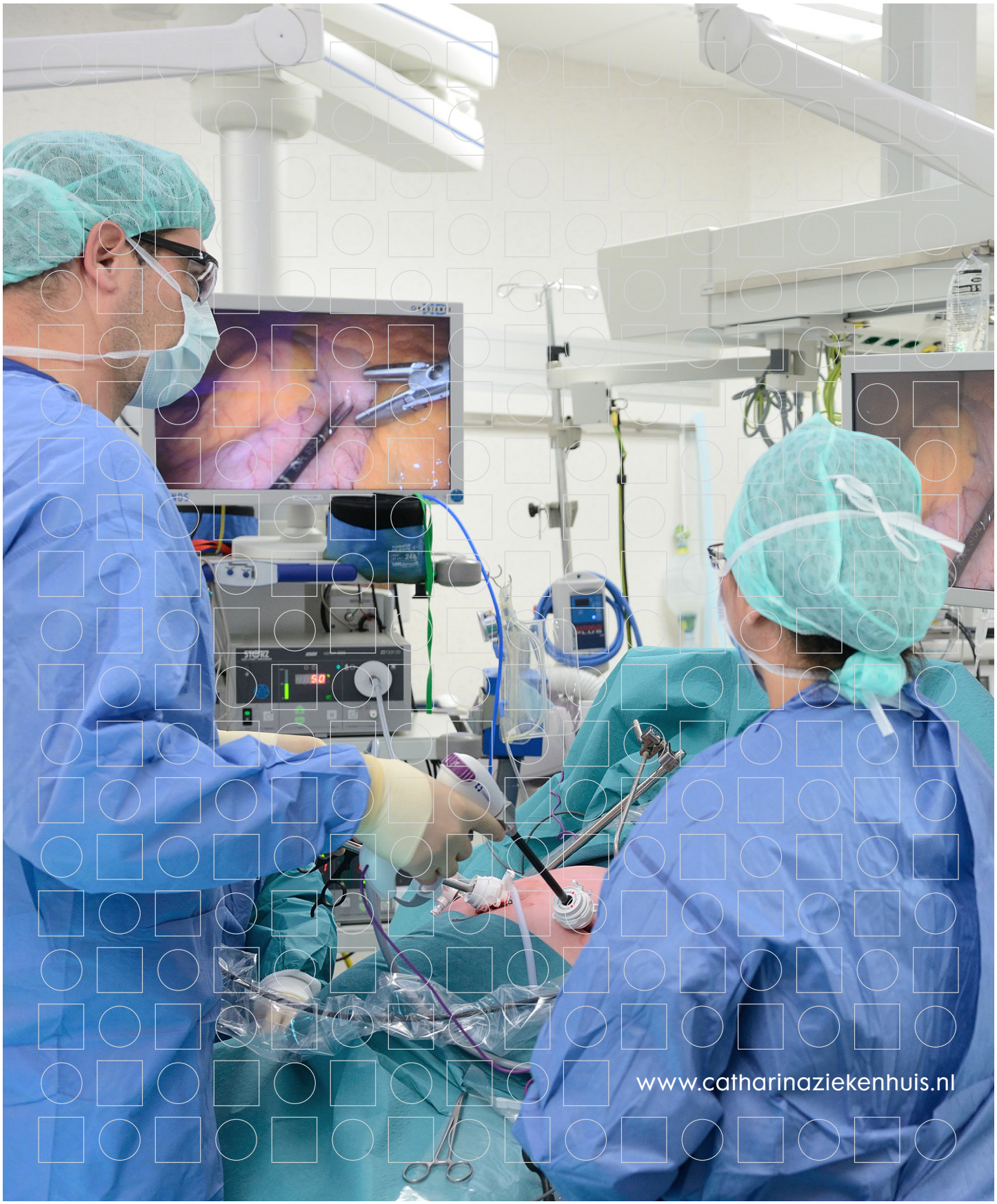
Wetenschappelijk jaaroverzicht

catharina
een santeon ziekenhuis

2017



Wetenschappelijk Jaaroverzicht 2017

Onder redactie van:
JMAH Jansen (Jolanda)
E Looije (Ellen)

Een uitgave van het Catharina Ziekenhuis
Eindhoven, 2018

Inhoudsopgave

“Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided”

Paracelsus (1493-1541)

Arts en Theoloog

Algemeen Klinisch Laboratorium

Absence of the spleen and the occurrence of primary red cell alloimmunization in humans

Evers D, van der Bom JG, Tijmensen J, de Haas M, Middelburg RA, de Vooght KMK, **van de Kerkhof D**, Visser O, Péquériaux NCV, Hudig F, Zwaginga JJ

Haematologica. 2017 Aug 102(8):e289-e292 Epub 2017 Apr 14

Geen abstract beschikbaar

Impactfactor: 7.702

Analytical evaluation of a new point of care system for measuring cardiac Troponin I

Kemper DW, Semjonow V, de Theije F, Keizer D, van Lippen L, Mair J, Wille B, Christ M, Geier F, Hausfater P, Pariente D, **Scharnhorst V, Curvers J**, Nieuwenhuis J

Clin Biochem. 2017 Mar;50(4-5):174-180. Epub 2016 Nov 12

OBJECTIVES: Point-of-care cardiac troponin testing with adequate analytical performances has the potential to improve chest pain patients flow in the emergency department. We present the analytical evaluation of the newly developed Philips Minicare cTnI point-of-care immunoassay.

DESIGN & METHODS: Li-heparin whole blood and plasma were used to perform analytical studies. The sample type comparison study was performed at 4 different hospitals. The 99th percentile upper reference limit (URL) study was performed using Li-heparin plasma, Li-heparin whole blood and capillary blood samples from 750 healthy adults, aging from 18 to 86years.

RESULTS: Limit of the blank, limit of detection and limit of quantitation at 20% coefficient of variation (CV) were determined to be 8.5ng/L, 18ng/L and 38ng/L respectively without significant differences between whole blood and plasma for LoQ. Cross-reactivity and interferences were minimal and no high-dose hook was observed. Total CV was found to be from 7.3% to 12% for cTnI concentrations between 109.6 and 6135.4ng/L. CV at the 99th percentile URL was 18.6%. The sample type comparison study between capillary blood, Li-heparin whole blood and Li-heparin plasma samples demonstrated correlation coefficients between 0.99 and 1.00 with slopes between 1.03 and 1.08. The method comparison between Minicare cTnI and Beckman Coulter Access, AccuTnI+3 demonstrated a correlation coefficient of 0.973 with a slope of 1.09. The 99th percentile URL of a healthy population was calculated to be 43ng/L with no significant difference between genders or sample types.

CONCLUSIONS: The Minicare cTnI assay is a sensitive and precise, clinical usable test for determination of cTnI concentration that can be used in a near-patient setting as an aid in the diagnosis of acute myocardial infarction.

Impactfactor: 2.434

Association of Blood Transfusion From Female Donors With and Without a History of Pregnancy With Mortality Among Male and Female Transfusion Recipients

Caram-Deelder C*, Kreuger AL, Evers D, de Vooght KM, **van de Kerkhof D**, Visser O, Péquériaux NC, Hudig F, Zwaginga JJ, van der Bom JG, Middelburg RA

JAMA. 2017 Oct 17;318(15):1471