Wijnhoven BP, van Laarhoven HW, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Ten Kate FJ, Creemers GM\*, Punt CJ, Plukker JT, Verheul HM, Bilgen EJ, van Dekken H, van der Sangen MJ\*, Rozema T, Biermann K, Beukema JC, Piet AH, van Rij CM, Reinders JG, Tilanus HW, Steyerberg EW, van der Gaast A; CROSS study group

Lancet Oncol. 2015 Sep;16(9):1090-8. Epub 2015 Aug 5

Voor abstract zie: *Chirurgie - Nieuwenhuijzen GA*

impactfactor: 24.690

**Sangen MJ van der**

**No prevention of radiotherapy-induced alopecia by scalp cooling**

van den Hurk C, de Beer F\*, Dries W\*, van de Sande I\*, Hermesen N\*, Breed W, van der Sangen M\* Radiother Oncol. 2015 Oct;117(1):193-4

Geen abstract beschikbaar

impactfactor: 4.363

**Sangen MJ van der**

**Radiation dose does not influence anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation and transhiatal esophagectomy**

Koëter M\*, van der Sangen MJ\*, Hurkmans CW\*, Luyer MD\*, Rutten HJ\*, Nieuwenhuijzen GA\*

Radiat Oncol. 2015 Mar 6;10(1):59

Voor abstract zie: *Chirurgie - Koëter M*

impactfactor: 2.546

**Toorn PP van der**

**A comprehensive evaluation of treatment accuracy, including end-to-end tests and clinical data, applied to intracranial stereotactic radiotherapy**

Seravalli E, van Haaren PM\*, van der Toorn PP\*, Hurkmans CW\*

Radiother Oncol. 2015 Jul;116(1):131-8

Voor abstract zie: *KFD - Haaren PM van*

impactfactor: 4.363

**Toorn PP van der**

**Hypofractionated versus conventionally fractionated radiotherapy for patients with prostate cancer (HYPRO): acute toxicity results from a randomised non-inferiority phase 3 trial**

Aluwini S, Pos F, Schimmel E, van Lin E, Krol S, van der Toorn PP\*, de Jager H, Dirksen M, Alemayehu WG, Heijmen B, Incrocci L

Lancet Oncol. 2015 Mar;16(3):274-83

**BACKGROUND:** In 2007, we began the randomised phase 3 multicentre HYPRO trial to investigate the effect of hypofractionated radiotherapy compared with conventionally fractionated radiotherapy on relapse-free survival in patients with prostate cancer. Here, we examine whether patients experience differences in acute gastrointestinal and genitourinary adverse effects.

**METHODS:** In this randomised non-inferiority phase 3 trial, done in seven radiotherapy centres in the Netherlands, we enrolled intermediate-risk or high-risk patients aged between 44 and 85 years with histologically confirmed stage T1b-T4 NX-OMX-0 prostate cancer, a PSA concentration of 60 ng/mL or lower, and WHO performance status of 0-2. A web-based application was used to randomly assign (1:1) patients to receive either standard fractionation with 39 fractions of 2 Gy in 8 weeks (five fractions per week) or hypofractionation with 19 fractions of 3.4 Gy in 6.5 weeks (three fractions per week). Randomisation was done with minimisation procedure, stratified by treatment centre and risk group. The primary endpoint is 5-year relapse-free survival. Here we report data for the acute toxicity outcomes: the cumulative incidence of grade 2 or worse acute and late genitourinary and gastrointestinal toxicity. Non-inferiority of hypofractionation was tested separately for genitourinary and gastrointestinal acute toxic effects, with a null hypothesis that cumulative incidences of each type of adverse event were not more than 8% higher in the hypofractionation group than in the standard fractionation group. We scored acute genitourinary and gastrointestinal toxic effects according to RTOG-EORTC criteria from both case report forms and patients' self-assessment questionnaires, at baseline, twice during radiotherapy, and 3 months after completion of radiotherapy. Analyses were done in the intention-to-treat population. Patient recruitment has been completed. This study is registered with [www.controlled-trials.com](http://www.controlled-trials.com), number ISRCTN85138529.

**FINDINGS:** Between March 19, 2007, and Dec 3, 2010, 820 patients were randomly assigned to treatment with standard fractionation (n=410) or hypofractionation (n=410). 3 months after radiotherapy, 73 (22%) patients in the standard fractionation group and 75 (23%) patients in the hypofractionation group reported grade 2 or worse genitourinary toxicity; grade 2 or worse gastrointestinal toxicity was noted in 43 (13%) patients in the standard fractionation group and in 42 (13%) in the hypofractionation group. Grade 4 acute genitourinary toxicity was reported for two patients, one (<1%) in each group. No grade 4 acute gastrointestinal toxicities were observed. We noted no significant difference in cumulative incidence by 120 days after radiotherapy of grade 2 or worse acute genitourinary toxicity (57.8% [95% CI 52.9-62.7] in the standard fractionation group vs 60.5% [55.8-65.3] in the hypofractionation group; difference 2.7%, 90% CI -2.99 to 8.48; odds ratio [OR] 1.12, 95% CI 0.84-1.49; p=0.43). The cumulative incidence of grade 2 or worse acute gastrointestinal toxicity by 120 days after radiotherapy was higher in patients given hypofractionation (31.2% [95% CI 26.6-35.8] in the standard fractionation group vs 42.0% [37.2-46.9] in the hypofractionation group; difference 10.8%, 90% CI 5.25-16.43; OR 1.6; p=0.0015; non-inferiority not confirmed).

**INTERPRETATION:** Hypofractionated radiotherapy was not non-inferior to standard fractionated radiotherapy in terms of acute genitourinary and gastrointestinal cancer for men with intermediate-risk and high-risk prostate cancer. In fact, the cumulative incidence of grade 2 or worse acute gastrointestinal toxicity was significantly higher in patients given hypofractionation than in those given standard fractionated radiotherapy. Patients remain in follow-up for efficacy endpoints.

*impactfactor:* 24.690

\* = Werkzaam in het Catharina Ziekenhuis

## **Spoedeisende hulp**

**Emmen-Bisselink CJ**

**[A woman with a finger deformation] - Een vrouw met een kromme pink**

C.J.A. Emmen-Bisselink

Ned Tijdschr Geneeskd. 2015;159:A8740

A 22-year-old woman presented with a congenital deformation of the little finger. This condition is named camptodactyly. It consists of a flexion contracture of the proximal interphalangeal joint

*impactfactor:* --

**Quintus A**

**Treatment of mallet fingers in Dutch hospitals: a nationwide survey of practice**

Haagsma A\*, de Boer HL\*, Quintus AC\*, Strikkeling NJ, Zeebregts CJ, Smit JM\*

Eur J Emerg Med. 2015 Jun;22(3):211-4. Epub 1 Mar 2014

*Voor abstract zie: Plastische Chirurgie - Haagsma A*

*impactfactor:* 1.583

**Thijssen WA**

**Complaints and Diagnoses of Emergency Department Patients in the Netherlands: A Comparative Study of Integrated Primary and Emergency Care**

Thijssen WA\*, van Miero E, Willekens M, Rebel J, Sandel MH, Giesen P, Wensing M

PLoS One. 2015 Jul 1;10(7):e0129739. eCollection 2015

**OBJECTIVE:** In the Netherlands, an increasing number of emergency departments (EDs) and general practitioner cooperatives collaborate by creating one Emergency-Care-Access-Point (ECAP). This has resulted in fewer patients at ECAP EDs. The objective of this study was to explore differences in patient characteristics, presented complaints and ED discharge diagnoses between EDs with an ECAP and EDs without an ECAP.

**METHODS:** A retrospective observational study was performed with 1800 consecutive patient records sampled from six EDs spread over the Netherlands in 2013. We extracted data on time and date of presentation, sex, age, presenting complaint, discharge diagnosis, origin and follow up.

**RESULTS:** At ECAP EDs, the mean age was 47.8 years (95%CI 46.1-49.4) compared to 41.3 (95%CI 39.7-42.9). Compared to non-ECAP EDs, more patients were referred by medical professionals (74.7% versus 46.8%), more patients received hospital admission (45.2% versus 29.0%) and fewer patients received GP follow-up (4.1% versus 16.9%). There was no significant difference in presenting complaints between ECAP and non-ECAP EDs. Most prevalent complaints were trauma (25.7% versus 29.7%), abdominal pain (12.1% versus 10.9%) and general symptoms (7.8% versus 4.8%). The most prevalent ED diagnoses significantly differed with fractures and dislocations (10.8%), sprains and strains (10.4%) and respiratory infections (6.8%) at ECAP EDs versus fractures and dislocations (10.7%), wounds (9.3%) and sprains and strains (8.9%) at non-ECAP EDs.

**CONCLUSION:** Compared to non-ECAP EDs, patients at ECAP EDs were older, medical professionals referred more patients and more patients received a hospital admission. We found some small differences in discharge diagnoses between ECAP EDs compared to non-ECAP EDs, but no difference in presented complaints.

*impactfactor:* 3.234

\* = Werkzaam in het Catharina Ziekenhuis

## Urologie

**Hendriks AJ**

**High acceptability of a newly developed urological practical skills training program**

de Vries AH\*, van Luijk SJ, Scherpbier AJ, Hendriks AJ\*, Koldewijn EL\* Wagner C, Schout BM

BMC Urol. 2015 Sep 4;15(1):93

**BACKGROUND:** Benefits of simulation training are widely recognized, but its structural implementation into urological curricula remains challenging. This study aims to gain insight into current and ideal urological practical skills training and presents the outline of a newly developed skills training program, including an assessment of the design characteristics that may increase its acceptability.

**METHODS:** A questionnaire was sent to the urology residents (n=?87) and program directors (n=?45) of all Dutch teaching hospitals. Open- and close-ended questions were used to determine the views on current and ideal skills training and the newly developed skills training program. Eight semi-structured interviews were conducted with 39 residents and 15 program directors. All interviews were audiotaped, fully transcribed, and thereafter analyzed.

**RESULTS:** Response was 87.4 % for residents and 86.7 % for program directors. Residents appeared to be still predominantly trained 'by doing'. Structured practical skills training in local hospitals takes place according to 12 % of the residents versus 44 % of the program directors ( $p < 0.001$ ). Ideally, residents prefer to practice certain procedures on simulation models first, especially in endourology. The majority of residents (92 %) and program directors (87 %) approved of implementing the newly developed skills training program ( $p = 0.51$ ). 'Structured scheduling', 'use of peer teaching' and 'high fidelity models' were indicated as design characteristics that increase its acceptability.

**CONCLUSIONS:** Current urological residency training consists of patient-related 'learning by doing', although more practice on simulation models is desired. The acceptability of implementing the presented skills-training program is high. Design characteristics that increase its acceptability are structured scheduling, the use of peer teaching and high fidelity models.

*impactfactor:* --

**Hermans T**

**Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial**

Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, Boll D\*, Boss EA, Hermans RH\*, Engelhart KC, Haartsen JE, Pijlman BM, van Loon-Baelemans IE, Mertens HJ, Nolting WE, van Beek JJ, Roukema JA, Zijlstra WP, Kruitwagen RF, van de Poll-Franse LV.

J Clin Oncol. 2015 Nov 1;33(31):3550-9. Epub 2015 Aug 24

*Voor abstract zie: Gynaecologie - Boll D*

*impactfactor:* 18.428

**Koldewijn EL**

**High acceptability of a newly developed urological practical skills training program**

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**CONCLUSIONS:** Current urological residency training consists of patient-related 'learning by doing', although more practice on simulation models is desired. The acceptability of implementing the presented skills-training program is high. Design characteristics that increase its acceptability are structured scheduling, the use of peer teaching and high fidelity models.

*impactfactor:* --

#### **Koldewijn EL**

##### **Patient Safety Risks of Basic Urological Procedures Performed by Junior and Senior Residents**

de Vries AH\*, Boute MC, Kuppen MC\*, van Merriënboer JJ, Koldewijn EL\*, Pelger RC, Schout BM, Wagner C

J Surg Educ. 2015 Sep-Oct;72(5):918-26. Epub 2015 Jun 24

*Voor abstract zie:* Urologie - Vries AH de

*impactfactor:* 1.379

#### **Koldewijn EL**

##### **Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie:* AKL - Geerts N

*impactfactor:* 2.824



## **Kuppen MC**

### **Patient Safety Risks of Basic Urological Procedures Performed by Junior and Senior Residents**

de Vries AH\*, Boute MC, Kuppen MC\*, van Merriënboer JJ, Koldewijn EL\*, Pelger RC, Schout BM, Wagner CJ Surg Educ. 2015 Sep-Oct;72(5):918-26. Epub 2015 Jun 24

Voor abstract zie: *Urologie - Vries AH de*

impactfactor: 1.379

## **Vries AH de**

### **High acceptability of a newly developed urological practical skills training program**

de Vries AH\*, van Luijk SJ, Scherpbier AJ, Hendriks AJ\*, Koldewijn EL\* Wagner C, Schout BM

BMC Urol. 2015 Sep 4;15(1):93

**BACKGROUND:** Benefits of simulation training are widely recognized, but its structural implementation into urological curricula remains challenging. This study aims to gain insight into current and ideal urological practical skills training and presents the outline of a newly developed skills training program, including an assessment of the design characteristics that may increase its acceptability.

**METHODS:** A questionnaire was sent to the urology residents (n=787) and program directors (n=45) of all Dutch teaching hospitals. Open- and close-ended questions were used to determine the views on current and ideal skills training and the newly developed skills training program. Eight semi-structured interviews were conducted with 39 residents and 15 program directors. All interviews were audiotaped, fully transcribed, and thereafter analyzed.

**RESULTS:** Response was 87.4 % for residents and 86.7 % for program directors. Residents appeared to be still predominantly trained 'by doing'. Structured practical skills training in local hospitals takes place according to 12 % of the residents versus 44 % of the program directors (p<0.001). Ideally, residents prefer to practice certain procedures on simulation models first, especially in endourology. The majority of residents (92 %) and program directors (87 %) approved of implementing the newly developed skills training program (p=0.51). 'Structured scheduling', 'use of peer teaching' and 'high fidelity models' were indicated as design characteristics that increase its acceptability.

**CONCLUSIONS:** Current urological residency training consists of patient-related 'learning by doing', although more practice on simulation models is desired. The acceptability of implementing the presented skills-training program is high. Design characteristics that increase its acceptability are structured scheduling, the use of peer teaching and high fidelity models.

impactfactor: --

## **Vries AH de**

### **Patient Safety Risks of Basic Urological Procedures Performed by Junior and Senior Residents**

de Vries AH\*, Boute MC, Kuppen MC\*, van Merriënboer JJ, Koldewijn EL\*, Pelger RC, Schout BM, Wagner C

J Surg Educ. 2015 Jun 24. pii: S1931-7204(15)00102-6

**OBJECTIVE:** To investigate the current performance of urological residents regarding basic urological procedures in relation to patient safety issues and the identification of specific training needs.

**DESIGN:** Observational data of 146 urethrocystoscopies (UCSs), 27 transrectal ultrasounds of the prostate (TRUSs), 38 transrectal ultrasound-guided prostatic biopsies (TRUSPs), and 30 transurethral resections of bladder tumor (TURBTs) were collected. Performance was evaluated using scoring lists including details on completeness of procedural steps, level of independence, time, and the incidence of unintended events. The causal factors contributing to the unintended events were identified by 2 expert urologists and classified according to the recognized PRISMA method.

**SETTING:** This study was performed in 5 teaching hospitals in the Netherlands.

**PARTICIPANTS:** We included 11 junior residents and 5 senior residents in urology in the final study cohort.

**RESULTS:** Senior residents showed a lower degree of completeness in material usage than junior residents did during UCS ( $p < 0.01$ ) and in preparation, material usage, and procedure during TRUSP (all  $p < 0.05$ ). In UCS and TURBT, senior residents received significantly less feedback than junior residents did (both  $p < 0.01$ ). Incidence of unintended events for junior vs senior residents was 11% and 4% in UCS, 0% and 7% in transrectal ultrasound of the prostate, 36% and 62% in TRUSP, and 41% and 23% in TURBT, respectively. Overall, unintended events were mainly caused by human factors, in particular, verification and skills-based issues.

**CONCLUSION:** Present performance of basic urological procedures involves a high percentage of unintended events, especially in TRUSP and TURBT, which are mainly caused by human factors and are a potential threat for patient safety. Junior residents are less independent but more thorough in the performance of UCS and TRUSP than senior residents are. Targeted skills training including assessment should be implemented before privileges for independent practice are granted to reduce the incidence of unintended events and optimize patient safety.

*impactfactor:* 1.379

## **Wijn RP**

### **Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

Geerts N\*, Jansz AR\*, Boonen KJ\*, Wijn RP\*, Koldewijn EL\*, Boer AK\*, Scharnhorst V\*

Clin Chim Acta. 2015 Jun 26;448:86-90

*Voor abstract zie:* AKL - Geerts N

*impactfactor:* 2.824

\* = Werkzaam in het Catharina Ziekenhuis

## Boeken

## Chirurgie

**Bode AS\*, Dekkers M\*, Oudheusden TR van\*, Teijink JA\*, and Luyer MD\***

**Part V Non-Occlusive Mesenteric Ischemia – Chapter 25: Clinical Presentation and Diagnosis – p. 337-342**

In: Mesenteric Vascular Disease : Current Therapy

Oderich, Gustavo S. (Ed.)

New York : Springer, 2015

ISBN: 978-1-4939-1846-1

**Oudheusden TR van\*, Dekkers M\*, Bode AS\*, Teijink JA\* and Luyer MD\***

**Part V Non-occlusive mesenteric ischemia, Chapter 26 Management and Results – p. 343-348**

In: Mesenteric Vascular Disease : Current Therapy

Oderich, Gustavo S. (Ed.)

New York : Springer, 2015

ISBN: 978-1-4939-1846-1

Haan Jacco J. de, Lubbers Tim, **Luyer Misha D\***, and Buurman Wim A

**Part XIV Enteral Aspects: Preclinical Studies, Chapter 130 Nutritional Modulation of Immune Response via Vagus Nerve: Preclinical Studies and Future Perspectives – p. 1713 - 1728**

In: Diet and Nutrition in Critical Care

Editors: Rajkumar Rajendram, Victor R. Preedy, Vinood B. Patel

New York : Springer, 2015

ISBN: 978-1-4614-7837-9

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Utrecht: De Tijdstroom, 2015

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Comorbiditeit bij COPD

Wouters EFM (red.)

Beuningen : Esculaap Media, 2015

ISBN: 9789491984105

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## Promoties

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**Wetenschapsavond  
Catharina Ziekenhuis  
2016**

## Presentaties

### Apotheek

#### Boerrigter E

#### **Therapeutic dalteparin in patients with renal insufficiency: 'Are we doing the right thing?'**

Emmy Boerrigter\*, Marijke J.E. Dekker, Arthur Wasylewicz, C.J.A.M. (Stijn) Konings, Volkher Scharnhorst, Rene J.E. Grouls, C.H.M. (Marieke) Kerskes

Achtergrond: Dalteparine wordt als voorkeursmiddel ingezet bij veel trombotische aandoening. Verondersteld wordt dat het gebruik van dalteparine bij patiënten met nierinsufficiëntie kan leiden tot accumulatie, met bloedingen als gevolg. Dosisreductie en monitoring wordt geadviseerd om dit te voorkomen, maar de evidence voor deze adviezen is zeer beperkt.

Doel: Onderzoeken of dosisreductie en monitoring van therapeutisch dalteparine noodzakelijk is bij patiënten met nierinsufficiëntie.

Opzet: Retrospectief onderzoek

Methode: Anti-Xa spiegels behorend bij patiënten opgenomen in het Catharina Ziekenhuis Eindhoven tussen 01-09-2011 en 01-09-2015 die behandeld werden met therapeutisch dalteparine, werden geïncludeerd. Het percentage sub- en suprathérapeutische anti-Xa topspiegels werd berekend. Meervoudige lineaire regressie werd gebruikt om te bepalen of de nierfunctie een significante voorspeller was voor de anti-Xa spiegel.

Resultaten: In totaal werden 205 spiegels geïncludeerd, waarvan 40 spiegels behoorden bij 32 patiënten die eenmaal daags dalteparine kregen en 165 spiegels bij 80 patiënten die tweemaal daags dalteparine kregen. Van de eenmaal daags gedoseerde patiënten had 67,5% een subtherapeutische anti-Xa spiegel, van de tweemaal daags gedoseerde patiënten 69,1%. Suprathérapeutisch was 2,5% en 5,5% van de anti-Xa spiegels behorende bij respectievelijk een- en tweemaal daags gedoseerde patiënten. Meervoudige lineaire regressie toonde aan dat, na correctie voor het aantal metingen per patiënt en de dagdosering dalteparine/opnamegewicht, de nierfunctie geen significante voorspeller was voor de anti-Xa spiegel.

Conclusie: Er is geen reden om aan te nemen dat dosisreductie van therapeutisch dalteparine noodzakelijk is bij patiënten met nierinsufficiëntie. Wellicht dienen de huidige richtlijnen voor dalteparine te worden aangepast.

### Chirurgie

#### Simkens GA

#### **Development of a Prognostic Nomogram for Patients with Peritoneally Metastasized Colorectal Cancer Treated with Cytoreductive Surgery and HIPEC**

Geert A. Simkens MD\*, Thijs R. van Oudheusden MD\*, Daan Nieboer MSc, Ewout W. Steyerberg PhD, Harm J. Rutten MD PhD FRCS (London)\*, Misha D. Luyer MD PhD\*, Simon W. Nienhuijs MD PhD\*, Ignace H. de Hingh MD PhD\*

Background: With the introduction of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), long-term survival in selected patients with colorectal

PM can be achieved. A tool to adequately predict survival in these patients may significantly improve patient selection and outcome.

**Aim:** This study aims to validate the peritoneal surface disease severity score (PSDSS) in patients with colorectal peritoneal metastases (PM) treated with CRS+HIPEC. If performance of the PSDSS is suboptimal, a new prognostic overall survival model will be developed.

**Methods:** Patients with colorectal PM undergoing CRS+HIPEC with intended complete cytoreduction between 2007 and 2015 were included. Statistical analyses, including internal validation, were performed with R software.

**Results:** A total of 200 patients underwent CRS+HIPEC. External validation of the PSDSS showed a Harrell's c statistic of 0.62. After analyses, four parameters were prognostic relevant factors for overall survival: Age, PCI-score, locoregional lymph node status, and signet ring cell histology. The weighted relevance of these parameters was turned into a prognostic nomogram that we termed COMPASS (Colorectal Peritoneal Metastases Prognostic Surgical Score). The COMPASS differentiated well and showed a Harrell's c statistic of 0.72 with a calibration plot showing good agreement.

**Conclusions:** This study externally validated the PSDSS and developed a new prognostic score: The COMPASS. This pre-cytoreduction nomogram adequately predicts overall survival of patients with colorectal PM undergoing CRS+HIPEC. It can be used as tool to assist in the decision of continuing cytoreduction and HIPEC and can provide valuable information for patients and surgeons in the follow-up period after CRS+HIPEC.

## Longgeneeskunde

**Gillis R**

### **An Asthma Diagnostic Consultation Service can make a significant contribution in obtaining an asthma diagnosis for primary care patients**

Ruby Gillis\*, F. Smeenk\*, W. van Litsenburg\*

**Background:** Previous studies showed us that General Practitioners (GPs) find it difficult to accurately diagnose asthma. This may result in both under and overdiagnosis. To support GPs in their diagnostic process of possible asthma patients a 'one-stop-shop' Asthma Diagnostic Consultation Service (ADCS) was set up.

**Research questions:** We retrospectively evaluated the effectiveness of this consultation service by analyzing the concordance between the GPs working hypotheses and the diagnoses set by the ADCS. Next we evaluated the consequences this had on the patients' pharmacotherapy. Lastly we evaluated whether the intention of being a 'one-stop-shop' service was really being met.

**Methods:** In total 659 patients were referred to the ADCS over a period of four years by 174 GPs. At this service the patients' medical history was taken and a physical examination and a Histamine Provocation Test (HPT) were carried out. We compared the GPs working hypotheses with diagnoses established at the ADCS and the medication patients used at entry of the ADCS with the medication they used when they were referred back to their GP.

**Results:** In 46% (n=303) of all referred patients an asthma diagnosis was excluded and 42% (n=275) were diagnosed with asthma. Twenty-five percent (n=163) of all patients were diagnosed by their GP with chronic rhinitis versus 40% (n=261) of the patients at the ADCS. Of the asthmatic patients 50% (n=137) were co-diagnosed with chronic rhinitis.

More than half of all patients received the advice to change pharmacotherapy (n=339), 12% (n=82) were advised to stop their medication and 10% (n=63) were advised to start medication. The 'one-stop-shop' principle was being met in 53% of patients. Ninety-one percent (n=599) of patients were referred back to their GP in most cases after a short period

of time and only 6% (n=41) of all patients are still under control at the ADCS because of a severe unstable asthma.

Conclusion: The ADCS contributed significantly to the diagnostic process. In 46% of the patients an asthma diagnosis was excluded. This ADCS led to a change in pharmacotherapy in 74% (n=484) of patients. Thereby, the ADCS was able to prevent over and under treatment of patients substantially. The 'one-stop-shop' policy was being met in the majority of patients.

## **Spoeoedeisende hulp**

### **Smits G**

#### **Procedural sedation in the emergency department by Dutch emergency physicians: a prospective multi-center observational study of 1711 adults**

Gaël SMITS\*, Maybritt KUYPERS, Lisette MIGNOT, Eef REIJNERS, Erick OSKAM, Karen VAN DOORN, Wendy THIJSEN\*, Erik KORSTEN\*

Background: In the (recent) past, painful procedures in Emergency departments were done with inadequate analgesia. In the last 5-10 years, newly trained Dutch Emergency physicians (EPs) have started to perform this under procedural sedation.

Objective: To describe the safety of procedural sedation in a country where emergency medicine (EM) is a relative new specialty.

Methods: This is a prospective observational study of adult patients undergoing procedural sedation in by Emergency Physicians or EM residents in eight hospitals. Data was collected on a standardized form. Primary outcome: adverse event rate.

Results: 1711 adult cases were included from 2006-2013. Propofol and midazolam were most used (63 and 29%). The adverse event rate was 11%, mostly hypoxia or apnea. No serious adverse events (aspiration, intubation, death, CPR, permanent neurological deficit) occurred. 90% of the indicated procedures (mostly hip & shoulder dislocations) could be successfully done in the ED.

Conclusion: Adverse events during procedural sedation occurred in 11% of patients. There were no serious adverse events. Procedural sedation – in a country where EM is a relatively new specialty – appears to be safe when performed by EPs or trained EM residents and has comparable adverse event rates as international studies.

## **Philips Research Eindhoven**

### **Petit C**

#### **Practical use of electronic early warning scores in a surgical ward: an observational study**

Clémence Petit, Louis Atallah, Rick Bezemer, Arthur Bouwman\*, Erik Korsten\*

Background and Goal of Study: Early Warning Scores (EWS) have become a common tool to identify patients at risk of deterioration. The aim of this observational study was to gain insight into the day-to-day application of digital EWS registration in a surgical unit.

Materials and Methods: This retrospective study included 384 patients from the Step Forward Unit, a general ward targeting patients who underwent major surgery. The vital signs were collected using Philips' IntelliVue Guardian Solution (Philips Medical Systems, Boeblingen, Germany), which also performed an automated calculation of the Modified Early Warning Score (MEWS).

Results and Discussion: The dataset contained 4923 spot-check observations, of which 12.6% were incomplete (i.e., not all required parameters were measured). The median time between consecutive complete sets of measurement was 6.7 hours (IQR: 5.0-11.5). This time interval became lower with higher MEWS scores (Figure 2). A majority of the measurements (80.0%) was done during 4 peak periods (Figure 3), in accordance with the 4 daily measurements required by the protocol. The measurements taken during off-peak hours were associated with higher MEWS (the proportion of MEWS superior or equal to 3 increased from 18.3% during the nursing rounds to 31.3% outside) and a higher rate of incomplete observations (19.0%, compared to 11.0% during the rounds).

Conclusions: Despite a suboptimal frequency of MEWS calculation, patients at greatest risk of deterioration seemed to benefit from extra measurements outside the routine nursing rounds, though more incomplete. Future systems should focus on better advising for the frequency of measurement and providing clinical decision support even with incomplete observations.

## Posters

### Algemeen Klinisch Laboratorium

**Coene KL\***

#### **Subclinical hypothyroidism: a 'laboratory-induced' condition?**

KLM Coene\*, AY Demir, MAC Broeren, P Verschuure, EGWM Lentjes and AK Boer\*

**Background:** In current literature and guidelines there is a tendency to define absolute thyroid stimulating hormone (TSH) concentrations at which patient follow-up or even pharmaceutical intervention should be initiated. As TSH concentrations depend on the analytical method/platform used for TSH quantification, absolute cut-off values may pose threats for uniform clinical decision making.

**Objective:** In this study we therefore set out to clarify to what extent the method/platform and the reference values applied for TSH influence the clinical interpretation of thyroid parameters.

**Method:** We retrospectively analyzed anonymous TSH results from the Dutch external quality program in relation to reference values advised by different manufacturers. We also examined TSH/free thyroxine (fT4) reference ranges and prevalence of thyroid pathology among different Dutch laboratories, including four cases in which a switch in measuring platform was made.

**Results:** Our data show that interpretation of thyroid parameters is not only influenced by between-method/platform variation, but is also substantially affected by the variation in TSH/fT4 reference intervals between laboratories. Additionally, we show that the transition to a novel analytical method/platform can result in a shift in the prevalence of thyroid pathology. Especially subclinical hypothyroidism stands out as a potentially 'laboratory-induced' condition. This is an undesirable situation, regarding the clinical implications of such a diagnosis for patients.

**Conclusion:** Our study emphasizes the need for (inter)national harmonization/standardization programs for the thyroid biomarkers TSH and fT4. Before the standardization of clinical management of thyroid disorders through guidelines can be successful, harmonization on a laboratory level is required first.

**Geerts N**

#### **Urine flow cytometry can rule out urinary tract infection, but cannot identify bacterial morphologies correctly**

N. Geerts\*, A.R. Jansz\*, K.J.M. Boonen\*, R.P.W.F. Wijn\*, E.L. Koldewijn\*, , A.K. Boer\*, V. Scharnhorst\*

The diagnosis of urinary tract infection (UTI) by urine culture is an expensive and time-consuming procedure. Using a screening method, to identify negative samples, would improve the procedure and reduce costs. Retrospective analysis of over 7000 urine samples indicated that with a cut-off value of  $> 200$  bacteria/?L, a sensitivity of 93.0%, a specificity of 63.5%, and a negative predictive value (NPV) of 96.2% is obtained. As a result the culturing of 49% of all samples could be avoided. Screening results can be improved by the introduction of gender-specific cut-off values. When a NPV of 95% is considered acceptable the unisex cut-off value of  $> 200$  bacteria/?L can be used for women (NPV 94.9%), but the cut-off value for men could be raised to  $> 400$  bacteria/?L without diminishing the NPV (NPV 95.0%).

Recently, Sysmex developed additional software for their urine flow cytometers. Besides measuring the number of bacteria present in urine, information is given on bacterial morphology, which may guide the physician in the choice of antibiotic. This software update

was evaluated. Bacteria are classified into two categories: 'rods' and 'cocci/mixed'. Compared to the actual morphology of the bacterial pathogen found, the 'rods' category scores reasonably well with 91% chance of classifying rod-shaped bacteria correctly. The 'cocci/mixed' category underperforms, with only 29% of spherical-shaped bacteria (cocci) classified as such. In its current version, the bacterial morphology software does not classify bacteria, according to their morphology, well enough to be of clinical use in this study population.

New findings

1. Analysis of 7322 samples led to a cut-off value of > 200 bacteria/?L (NPV of 96.2%).
2. Screening results can be improved by the introduction of gender-specific cut-off values.
3. Foreknowledge on bacterial morphology, as indicated by urine flow cytometry, did not lead to changes in antibiotic choice.

## **Schmitz E**

### **Therapeutic drug monitoring of infliximab: performance evaluation of three commercial ELISA kits**

E.M.H. Schmitz\*, D. van de Kerkhof\*, D. Hamann, J.L.J. van Dongen\*, P.H.M. Kuijper\*, L. Brunsveld\*, V. Scharnhorst\*, M.A.C. Broeren\*

Background: Therapeutic drug monitoring (TDM) of infliximab (IFX, Remicade®) can aid to optimize therapy efficacy. Many assays are available for this purpose. However, a reference standard is lacking.

Goal: Therefore, we evaluated the analytical performance, agreement and clinically relevant differences of three commercially available IFX ELISA kits on an automated processing system.

Methods: The kits of Theradiag (Lisa Tracker Infliximab), Progenika (Promonitor IFX) and apDia (Infliximab ELISA) were implemented on an automated processing system. Imprecision was determined by triplicate measurements of patient samples on five days. Agreement was evaluated by analysis of thirty patient samples and four spiked samples by the selected ELISA kits and the in-house IFX ELISA of Sanquin Diagnostics (Amsterdam). Therapeutic consequences were evaluated by dividing patients into four treatment groups using cut-off levels of 1, 3 and 7 µg/mL and determining assay concordance.

Results: Within-run and between-run imprecision were acceptable ( $\leq 12\%$  and  $\leq 17\%$ , respectively) within the quantification range of the selected ELISA kits. The apDia assay had the best precision and agreement to target values. Statistically significant differences were found between all assays except between Sanquin Diagnostics and the Lisa Tracker assay.

The Promonitor assay measured the lowest IFX concentrations, the apDia assay the highest. When patients were classified in four treatment categories, 70% concordance was achieved.

Conclusions: Although all assays are suitable for TDM, significant differences were observed in both imprecision and agreement. Therapeutic consequences were acceptable when patients were divided in treatment categories, but this could be improved by assay standardization.



# Apotheek

## Taks M

### The implementation of a treatment algorithm for Infliximab in inflammatory bowel disease patients

M. Taks, MSc\*, P.A.R.R. Pijls, MSc\*, R.J.E. Grouls\*, PharmD, PhD, R. ten Broeke\*, PharmD, PhD, L.J.J. Derijks, PharmD, PhD, J. Curvers\*, PhD, L.P.L. Gilissen, PhD, MD\*

Introduction: The anti-TNF-alpha inhibitor infliximab (IFX) is an effective and safe therapy for many inflammatory bowel disease (IBD) patients. However, there are still patients who do not achieve remission despite infliximab therapy. Therapeutic drug monitoring (TDM) allows for a more cost-effective use of IFX by monitoring IFX trough levels and anti-IFX antibody (ATI) formation. Recently, several IFX treatment algorithms for TDM have been published, but their effectiveness have never been validated in daily practice. Therefore, the aim of our study was to investigate the use of an IFX treatment algorithm for our IBD population, focusing on remission rates and drug costs.

Methods: In this prospective intervention study, IBD patients > 18 years treated with IFX were asked to participate in this study. Remission rates were assessed by use of fecal calprotectin levels and a validated questionnaire. IFX trough levels and ATI's were determined at baseline and at the third IFX infusion. If needed, a therapy adjustment was performed during the second IFX infusion.

Results: 62 IBD patients were treated with IFX, of which 33 patients agreed to participate in this study. 13 (39%) patients required and agreed to therapy adjustments of which 4 (12%) patients discontinued IFX treatment because of undetectable trough levels IFX and ATI formation. Remission rates at baseline and at third infusion were both 28 (85%). An annual cost reduction in drug costs of 47.026€ (7,4%) was realized using this treatment algorithm.

Conclusion: The studied treatment algorithm can be helpful in optimizing IFX therapy of IBD patients.

# Cardiologie

## Hoorn CJ

### Review on Factors Influencing Physician Guideline Adherence in Cardiology

C.J.G.M. Hoorn\*, H.J.G.M. Crijns\*, A.T.M. Dierick-van Daele\*, L.R.C. Dekker\*

Background: Cardiovascular disease (CVD) is the most common cause of death in Western countries, physician adherence to guidelines is often suboptimal, resulting in impaired patient outcome and prognosis. Multiple studies have been conducted to evaluate patterns and influencing factors of patient adherence, but little is known about factors influencing physician guideline adherence.

Aims: This review aims to identify influencing factors for physicians guideline adherence relevant to cardiology and to provide insights and suggestions for future improvement.

Methods: A literature search for studies in adults with any cardiac condition, published until September 2015 in PubMed and Cochrane, was done. Observational studies, randomised controlled trials (RCTs) and reviews were included. The methodological quality of the publications was evaluated using The Strobe Checklist.

Results: Out of 477 studies eight prospective cross-sectional studies were selected, which were all conducted in multiple centres. An important link between male patients, physicians' medical specialty, type of centre, and physician adherence was found.

Conclusion: Besides the small number of retrieved articles, only few patient characteristics were analysed. Female and elderly patients, physicians without cardiologic specialization and primary care centres are inextricably linked to physician noncompliance. It is expected that

treating physicians have difficulties applying the guidelines for the increased number of aging and complex patients. Active involvement of the physicians during guideline development and implementation, as well as the use of guideline decision support tools are recommended to improve guideline adoption, resulting in improvement in patient outcome. Vernieuwende elementen

Cardiologische zorg wordt gefragmenteerd geleverd in verschillende zorgniveaus en medische specialismen, hierdoor is er een suboptimale guideline adherence. Optimalisatie van samenwerking en communicatie tussen deze verschillende groepen is noodzakelijk om kwaliteit van zorg te waarborgen en patiëntenresultaten te verbeteren in een tijdperk waar complexe, oudere patiënten niet ongewoon zijn.

## Chirurgie

### Brinkman DJ

#### **The effect of sarcopenia and visceral obesity on the inflammatory response in colorectal surgery**

B.J.J. Smeets\*; D.J. Brinkman\*; E.C.J. Horsten\*; J.A. Langius; H.J.T. Rutten\*; W.J. de Jonge; M.D.P. Luyer\*

Introduction: Sarcopenia and visceral obesity (VO) have been suggested to increase postoperative complications in colorectal surgery by altering the inflammatory response. However, clinical evidence to support this hypothesis is scarce.

Aim: To investigate the effects of sarcopenia and VO on inflammation and complications following colorectal surgery.

Materials and Methods: A post-hoc analysis was performed in 79 patients using data from a randomized placebo-controlled trial in which perioperative gum chewing reduced postoperative complications and inflammation. Sarcopenia and VO were assessed using computed tomography image analysis. Plasma concentrations of interleukin (IL) 8 and soluble tumor necrosis factor receptor 1 (TNFRSF1A) were measured preoperatively and 4 hours after start of surgery. Clinical data were prospectively registered in a database.

Results: IL-8 concentrations were higher in patients with versus without sarcopenia before surgery (0 [0-6.01] vs 0 [0-0] pg/ml,  $p = 0.011$ ) and after surgery ( $352 \pm 268$  vs  $239 \pm 211$  pg/ml,  $p = 0.048$ ). TNFRSF1A was higher in patients with versus without VO only before surgery (0.49 [0.28-1.36] vs 0.40 [0.25-1.19] ng/ml,  $p = 0.036$ ). Linear regression analysis identified gum chewing ( $p = 0.034$ ) and sarcopenia ( $p = 0.034$ ) as independent predictors of postoperative IL-8 concentrations. Gum chewing reduced postoperative IL-8 ( $215 \pm 204$  vs  $376 \pm 249$  pg/ml,  $p = 0.016$ ) and TNFRSF1A ( $0.75 [0.59-0.94]$  vs  $0.92 [0.70-1.04]$  ng/ml,  $p = 0.044$ ) in patients with VO. Sarcopenia and VO were not associated with any postoperative complication.

Conclusion: Sarcopenia increases IL-8 before and early after colorectal surgery, while VO may increase preoperative TNFRSF1A. Gum chewing may reduce the postoperative inflammatory response in patients with VO.

### Hageman D

#### **Effect van diabetes mellitus op de resultaten van gesuperviseerde looptherapie voor claudicatio intermittens: een systematisch review**

David Hageman\*, Lindy N.M. Gommans\*, Marc R.M. Scheltinga, Joep A.W. Teijink\*

Introductie: Patiënten met perifere arterieel vaatlijden en diabetes mellitus (DM) hebben vaak atypische symptomen, slechtere onderste extremitateit functie en snellere ziekteprogressie. Mogelijk worden ook de resultaten van gesuperviseerde looptherapie

(GLT) bij patiënten met claudicatio intermittens (CI) beïnvloedt door de aanwezigheid van DM. Het doel van dit onderzoek was om de bewijslast van de mogelijke invloed van DM op de resultaten van GLT bij patiënten met CI samen te vatten en hiaten in de literatuur te identificeren.

Methoden: Artikelen werden verkregen door middel van een literatuurzoekopdracht in MEDLINE, EMBASE en CENTRAL. Twee auteurs beoordeelden onafhankelijk van elkaar gerandomiseerde en niet-gerandomiseerde onderzoeken die het effect van DM op de loopafstand na GLT onderzochten bij patiënten met CI. Geschikte studies onderzochten GLT bij zowel diabetische als niet-diabetische patiënten met CI. Onderzoeken werden beoordeeld op methodologische kwaliteit met behulp van de 'Cochrane Collaboration's tool for assessing risk of bias'. Uitkomstmaten waren (verandering in) maximale, pijnvrije en functionele loopafstand (meters).

Resultaten: De literatuurzoekopdracht leverde 903 potentieel relevante en unieke artikelen op. Na screening van de titels en abstracts en de daaropvolgende full-text evaluatie werden 3 artikelen geïnccludeerd. Alle onderzoeken hadden een low risk of bias. De drie artikelen rapporteerden alle maximale loopafstand (MLA, n = 845), twee rapporteerden daarnaast pijnvrije loopafstand (PVLA, n = 87) en één rapporteerde functionele loopafstand (FLA, n = 758). Verbetering in MLA, PVLA en FLA werd gezien voor zowel de diabetische als niet-diabetische groep patiënten met CI. In één onderzoek was de MLA na drie maanden follow-up 111 meter (128%) groter in de niet-DM groep in vergelijking met de DM-groep (niet-DM: 198 meter vs. DM: 87 meter, p = 0,056). In een ander onderzoek had de niet-DM groep een significante toename in PVLA na drie maanden follow-up terwijl hier geen sprake van was in de DM-groep. Echter, in het grootste onderzoek van deze review werd geen effect van DM op de MLA en FLA na GLT beschreven.

Conclusie: Patiënten met CI en DM verbeteren in loopafstand na GLT. Hoewel er tegenstrijdige resultaten worden gemeld over het effect van DM wanneer diabetische en niet-diabetische patiënten met CI onderling worden vergeleken, zijn er geen argumenten gevonden om diabetische patiënten GLT te onthouden.

## **Hageman D**

### **Minimale correlatie tussen fysieke capaciteit en dagelijkse activiteit bij patiënten met claudicatio intermittens**

David Hageman\*, Lindy N.M. Gommans\*, Ingeborg Jansen\*, Robbin de Gee\*, Rob C. van Lummel\*, Nicole Verhofstad\*, Marc R.M. Scheltinga, Joep A.W. Teijink\*

Introductie: Behandelresultaten van patiënten met claudicatio intermittens (CI) worden doorgaans uitgedrukt in loopcapaciteit (maximale loopafstand in meters), zoals gemeten tijdens een gestandaardiseerde loopbandtest (LT). De loopcapaciteit weerspiegelt waartoe een patiënt in een gecontroleerde omgeving maximaal in staat is en maakt onderdeel uit van de fysieke inspanningscapaciteit (FIC). Dagelijkse fysieke activiteit (FA), gedefinieerd als de totale hoeveelheid beweging per dag, wordt in toenemende mate gezien als een sterke voorspeller van morbiditeit en mortaliteit bij patiënten met CI. Daarnaast suggereren recente inzichten dat een toename in FIC niet automatisch leidt tot een toename in dagelijkse FA. De exacte relatie tussen FIC en FA bij patiënten met CI is echter nog onduidelijk.

Methoden: Er werd een cross-sectioneel onderzoek verricht naar de correlatie tussen verschillende FIC uitkomsten en FA in een algemene CI populatie. FIC werd bepaald met een viertal veel gebruikte testen (Gardner-Skinner loopbandtest (LT), physical performance battery, timed up and go test en zes minuten wandeltest (6MWT)). FA werd gemeten tijdens zeven opeenvolgende dagen met behulp van een tri-axiale accelerometer (DynaPort MoveMonitor). Vijf FA componenten (liggen, zitten, staan, schuifelen en bewegen) en vier

parameters (totale duur, aantal periodes, gemiddelde duur per periode en gemiddelde bewegingsintensiteit per periode) werden geanalyseerd. Correlatiecoëfficiënten tussen FIC en FA componenten werden vervolgens bepaald.

Resultaten: Gegevens van 46 patiënten waren beschikbaar voor deze analyse. De CI patiënten waren 81% van de dag sedentair (liggen en zitten) en de resterende 19% van de tijd fysiek actief (staan, schuifelen en bewegen). Over het algemeen werden zeer zwakke tot matige correlaties (Spearman correlatiecoëfficiënten variërend tussen 0,025 en 0,663) gevonden. Matige correlaties (welke als relevant beschouwd mogen worden) werden gevonden tussen zowel de LT uitkomsten als de 6MWT en diverse componenten van FA. Functionele loopafstand (gemeten met de LT) correleerde bijvoorbeeld redelijk goed met het aantal stappen per dag (Spearman correlatiecoëfficiënt = 0,663,  $p = <0.01$ ).

Conclusie: FIC en FA correleren slecht tot matig bij patiënten met CI. Het wordt daarom zinvol geacht om FA als nieuwe uitkomstmaat en toekomstig behandeldoel voor patiënten met CI te gaan gebruiken.

## **Hageman D**

### **Wanneer wordt gesuperviseerde looptherapie voor claudicatio intermittens zinvol geacht: een landelijk onderzoek onder vaatchirurgen**

David Hageman\*, Gert-Jan Lauret\*, Lindy N.M. Gommans\*, Mark J.W. Koelemay, Marc R.H.M. van Sambeek\*, Joep A.W. Teijink\*

Introductie: Huidige internationale richtlijnen over de behandeling van claudicatio intermittens (CI) bevelen gesuperviseerde looptherapie (GLT) aan als eerste keuze therapie. In een landelijk onderzoek onder Nederlandse vaatchirurgen uit 2011 werden argumenten gerapporteerd om niet te verwijzen voor GLT, zoals de aanwezigheid van cardiopulmonale co-morbiditeit.<sup>1</sup> Geconcludeerd werd dat deze schijnbare contra-indicaties voor SET in feite juist indicaties zijn voor deelname aan een trainingsprogramma. Het doel van het huidige onderzoek was om vier jaar later de inzichten en overwegingen onder Nederlandse vaatchirurgen bij het voorschrijven van GLT opnieuw te beoordelen.

Methoden: Nederlandse vaatchirurgen, fellows en differentianten vaatchirurgie werd gevraagd een enquête met 26 vragen in te vullen tijdens de Vaatdagen 2015 of via een website. De enquête bestond uit elf ja/nee-vragen, negen multiplechoicevragen en zes openvragen over factoren die relevant en/of belangrijk geacht worden bij het voorschrijven van GLT, zoals specifieke patiëntkenmerken en co-morbiditeit. Data-extractie werd gedaan door twee auteurs onafhankelijk van elkaar. Data-analyse werd verricht in SPSS 19 software (IBM Corporation, Armonk, New York).

Resultaten: In totaal voltooiden 124 respondenten (82% man, gemiddelde leeftijd 46 jaar), waaronder 104 vaatchirurgen, de enquête. GLT werd nuttig geacht bij CI patiënten met COPD (86% van de respondenten) of chronisch hartfalen (75%). Voor patiënten met CI door een aorta-iliacale stenose/occlusie werd GLT minder vaak als nuttig beoordeeld (63%). Invalidering in het arbeidsproces (90%), beperking in algemene dagelijkse levensverrichtingen (87%) en de anatomische locatie van de stenose/occlusie (70%) werden door respondenten beschouwd als de belangrijkste factoren in de beslissing om over te gaan op een vasculaire ingreep. De enkel-arm index (13%), financiële situatie van de patiënt (15%) en loopafstand gemeten tijdens een loopbandtest (28%) werden door een minderheid als belangrijk beoordeeld. GLT in voorbereiding op of in navolging van een vasculaire interventie werd door respectievelijk 77% en 84% van de respondenten als nuttig beschouwd.

Conclusie: Ten opzichte van de resultaten uit 2011 lijkt sprake van een positievere houding van Nederlandse vaatchirurgen ten aanzien van GLT voor CI patiënten met cardiopulmonale co-morbiditeit (2011: hartfalen 70% en COPD 66% vs. 2015: hartfalen 75% en COPD 86%). Bij

patiënten met een aorta-iliacale stenose/occlusie blijft GLT echter nog onderbenut (2011: 71% vs. 2015: 63%).

#### **Houten MM van den**

#### **Cost-Effectiveness of Supervised Exercise Therapy Compared with Endovascular Revascularization for Intermittent Claudication**

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**Background:** Current guidelines recommend supervised exercise therapy (SET) as the preferred initial treatment for patients with intermittent claudication (IC). The availability of SET programs is however limited and such programs are usually not reimbursed. Evidence on the long-term cost-effectiveness of SET compared to endovascular revascularization (ER) as primary treatment for IC is required for successful implementation in clinical practice.

**Methods:** A Markov model was constructed to determine the incremental costs, incremental quality-adjusted-life years and incremental cost-effectiveness ratio of SET versus ER for a hypothetical cohort of patients with newly diagnosed IC, from the Dutch healthcare payer's perspective. In case of primary treatment failure possible secondary interventions were repeat ER, open revascularization, or major amputation. Data sources for model parameters included original data from two randomized controlled trials, as well as evidence from the medical literature. The robustness of the results was tested with probabilistic- and one-way sensitivity analysis.

**Results:** Considering a 5-year time horizon, probabilistic sensitivity analysis revealed that SET was associated with cost-savings (-€6412, 95% credibility interval; -€11 874 to -€1939) compared to ER. The mean difference in effectiveness was -0.07 quality-adjusted-life years (95% CI; -0.27 to 0.16). ER was associated with an additional €91 600 (US \$118 164) per quality-adjusted-life year gained as compared with SET. SET remained the most cost effective option in one-way sensitivity analysis using alternate assumptions.

**Conclusions:** SET is a more cost-effective primary treatment for IC compared to ER. These results support implementation of supervised exercise programs in clinical practice.

#### **Mannetje Y 't**

#### **Late single-center outcome of the Talent Abdominal Stent Graft after a decade of follow-up**

Y.W. 't Mannetje\*, P.P.H.L. Broos\*, R.F.A. van Poppel\*, M.R.H.M. van Sambeek\*, J.A.W. Teijink\*, Ph.W.M. Cuypers\*

**Objective:** Lifelong yearly surveillance is advised after endovascular abdominal aortic aneurysm repair (EVAR) for abdominal aortic aneurysms (AAA). This follow-up requires a substantial amount of healthcare resources. The aim of this paper is to assess the occurrence of stent graft related complications and secondary interventions during a minimum of ten-year follow-up after elective EVAR.

**Methods:** Patients treated in a high-volume endovascular center in The Netherlands with the Talent infrarenal stent graft (Medtronic Vascular, Santa Rosa, CA, USA) between June 1999 and February 2005, were included. Patients with previous aortic surgery or emergency interventions were excluded. Our primary outcome was clinical success up to 10-years. Secondary endpoints were technical success and survival.

**Results:** A total of 149 patients were included, 91.9% were male. The mean age was  $70.2 \pm 7.8$  years. A stent graft was implanted in 98% of patients; technical success was achieved in 89.9%. Clinical success after 30 days, 1 year, 5 and 10 years was 81.1%, 74.3%, 70.3% and 65.5%, respectively. In 30 patients (20.7%) a secondary intervention was required, 80.0% of first secondary interventions occurred within the first 5 years. Six late conversions were

necessary due to stent graft infection (2), migration (2), or persisting endoleak (2). The 5- and 10-year overall survival rates were 55.2% and 38.6%, respectively.

Conclusion: The risk of EVAR-related complication is highest in the first 5 years. Consequently the main focus should be on that period, further follow-up must not be neglected, as complications occur up to 10 years after treatment.

**Mannetje Y 't**

### **Outcomes after abandoning routine pre-emptive coil embolization of the internal iliac artery in endovascular aneurysm repair**

Y.W. 't Mannetje\*, P.P.H.L. Broos\*, M.R.H.M. van Sambeek\*, J.A.W. Teijink\*, Ph.W.M. Cuypers\*

Objectives: Coil embolization of the internal iliac artery (IIA), prior to endovascular exclusion of common iliac artery (CIA) aneurysms, remains controversial. We analysed outcomes of a strategy abandoning pre-emptive coil embolization in all cases. Our aim is to determine if this strategy is safe, effective and well tolerated by the patients.

Methods: All patients receiving a stent graft that extended into the external iliac artery, operated between January 2010 and November 2010, were included. Preoperative imaging was reviewed to determine aneurysm morphology, and follow-up imaging and symptoms were recorded. The primary outcome was the occurrence of type-II endoleaks, aneurysm growth and the occurrence of buttock claudication.

Results: A total of 88 patients (95.5% male; mean age  $73.9 \pm 8.7$  years), including 92 covered IIAs, were included. The median CIA diameter was 37mm (range 9-90). The procedure was elective in 68.2%. The IIA was intentionally covered in 83.0% of patients. The 30-day mortality was 5.7%, mean follow-up was  $26.9 \pm 18.2$  months. A total of 14 (16.9%) patients required a secondary intervention. Three type-II endoleaks originating from a covered IIA were recorded; one was accepted, one required an intervention because of aneurysm growth, and one patient died before any treatment was initiated. Buttock claudication was reported in 27.7% and persisted after one year in 4.8% of the cases only. No severe ischemic IIA related complications were reported.

Conclusion: Overstenting the IIA without pre-emptive coil embolization is safe, has a low risk for type-II endoleaks and aneurysm growth and buttock claudication is rare. This revised strategy saves both operating time and resources.

**Oudheusden TR van**

### **Poor outcome after cytoreductive surgery and HIPEC for colorectal peritoneal carcinomatosis with signet ring cell histology**

T.R. van Oudheusden\*, H.J. Braam\*, S.W. Nienhuijs\*, M.J. Wiezer\*, B. van Ramshorst\*, M.D.P. Luyer<sup>8</sup>, I.H.J.T. de Hingh\*

Background: Signet ring cell cancer (SRCC) patients have a poor oncologic outcome. The aim of this study was to determine whether the potential drawbacks of HIPEC outweigh the benefits in patients with peritoneally metastasized SRCC.

Methods: Patients with PC of colorectal origin referred to two tertiary centers between April 2005 and December 2013 were identified and retrospectively analyzed. Data were compared between SRCC histology and other differentiations.

Results: Three-hundred-fifty-one patients were referred for CRS+HIPEC among which 20 (5.7%) patients were identified with SRCC histology. CRS+HIPEC was performed in 16 of these 20 (80%) and 252 out of the 331 remaining patients (76.1%). A higher proportion of patients in the SRCC-group were diagnosed with N2 stage (62.5% vs. 36.1%,  $P=0.04$ ). A macroscopic complete resection was achieved in 87.5% and 97.2% respectively ( $P=0.04$ ).

Median survival was 14.1 months compared to 35.1 months ( $P < 0.01$ ). Recurrence occurred in 66.7% of the SRCC patients and in 43.7% of the other histology patients ( $P = 0.07$ ).

Conclusion: Patients with SRCC and PC treated with CRS + HIPEC have a poor median survival only slightly reaching over 1 year. In case of doubt of eligibility, the presence of SRCC should refrain a surgeon from performing CRS and HIPEC.

Vernieuwende elementen:

Deze studie laat zien dat het hebben van een peritoneaal gemetastaseerd zegelringcarcinoom prognostisch dramatisch is en is daarmee een belangrijke boodschap voor chirurgen, MDL artsen en Internisten/Oncologen wat betreft welk behandelingspad er gekozen moet worden en hoe ze patiënten moeten inlichten.

## **Rovers K**

### **Hospital of diagnosis affects the likelihood of undergoing surgery and overall survival in patients diagnosed with colorectal peritoneal carcinomatosis**

Koen Rovers\*

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) for colorectal peritoneal carcinomatosis (PCRC) is centralised, whereas the diagnosis is made in all hospitals. This study aims to assess whether hospital of diagnosis affects the likelihood of undergoing CRS+HIPEC and overall survival (OS).

Methods: Between 2005-2014, all PCRC patients potentially eligible for CRS+HIPEC in the Netherlands were selected. Hospitals were classified as HIPEC-centre (HC) or non-HIPEC centre (NHC). For survival analysis, hospitals were classified as high-probability-centre (HPC, >20% of patients underwent CRS+HIPEC), medium-probability-centre (MPC, 10-20% of patients underwent CRS+HIPEC) or low-probability-centre (LPC, <10% of patients underwent CRS+HIPEC). Logistic regression and Cox regression analysis were used to assess the relationship between hospital of diagnosis and the likelihood of undergoing CRS+HIPEC and OS, respectively.

Results: 2661 patients, diagnosed in 91 hospitals, were included. Between hospitals of diagnosis, the percentage of patients receiving CRS+HIPEC ranged from 0%-53%, median OS ranged from 3.1-28.3 months, and 3-year OS ranged from 0%-42%. Patients diagnosed in HC were more likely to receive CRS+HIPEC than patients diagnosed in NHC (33% vs 13%, OR 3.46 [2.24–5.33]). Median OS was 14.2, 10.1, and 8.2 months for patients diagnosed in HPC, MPC and LPC, respectively ( $p < 0.01$ ). On multivariate analysis, patients diagnosed in HPC had higher OS compared to patients diagnosed in MPC (HR 0.84 [0.74–0.95]). Patients diagnosed in LPC had lower OS (HR 1.18 [1.07–1.30]).

Conclusion: The large variation in probability of receiving CRS+HIPEC and OS between hospitals of diagnosis indicates suboptimal patient selection and potential underuse of CRS+HIPEC.

## **Smeets B**

### **Beneficial effects of early enteral nutrition after major rectal surgery: a possible role for conditionally essential amino acids? Results of a randomized clinical trial**

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Background: In a previous study comparing early enteral nutrition (EEN) versus early parenteral nutrition (EPN) after major rectal surgery, EEN reduced postoperative ileus, anastomotic leakage and hospital stay. Other studies show that plasma glutamine concentration represents poor prognosis in ICU-patients.

**Objective:** The aim was to investigate the beneficial effect of EEN versus EPN in relation to plasma concentrations of glutamine, citrulline and arginine.

**Methods:** This is a preplanned substudy of a previous prospective, randomized, open-label, single centre study, comparing EEN versus EPN in 123 patients at high risk of postoperative ileus after surgery for locally advanced or locally recurrent rectal cancer. Eight hours after the surgical procedure artificial nutrition was started in hemodynamically stable patients, stimulating oral intake in both groups. Blood samples were collected to measure plasma glutamine, citrulline and arginine concentrations using a validated ULPC-tandem mass spectrometric method.

**Results:** Baseline concentrations were comparable for both groups. Directly after rectal surgery, a decrease in plasma amino acids was observed. Plasma glutamine concentrations were higher in the parenteral group than in the enteral group on postoperative day 1 ( $p=0.027$ ) and day 5 ( $p=0.008$ ). Arginine concentrations were also significantly increased in the parenteral group at day 1 ( $p<0.001$ ) and day 5 ( $p=0.001$ ).

**Conclusions:** Lower plasma glutamine and arginine concentrations were measured in the enteral group, while a better clinical outcome was observed. We conclude that plasma amino acids do not provide a causal explanation for the observed beneficial effects of EEN after major rectal surgery.

## **Smeets B**

### **The effect of early vs late enteral nutrition on anastomotic leakage after lower intestinal surgery; a systematic review and meta-analysis**

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**Background:** Early start of enteral nutrition is an essential part of fast-track protocols in colorectal surgery. Recently, early enteral nutrition has been shown to significantly reduce anastomotic leakage. However, the relation between early enteral nutrition and anastomotic leakage is not well understood.

**Objectives:** To determine the effect of early enteral nutrition compared to late enteral nutrition on anastomotic leakage in patients undergoing lower intestinal surgery.

**Methods:** The Pubmed, Embase, Medline and Cochrane databases were systematically searched. Randomized controlled trials comparing early vs late enteral nutrition in patients undergoing lower intestinal surgery were included. A meta-analysis was performed for anastomotic leakage using the Mantel-Haenszel method.

**Results:** Nine studies met eligibility criteria. Early enteral nutrition significantly reduced anastomotic leakage (OR 0.40; 95% CI 0.17-0.95;  $p=0.04$ ), however substantial heterogeneity was present between studies with regard to perioperative protocols and definitions for anastomotic leakage.

**Conclusion:** Early enteral nutrition following colorectal surgery reduces anastomotic leakage. However, anastomotic leakage is often not well defined and the incidence is low. Further prospective studies are needed to elucidate the effect of early enteral nutrition on anastomotic leakage.



## Gynaecologie

**Kuijs MG**

### **The Risk of Concurrent Ovarian Malignancy in Patients with Endometrial Carcinoma**

Maudi GGA Kuijs\*, Louis JM van der Putten, Ralph H Hermans\*, Nicole PM Ezendam, Johanna MA Pijnenborg

**Background** Endometrial carcinoma (EC) is the most common gynecological malignancy in western countries. Primary treatment consists of hysterectomy and bilateral salpingo-oophorectomy (BSO). Although most patients are postmenopausal, about 14% are premenopausal. In these women BSO results in iatrogenic menopause, which is associated with reduced life expectancy and quality of life.

**Objective** Investigate the prevalence of ovarian spread of EC in patients below and above the age of 50 years and discuss the safety of ovarian preservation in premenopausal women.

**Methods** Data of all patients diagnosed with endometrioid EC between 2010 and 2013 were retrieved from the Netherlands Cancer Registry. Primary outcome was the prevalence of ovarian metastasis, defined as FIGO stage IIIA, in patients aged  $\leq 50$  or  $> 50$  at diagnosis. In addition, discordance between clinical and FIGO stage was determined.

**Results** In total, 6240 patients were diagnosed with endometrioid EC. Mean age at diagnosis was 67 years (SD 11), and 347 patients (5.6%) were  $\leq 50$  years of age. In patients  $> 50$  years, 92% had FIGO I/II and 2.4% FIGO IIIA. This was respectively 89% and 4.3% in patients  $\leq 50$  years. Both clinical and FIGO stage were known in 3324 patients. In patients  $> 50$  years 59 out of 2742 patients (2%) with clinical stage I EC had FIGO IIIA or higher, whereas in patients  $\leq 50$  years this was 1 out of 148 (0.7%).

**Conclusion** Ovarian preservation should be considered for patients  $\leq 50$  years with clinical stage I endometrioid EC.

## Inwendige geneeskunde

**Bie AJ de**

### **Digital dynamic checklists can improve checklist acceptance and compliance to best eligible practice in the Intensive Care Unit**

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**Background:** Checklists can reduce medical errors in a cost-effective manner. However, the use of checklists is hampered by lack of acceptance and compliance.

**Methods:** This simulation based study tested the first dynamic clinical checklist (DCC) for an Intensive Care (IC) ward round. Through decision support and workflow technology is the DCC connected to the electronic health record and therefore able for providing checklist items that are specific to the patient and to the role of the caregiver. A gold standard was established for six typical IC scenarios to objectify which items needed to be checked. Clinicians of the IC compared the DCC with the local standard of care. The primary outcomes were the caregiver satisfaction score and the percentages of checked items overall and of critical items needing a direct intervention.

**Results:** In total twenty participants were included, who performed 116 scenarios. The median percentage of checked items was 100% with the DCC, compared to 75% for the scenarios completed with the local standard of care ( $p < 0.001$ ). Of the critical items remained 23% unchecked in the scenarios performed with the local standard of care, in contrast to 0% if the DCC was used ( $p < 0.001$ ). The mean satisfaction score was 4.13 out of 5.

Conclusion: This simulation study indicates that a DCC significantly increases compliance to best practice by decreasing the percentage of unchecked items during IC ward rounds, while the user satisfaction rate remains high. More, real life, clinical research is required to further evaluate this new kind of checklist.

Vernieuwende elementen: De dynamische checklists zijn vernieuwend doordat ze relevante specifieke items van een individuele patiënt presenteren aan een specifiek zorgverlener in tegenstelling tot de huidige statische papieren checklist. Hierdoor wordt de checklist weer een cognitief hulpmiddel, passend in de dagelijkse workflow van de zorgverlener, ipv een last die meer papierwerk genereert.

## **Munnik ES de**

### **Let's talk about sex: Barriers and facilitators for discussing sexual risk behavior with HIV positive men who have sex with men by HIV nurses.**

Suzanne de Munnik

HIV positive MSM are often diagnosed with sexually transmitted infections (STI), suggesting sexual risk behavior. HIV nurses discussing sexual risk behavior with MSM could improve health promotion in this group. We would like to get more insight into the psychosocial determinants that influence whether HIV nurses discuss sexual risk behavior.

Method: A questionnaire was conducted among the HIV nurses. We assessed factors from the theory of planned behavior, and factors from a previous qualitative study. Determinants that were assessed included attitudes, subjective norms, and also shame and attention for prevention. Outcomes were self-reported frequency of discussing sexual risk behavior (5-point likert scale), and intention to discuss sexual risk behavior (sum score 4 items; range 4-24,  $\alpha = .76$ ).

Results: A total of 60 out of 79 HIV nurse completed the questionnaire. Participants reported high intentions to discuss sexual risk behavior ( $M = 17$ ,  $SD = 3$ ). Intentions to discuss sexual risk behavior was higher among men, non-heterosexuals. Participants who followed the Mainline course had more positive attitudes, and had the time or saw it as a priority to discuss sexual risk behavior ( $R^2 = .54$ ). Self-reported discussion was associated with higher intentions to discuss sexual risk behavior, higher experienced knowledge, and being a nurse practitioner ( $R^2 = .60$ ).

Discussion: HIV nurses report high intentions and frequency of discussing sexual risk behavior among HIV positive MSM. However, these MSM increasingly become co-infected with STI. Efforts to improve discussing of sexual risk behavior could focus on getting more insights into what exactly is discussed. We could also explore whether the self-reported frequency of discussing sexual risk behavior corresponds with practice or are biased.

## **Razenberg LG**

### **Challenging the dogma of colorectal peritoneal metastases as an untreatable condition: results of a population based study**

Lieke G.E.M. Razenberg, MD\*, Valery E.P.P. Lemmens, PhD, Geert-Jan Creemers, MD, PhD\*, Ignace H.J.T. de Hingh, MD, PhD\*

Background/purpose: In spite of the lack of high-level evidence to support either systemic or surgical treatment of patients with peritoneal metastases (PM) of colorectal cancer (CRC), treatment of these patients is increasingly intensified. This study aims to provide insight into the impact of this trend on survival of these patients in a large unselected population.

Methods: All consecutive CRC patients presenting with PM between 1995 and 2014 were extracted from the Netherlands Cancer Registry ( $n=1661$ ). Trends in treatment and overall survival were assessed in four time periods related to the availability of different systemic and loco-regional treatment modalities.

Results: In total, 1273 PM patients received treatment (77%). Treatment with systemic therapy increased from 22.5% in 1995-1999 to 56% in 2010-2014 ( $p < 0.0005$ ). Since 2005, a strong increase in the use of loco-regional treatment modalities (CRS-HIPEC, surgery for metastases) was observed. Overall survival improved from 6.0 months in 1995-2000 to 12.5 months in 2010-2014 ( $p < 0.0001$ ), regardless of the extent of metastatic disease. In multivariable regression analysis, the beneficial influence of recent diagnosis (2010-2014) was associated with the increased implementation of systemic therapy and loco-regional treatment.

Conclusion: CRC patients presenting with PM are increasingly offered a multi-disciplinary approach incorporating both systemic and loco-regional treatment. Concomitantly, an increased overall survival for the entire cohort of PM patients was observed, compellingly challenging the dogma of PM as an untreatable condition. In spite of the lack of data from randomized trials, patients with PM should be considered for treatment whenever possible.

## Longgeneeskunde

### Dumoulin DW

#### **Large variation between hospitals in the percentage of patients with stage IIIB / IV lung cancer who receive chemotherapy and strong correlation of being treated with chemotherapy and survival**

D.W. Dumoulin\* and B.E. van den Borne\* on behalf of Santeon's 'Care for Outcome' group

Background: 'Care for Outcome' is a Value Based Health Care project of Santeon (a cooperation of seven leading, top clinical hospitals spread across the Netherlands) in which outcome measures for lung cancer are being measured and reported on a yearly base. In this observational study we report differences in outcome of the 6 participating hospitals.

Methods: In this retrospective study, data of all lung cancer patients from the Santeon hospitals who were diagnosed between 1-1-2008 and 31-12-2012 was analysed. Primary endpoint in this analysis is mortality. Logistic regression analysis was performed to identify correlating factors for outcome.

Results: Data of 5922 lung cancer patients was collected. Of these, 3584 (61%) patients had stage IIIB or IV disease. With logistic regression analysis, tumour stage, performance status, age, co morbidity and treatment with or without chemotherapy were significant factors for survival. Of these factors, treatment with or without chemotherapy was the strongest of all. The percentage of patients receiving chemotherapy was significantly different between hospitals, ranging from 36% to 59% (mean 47,6%). The median survival of patients treated with or without chemotherapy (excluding those who died within 45 days and therefore passing the 'immortal time bias' effect was 124 (95%BI 116-132) and 295 (95%BI 281-309) days ( $p < 0.001$ ), respectively (survival difference: 171 days). This significant difference persisted after correction of tumour stage, performance state, age and co morbidity.

Conclusion: There is a strong variation between hospitals in the percentage of patients with stage IIIB / IV lung cancer who receive chemotherapy. This variation is strongly correlated with survival. Performance status, age and co morbidity are also correlated with survival, however less strongly than chemotherapy.

## Medische psychologie

### Henken HT

#### **Cognitive behavioural group therapy for bipolar disorder: a case series design**

HT Henken\*, EJ Regeer, J Lobbestael, S Demacker, K Berg van den\*, RW Kupka

Background: Guidelines for bipolar disorder (NICE, 2006; Nolen et al, 2008) emphasize the use of cognitive behavioural therapy (CBT) as a psychological intervention in the treatment of bipolar disorder, but relatively little research is conducted in this area (APA, 2010; Hirschfeld, 2005; NICE, 2006; Nolen et al, 2008). To our knowledge, no Dutch CBT protocol for bipolar disorders is validated in research, or even considered evidence-based practice. Moreover, CBT is mostly administered as individual, not group treatment.

Objective: We conducted a preliminary study to generate hypotheses on the efficacy of a cognitive behavioural group intervention for bipolar disorder, which can be tested in further analytic studies, by following the level of mood (and other) symptoms over time, and by assessing whether changes in dysfunctional attitudes and sense of mastery over life outcomes occur.

Methods: Data were obtained from patients recruited from three mental health departments, diagnosed with bipolar I or II disorder, who participated in the group intervention. An A-B multiple baseline case series design was used, involving a baseline, treatment and follow-up phase.

Results/conclusions: Data collection will be completed in February 2016 and followed by data analyses.

## Operatiekamers

### Stepaniak PS

#### **Constraints on the Scheduling of Urgent and Emergency Surgical Cases: Surgeon, Equipment, and Anesthesiologist Availability**

Pieter S. Stepaniak PhD\*, Franklin Dexter MD PhD

Introduction: Computer simulation is used to evaluate use of dedicated operating rooms (ORs) for urgent and emergency (add-on) surgical cases versus the same amount of OR time interspersed throughout the day in many ORs and/or at the end of the day. Simulations are limited because of absence of prior quantitative data on the relative incidence of surgeon, equipment, and anesthesiologist availability as a constraint influencing when cases start.

Methods: We prospectively obtained a series of 6 weeks (N = 30 days) of add-on cases announced (submitted) in the period 7:30 AM through 4:59 PM Monday through Friday at an 18 OR Level 2 trauma teaching hospital in The Netherlands. When an urgent or emergency case (add-on) was announced, the OR scheduler evaluated which of the ORs were both clinically suitable for the procedure and either currently open or would be open within 30 minutes.

Results: The ratio of mean cases per day with surgeon versus OR availability as a constraint was 96.1% (99% confidence interval 64.6% to 127.8%). The ratio can be considered (in simulation) as equaling 1.0 (P = 0.83, mean  $1.02 \pm 0.10$  [SE], median 1.00, N = 30 days). The ratios of mean cases each day with equipment as constraint (e.g., C arm) versus OR availability as a constraint was negligible (mean  $0.03 \pm 0.02$ , median 0.00, P < 0.0001 relative to 1.0). Lack of an anesthesiologist limiting when the add-on case starts could be neglected entirely (P < 0.0001, ratios mean  $0.00 \pm 0.00$ , median 0.00).

Conclusions: Surgeon and OR availability can be equally (1:1) limiting when cases start. Before individual hospitals apply current papers that are based on ORs being constraints, some hospitals may need also to consider surgeon availability as limiting.

## Orthopedie

### Kamp MC

#### **Incidence of Congenital Idiopathic Clubfoot in The Netherlands**

Arnold T. Besselaar\*, Maud C. Kamp\*, Max Reijman, M.C. (Marieke) van der Steen\*

**Background/aim:** The idiopathic clubfoot (talipes equinovarus adductus) is a common orthopaedic problem, with an estimated incidence of approximately 1 per 1000 live births. There are no nationwide studies in the Netherlands to confirm these estimates. Because lack of a central registration program, we performed a cross-sectional nationwide multicenter study in order to assess the incidence of the congenital idiopathic clubfoot in the Netherlands over 2 consecutive years.

**Patients and methods:** The twenty-one accredited clubfoot treatment center in the Netherlands were approached for data collection, in collaboration with the Workgroup Children Orthopaedics. All the idiopathic clubfoot cases born during 2013-2014 were analyzed with special reference to gender, affected foot (unilateral/bilateral), regional distribution and seasonal variation.

**Results:** Among the 346.522 live births recorded between January 2013 and December 2014, 233 idiopathic clubfoot cases were registered (data of 15 clubfoot treatment centers). The interim incidence of the congenital idiopathic clubfoot during 2013 and 2014 was 0.67 per 1.000 live births. The clubfoot demonstrates a male-to-female ratio of 2:1 and in approximately half of the cases it includes a bilateral deformity. Based on the current available data there is no significant seasonal variation and regional distribution in occurrence of the clubfoot.

**Interpretation:** We estimated the incidence of the clubfoot using data from accredited clubfoot treatment center in the Netherlands. Sex distribution and laterality of the clubfoot is in accordance with previous reports. Due to incompleteness of the data, the exact incidence of the clubfoot remains unknown. This study underscores the importance of a central birth defect registration program in the Netherlands.

**Vernieuwende elementen studie:**

De huidige data is gebaseerd op de beschikbare data in 15 van de 21 erkende klompvoet behandelcentra (betreffende resterende ziekenhuizen loopt de data-overdracht). Om accurate gegevens te verkrijgen wordt deze data aangevuld en geverifieerd met de beschikbare gegevens van de Nederlandse Vereniging Klompvoeten, EUROCAT-NNL, Prenatale Screeningcentra Nederland en het CBS.

### Martens N

#### **Predicting complications with comorbidity indices in total knee and hip arthroplasty**

Nick Martens\*, dr. M.C. van der Steen\*, dr. M. Reijman, researcher, dr. J.G.E. Hendriks, drs. R.W.T.M. van Kempen,

**Background.** Total hip or knee arthroplasty (THA or TKA) are common, successful and safe orthopaedic interventions for the treatment of osteoarthritis. With the ageing population also an increase of comorbidities is seen. Having comorbidities is related to more post-operative complications and decreased functional outcome. The aim of this study was to examine if there is a relation between the score on comorbidity indices and the development of post-operative complications in our patient population.

**Methods.** All patients of "Coöperatie Orthopedie Groot Eindhoven" who underwent a TKA or THA in 2014 were included in this retrospective cohort study. Medical records were reviewed for complications, ASA and in order to fill out the Functional Comorbidity Index (FCI) and Charlson Comorbidity Index (CCI).

Results. A total of 1233 patients were included whereof 494 TKA and 739 THA. The average BMI was significantly higher in the TKA group ( $<0.001$ ). Further demographics were comparable between groups. The order of the scores on the indices were similar but the TKA group scored slightly higher for the FCI, while THA group scored slightly higher on the CCI and ASA. Only for the THA group a significant relation between the scores on the indices and complications was found.

Conclusion. Overall this project provided valuable information on comorbidities and complications in our patient population that can be used both clinically and for further research purposes. Only for the THA is proven that a higher score on the ASA, FCI or CCI is related to having a greater chance of developing a post-operative complication.

## **Plastische Chirurgie**

### **Zeeuw FT van der**

#### **Invloed van een oral-facial-digital-1 osteoblast specifieke mutatie op middengezicht morfologie**

Frederique T. van der Zeeuw\*, Hadeel al Lami, William B. Barrell, Karen J. Liu,

Achtergrond: De meest voorkomende congenitale aangezihtsafwijking is de orofaciale schisis die voorkomt in 1:1250 levendgeborenen waarvan ongeveer 30--50% syndroomaantal is. Eén van deze syndromen is het oral---facial---digital syndroom type1. Het syndroom wordt o.a. gekenmerkt door cranio---faciale afwijkingen (o.a. microretrognathie, hypertelorisme en cheilo---gnatho--- en/of palatoschisis) en handmalformaties (o.a. brachydactyly, clinodactyly en polydactyly). Het is een syndroom met een hoge mate van fenotypische variabiliteit, welke nog grotendeels onbegrepen is. Door deze grote fenotypische variabiliteit is er onzekerheid over de precieze invloed van het OFD1 gen op middengezicht morfologie. Osteoblast specifieke deleties van het gen in muizen kunnen ons hier inzicht in geven.

Methoden: Muizen met een osteoblast specifieke deletie van *Ofd1* zijn gegenereerd gebruikmakend van twee genetisch gemanipuleerde ciliopathie muislijnen (? *Osx::cre/+* en ? *Ofd fl/fl*) waarna deze zijn vergeleken met een wildtype controlegroep. Controle van de genotypes werd uitgevoerd met PCR. Embryo's werden uitgenomen op 15.5DPC (days post coitus) en 18.5DPC. Op de embryo's werden (1) whole---mount skelet studies uitgevoerd, (2) coronale en sagittale doorsneden van ledematen en schedels gemaakt en gekleurd en (3) micromass assay's van het aangezicht en de ledematen gedaan. De postnatale fase (op postnatale dagen P0, P7 en P22) werd beoordeeld door zowel skelet studies als microCT reconstructies.

Resultaten: Deze experimenten geven ons meer duidelijkheid over de bot fenotypes in *Ofd1* muizen en het moleculaire mechanisme achter de aandoening. Microretrognathie van de mandibula is naar onze verwachting te wijten aan hyperossificatie in de intramembraneuze ossificatie---locaties in de mandibula. Daarnaast blijkt er sprake te zijn van verkorte ledematen en polydactyly.

Conclusie: Onze resultaten geven inzicht in de invloed van mutaties van het *Ofd1* gen op middengezicht morfologie in muizen. Muizen geven ons die mogelijkheid omdat een geïsoleerde mutatie gegenereerd kan worden. In mensen zal door de invloed van mogelijke andere mutaties op het fenotype, niet zeker zijn of de oorzaak hiervan de OFD1 mutatie is. Dit onderzoek, waarin een osteoblast specifieke deletie binnen het *Ofd1* gen wordt gegenereerd, geeft ons een duidelijker inzicht in de hoge ossale fenotypische variabiliteit van dit syndroom en de redenen hierachter.

## Radiologie

### Nerad E

#### **Diagnostic accuracy of computed tomography for local staging of colon cancer: a systematic review and meta-analysis.**

E. Nerad\*, M.J. Lahaye, M. Maas, H.C.M van den Bosch\*, G.L. Beets, P. Nelemans, R.G.H. Beets-Tan

Purpose: To determine the diagnostic value of pre-operative computed tomography (CT) in detecting colon carcinomas with invasion beyond the bowel wall and the presence of malignant lymph nodes.

Methods and Materials: The meta-analysis was conducted according to PRISMA guidelines. A literature search of Ovid, Embase and Pubmed was performed to identify studies reporting on the accuracy of CT for local staging of colon carcinomas. Data extraction was performed by two observers in consensus. The sensitivity, specificity, and diagnostic odds ratio (DOR) were calculated using a bivariate random effects model and summary receiver operating curves (sROC) were generated.

Results: Twenty studies fulfilled all the required inclusion criteria. The pooled sensitivity, specificity, DOR for detection of tumour invasion beyond the bowel wall were 90% (95%CI 83-95%); 69% (95%CI 62-75%); 20,6 (CI 20-41%) respectively. For detection of invasion depth of 5mm beyond the bowel wall these values were 77% (CI: 66-85%); 70% (CI: 53-83%); 7.8 (CI: 4.2-14.2) and nodal involvement; 71% (CI: 58-81%); 66% (CI: 46-83%); 4.8 (CI: 2.5-9.4%).

Conclusion: CT is reliable in detecting colon carcinomas with tumour invasion through the bowel wall (T1/T2 versus T3/T4). However detecting tumour invasion of > 5mm from the bowel wall (T1/T3ab and T3cd/T4) tumours and especially nodal involvement remain a challenge for CT.

Vernieuwende elementen: There might be a paradigm shift in the treatment of colon cancer in the near future due to the FOXTROT study which evaluates neoadjuvant treatment in patients selected by CT.

Knowledge of the accuracy in pre-operative staging of colon cancer by CT, which is the purpose of this study, seems imperative.

## Urologie

### **Bilt - Sonderegger EH van de**

#### **Glijmiddel tijdens urologische instrumentatie: met of zonder lidocaïne?**

E.H.M. van de Bilt-Sonderegger\*, Dr. E.L. Koldewijn \*

Introductie: Op de urologische functieafdeling worden dagelijks urethrocystoscopen of katheters via de urethra ingebracht. Het gebruik van glijmiddel voorkomt beschadiging van het slijmvlies van de urethra en maakt het onderzoek zo comfortabel mogelijk voor zowel patiënt als zorgverlener. Meestal wordt gebruik gemaakt van een glijmiddel met lidocaïne. Dit onderzoek is gestart om aan te tonen of er een verschil is in pijnbeleving bij de patiënten, waarbij wel of geen lidocaïne toegevoegd is aan het glijmiddel.

Materiaal en Methoden : Het observationeel onderzoek is uitgevoerd onder 86 patiënten die behandeld werden op het urologisch behandelcentrum op een van de twee onderzoekkamers. In onderzoekkamer 1 kreeg men glijmiddel met lidocaïne en in onderzoekkamer 2 zonder lidocaïne. Deze patiënten ondergingen een cystoscopie of kregen een blaaskatheter ingebracht. Alle patiënten kregen dezelfde vragenlijst met 3 vragen. Hierin werd hen de vraag gesteld of zij eerder glijmiddel toegediend hadden gekregen, hoe zij de pijn ervaarden tijdens het inbrengen van een cystoscoop/katheter en de pijnbeleving na de

instrumentatie. Men kon deze pijn aangeven door een VASscore te geven aan de pijn op een schaal tussen 0-10. De continue variabelen zijn getoetst dmv Mann-Whitneytest. De categorische variabelen zijn geanalyseerd door de Chikwadrattest

Resultaten: Patiënten uit de groep zonder lidocaïne (n=43) ervaren significant minder pijn, dan de groep met lidocaine (n=43) (p: 0.009) De mediane waarde in de VAS score in de lidocaine groep is 3 (min 0-max 9) en in groep zonder lidocaïne 1 (min 0- max 8) = (p0,024)

Conclusie: Patiënten die worden voorbehandeld met een glijmiddel zonder lidocaïne geven minder pijn aan tijdens urethrocystoscopie of het inbrengen van een katheter. Dit verschil is statistisch significant, zodat kan worden geconcludeerd dat instilleren zonder lidocaine een beter effect heeft op de pijnbeleving van de patiënt. In de literatuur is nauwelijks evidence te vinden met betrekking tot pijnbeleving en gebruik van glijmiddel met of zonder lidocaine, zodat een vervolgonderzoek gewenst is om dit verschil te kunnen verklaren.

## **Genugten HG**

### **The Simbla TURBT Simulator in Urological Residency Training: From Needs Analysis to Validation**

Anna H. de Vries\*, Hilde G.J. van Genugten\*, Ad J.M. Hendrik\*<sup>1</sup>, Evert L. Koldewijn\*, Barbara M.A. Schout, Irene M. Tjiam, Jeroen J.G. van Merriënboer, Cordula Wagner

Objective: To investigate the value of the physical 'Simbla' TURBT simulator as an educational tool within urological residency training, by means of a Training Needs Analysis (TNA) and assessment of its feasibility, acceptability, and face, content and construct validity.

Methods: To analyse the training needs for TURBT, procedural steps and pitfalls were identified, and the TNA was completed during an expert consensus meeting. Participants (n=76) were divided into three groups based on their experience in TURBT: novices, intermediates, and experts. Participants performed two standardized TURBT procedures on the simulator. Face and content validity as well as feasibility and acceptability were assessed with a quantitative survey. Construct validity was assessed by comparing the performance of novices, intermediates and experts on resection time, quality of tumour resection and overall performance.

Results: Of the 21 procedural steps and 17 pitfalls defined in TNA, 13 steps and 8 pitfalls were covered by the Simbla. Participants rated the Simbla's overall realism (face validity) with a score of 8 out of 10 (range 6-9). The simulator was judged to be most useful (content validity) for learning eye-hand coordination: score 8(6-10). All aspects regarding realism and usefulness were rated above the acceptability threshold of 6/10. Intermediates (100%) and experts (96%) considered the Simbla to be a useful educational tool within the urological curriculum. Resection time was longer for novices than for experts (p<0.05) (construct validity). In addition, the overall performance of novices was rated lower compared to intermediates and experts, and novices showed more irradical resections and bladder perforations (all p<0.05).

Conclusions: The Simbla TURBT simulator is a valid, feasible and acceptable educational tool for training procedural skills and may be implemented in the urological curriculum to complement learning in clinical practice. TNA is valuable in defining training objectives and evaluating the educational value of a simulator.



## **Technische Universiteit Eindhoven**

### **Koopmans PJ**

#### **Validation of the new ADM stiffness measure, to gain precise and reliable ankle torque measures to detect clubfoot stiffness**

P.J.J.Koopmans, Dr. M.C. v.d. Steen, Dr. M. Reijman, Dr. ir. B. v. Rietbergen, Drs. A.T. Besselaar\*

One out of 1000 children is born with clubfoot, a deformation of the foot characterized by equinus, cavus, varus and adductus. Nowadays clubfoot is treated with the Ponseti method, including a casting and bracing phase where the foot is corrected for all deformations, leading to a totally functional foot after four years. However, up to fifteen percent of the clubfoot children will have a relapse during or after treatment. Stiffer clubfeet have a higher tendency to relapse, however it is not yet possible to quantify this stiffness.

The current research project focuses on a new method to measure stiffness with the use of the abduction dorsiflexion mechanism (ADM) brace. This brace is used in clinical practice and was modified to measure ankle torque. For validation of the ADM stiffness measure repeatability, reliability and torque-angle relationships were analyzed. To investigate torque in clubfeet both clubfoot (n: 49, age:  $4,3 \pm 2,1$ ) and healthy (n:18, age:  $4,6 \pm 1,9$ ) children were included, from which the torque of both feet was measured over  $15^\circ$  rotation toward dorsiflexion and abduction.

Results show that the ADM stiffness measure is reliable but not precise enough and does not match the expected torque-angle relationships. Between the healthy and clubfeet no significant torque differences were found, indicating that the ADM stiffness measure may be too simplistic to measure ankle stiffness. A foot model may give insight in what parts of the foot influence stiffness to conclude whether or not we can measure clubfeet stiffness.

Innovative elements

Researchers and orthopedic surgeons claim that stiffness is one of the factors ranking the severity and the tendency for a relapse of a clubfoot. In this study we made a first step in quantification of the stiffness parameter in clubfoot patients in a clinical environment.

### **Scheepers MR**

#### **Rotating magnetic particle pairs for studying magnetic particle aggregation in blood plasma**

M.R.W. Scheepers, L.J. van IJendoorn, M.W.J. Prins

Background: Magnetic particles are often used in biophysical research and in many applications. An example of a biosensor using magnetic particles is the MiniCare system of Philips that uses the Magnotech Technology. One of the challenges of this biosensor is to avoid non-specific aggregation of the magnetic particles in blood plasma, because this irreversible particle clustering can produce a variability in the outcome of the measurements.

Aim: The aim of this project is to develop a method to study the interaction between magnetic particles in blood plasma. A study will be performed on the interaction between magnetic particles in different experimental conditions: Different solution conditions, different solution additives and different particle functionalizations.

Method: To obtain information about different pathways of aggregation, experiments will be performed with single particle resolution. For this purpose single pairs of particles will be observed over time. First, a primary particle is bound to a surface by a rotationally restricted bond. Then with a constant magnetic field, a secondary particle is trapped on the primary particle by attractive dipole-dipole interaction. By rotating the magnetic field, the secondary

particle will start rotating. Aggregation can be detected as particle pairs stop rotating when a bond is formed between them.

Results: The first results have to be obtained with a model system, to test the experimental method. Both particles are functionalized against different epitopes of troponin. In this way a bond between the primary and secondary particle can be induced specifically by introducing troponin in the system.

Conclusion -

Innovativeness: Research on the use of magnetic particles in biosensor applications is often only performed in buffer solutions. In this research experiments will be performed to quantify the interaction between magnetic particles not only in buffer solutions, but also in blood plasma.

**Tabellen**

**Tabel 1: Overzicht aantal publicaties**

<b>Specialisme</b>	<b>Tijdschrift artikelen</b>	<b>Promoties</b>	<b>Boeken</b>	<b>Hoofdstuk</b>	<b>Totaal</b>
Algemeen Klinisch Laboratorium	7				7
Anesthesiologie	9				9
Apotheek	5				5
Cardiologie	38	1			39
Cardiothoracale chirurgie	10				10
Chirurgie	105	6		4	115
Dermatologie	11				11
Gynaecologie	16	1			17
ICMT	1				1
Intensive Care	1				1
Inwendige geneeskunde	17				17
Kindergeneeskunde	9				9
Klinische Fysica	7			1	8
Kwaliteit	3	1			4
Longgeneeskunde	11			1	12
Maag, darm en leverziekten	10				10
Medische psychologie	3				3
Mondziekten en kaakchirurgie	1				1
Neurologie	4				4
Nucleaire geneeskunde	3				3
Onderwijs en Onderzoek	3				3
Orthopedie	5				5
Pamm	7	1			8
Plastische chirurgie	3				3
Radiologie	11	1			12
Radiotherapie	7				7
Spoedeisende hulp	2	1			3
Urologie	2				2
<b>Totaal</b>	<b>311</b>	<b>12</b>		<b>6</b>	<b>329</b>

**Tabel 2 Wetenschapsavond**

<b>Specialisme</b>	<b>Wetenschaps avond 2016 Presentaties</b>	<b>Wetenschaps avond 2016 Posters</b>	<b>Totaal</b>
Algemeen Klinisch Laboratorium		3	3
Apotheek	1	1	2
Cardiologie		1	1
Chirurgie	1	11	12
Gynaecologie		1	1
Inwendige geneeskunde		3	3
Longgeneeskunde	1	1	2
Medische psychologie		1	1
Operatiekamers		1	1
Orthopedie		2	2
Plastische Chirurgie		1	1
Radiologie		1	1
Spoedeisende hulp	1		1
Urologie		2	2
Philips Research Eindhoven	1		1
Technische Universiteit Eindhoven		2	2
<b>Totaal</b>	<b>5</b>	<b>31</b>	<b>36</b>

**Tabel 3: Overzicht aantal artikelen en gemiddelde impactfactor per specialisme**

<b>Specialisme</b>	<b>Artikelen met impactfactor</b>	<b>Artikelen zonder impactfactor</b>	<b>Totaal aantal artikelen</b>	<b>Gemiddelde impactfactor</b>	<b>Standaard deviatie</b>
Algemeen Klinisch Laboratorium	6	1	7	4.526	4.714
Anesthesiologie	8	1	9	3.258	1.916
Apotheek	4	1	5	6.523	10.223
Cardiologie	38	0	38	5.665	7.742
Cardiothoracale chirurgie	8	2	10	2.656	2.107
Chirurgie	91	14	105	5.279	8.555
Dermatologie	11	0	11	3.223	0.811
Gynaecologie	14	2	16	4.426	5.519
ICMT	1	0	1	2.004	0
Intensive Care	1	0	1	6.312	0
Inwendige geneeskunde	16	1	17	5.947	10.315
Kindergeneeskunde	8	1	9	4.954	3.948
Klinische Fysica	6	1	7	3.092	1.798
Kwaliteit	3	0	3	2.824	1.046
Longgeneeskunde	10	1	11	5.737	6.668
Maag, darm en leverziekten	9	1	10	7.263	6.708
Medische Psychologie	3	0	3	2.702	1.039
Mond en Kaakchirurgie	1	0	1	1.261	0
Neurologie	4	0	4	6.057	1.508
Nucleaire geneeskunde	1	2	3	1.093	1.893
Onderwijs en Onderzoek	1	2	3	0.774	1.341
Orthopedie	4	1	5	2.203	1.636
Pamm	6	1	7	3.690	2.232
Plastische chirurgie	2	1	3	1.001	0.871
Radiologie	11	0	11	8.772	15.667
Radiotherapie	5	2	7	13.533	20.517
SEH	1	1	2	1.617	2.287
Urologie	1	1	2	0,690	0.975
<b>Totaal</b>	<b>274</b>	<b>37</b>	<b>311</b>	<b>5.102</b>	<b>8.002</b>

**Tabel 4: Impactfactor per tijdschrift**

<b>Titel</b>	<b>Impact factor</b>	<b>Titel</b>	<b>Impact factor</b>
Acta Anaesthesiol Scand	2.322	Br J Surg	5.542
Acta Derm Venereol	3.025	Brain Res	3.028
Acta Diabetol	2.399	Breast	2.381
Acta Oncol	2.997	Breast Cancer Res Treat	3.940
Alcohol Alcoholism	2.889	Breast J	1.411
Am Heart J	4.463		
Am J Cardiol	3.276	Camb Q Healthc Ethics	0.682
Am J Obstet Gynecol	4.704	Cancer Epidemiol	2.711
Am J Respir Crit Care Med	12.996	Catheter Cardiovasc Interv	2.107
Anaesth Intensive Care	1.296	CELL TISSUE RES	3114
Anaesthesia	3.382	Cerebrovasc Dis	3.754
Ann N Y Acad Sci	4.383	Chron Respir Dis	2.694
		Circ Arrhythm	
Ann Oncol	7.040	Electrophysiol	4.513
Ann Surg Oncol	3.930	CLIN CARDIOL	2151
Ann Thorac Surg	3.849	Clin Chem Lab Med	2.707
Ann Vasc Surg	1.170	Clin Chim Acta	2.824
Anticancer Res	1.826	Clin Colorectal Canc	2.813
Appetite	2.691	Clin Endocrinol	3.457
Artif Organs	2.050	Clin Exp Dermatol	1.092
		Clin Infect Dis	8.886
Best Pract Res Clin Gastroenterol	3.478	Clin Lung Cancer	3.104
Bioanalysis	3.003	Clin Nutr	4.476
		Cochrane Database Syst	
Biomed Res Int	1.579	Rev	6.032
BJOG	3.448	Colorectal Dis	2.351
BMC Cancer	3.362	Crit Care Med	6.312
BMC Pregnancy Childbirth	2.190		
BMC Surg	1.397	Dermatology	1.569
BMC Womens Health	1.495	Dis colon rectum	2.615
BMJ	17.445	Dis Esophagus	1.782
Br J Cancer	4.836		
Br J Dermatol	4.275	Emerg Infect Dis	6.750

Br J Radiol	2.026	Endoscopy	5.053
Eur Heart j	15.203	Int J Cancer	5.085
Eur J Cancer	5.417	Int J Cardiol	4.036
Eur J Cardiothorac Surg	3.304	Int J Gynecol Cancer	1.958
Eur J Emerg Med	1.583	Int J Lab Hematol	1.819
Eur J Endocrinol	4.069	Int J Med Inform	2.004
Eur J Gastroenterol Hepatol	2.253	Int J Pharm	3.650
Eur J Heart Fail	6.526	INT ORTHOP	2.025
Eur J Neurosci	3.181	Int Urogynecol J	1.961
		Interact Cardiovasc Thorac Surg	1.155
Eur J Nucl Med Mol Imaging	5.383	Invest Radiol	4.437
Eur J Obstet Gyn R B	1.695		
Eur J Pediatr	1.907	J Am Acad Dermatol	4.449
Eur J Prev Cardiol	3.319	J Am Coll Cardiol	16.503
Eur J Radiol	2.369	J Am Coll Surg	5.122
Eur J Surg Oncol	3.009	J Anat	2.097
Eur J Vasc Endovasc Surg	3.490	J Anesth	1.176
Eur Radiol	4.014	J Antimicrob Chemother	5.313
Eur Respir J	7.636	J Card Fail	3.051
Eurointervention	3.769	J Cardiovasc Magn Reson	4.556
Exp Dermatol	3.762	J Clin Endocrinol Metab	6.209
		J Clin Oncol	18.428
Front Microbiol	3.989	J Electrocardiol	1.361
		J Endourol	1.708
Gastroenterology	16.716	J Endovasc Ther	2.826
Gastrointest Endosc	5.210	J Eur Acad Dermatol	
		Venereol	2.826
Gut	14.660	J Geriatr Oncol	1.859
Haematologica	5.814	J Health Commun	1.617
Heart	5.595	J Hosp Infect	2.544
Heart Rhythm	5.076	J Infect Dis	5.997
Hernia	2.050	J Mech Behav Biomed	
		Mater	3.417
HPB	2.675	J Med Internet Res	3.428
Hum Reprod	4.569	J Minim Invasive gynecol	1.830
		J Pediatr Gastroenterol	
IEEE J Biomed Health Inform	1.440	Nutr	2.625



J Plast Reconstr Aesthet Surg	1.421	PLoS One	3.234
J Stroke Cerebrovasc Dis	1.669		
J Surg Educ	1.379	Qual Life Res	2.486
J Surg Oncol	2.644		
J Thromb Haemost	5.720	Radiat Oncol	2.546
J Vasc Access	0.846	Radiology	6.867
J Vasc Surg	3.021	Radiother Oncol	4.363
JACC Cardiovasc Imaging	7.188	Respir Med	3.086
JACC Cardiovasc Interv	7.345	Respir Res	3.093
JAMA	35.289	Rheumatology (Oxford)	4.475
lancet	45.217	Scand J Urol	1.247
Lancet Oncol	24.690	Stroke	5.723
Lung Cancer	3.958	Surg Endosc	3.256
Lymphat Res Biol	1.709	Surg Obes Relat Dis	4.066
		Surgery	3.380
Med Phys	2.635		
Mol Genet Metab	2.625	Ther Drug Monit	2.376
Muscle Nerve	2.283	Thorax	8.290
		Trials	1.731
N Engl J Med	55.873		
Nat Rev Gastroenterol Hepatol	12.610	Urol Oncol	2.768
Neth Heart J	1.837		
Neth J Med	1.969	Value Health	3.279
Neurology	8.250		
		World J Gastroenterol	2.369
Obes Facts	2.245	World J Gastrointest Surg	2.798
Obes Surg	3.747	World J Surg	2.642
Oral Surg Oral Med Oral Pathol			
Oral Radiol	1.261		
Pacing Clin Electrophysiol	1.129		
Pediatr Infect Dis J	2.723		
Perfusion	0.935		
Phys Med Biol	2.761		
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Het Catharina Ziekenhuis maakt deel uit van Santeon



Het Catharina Ziekenhuis is lid van de vereniging  
van Samenwerkende Topklinische Ziekenhuizen

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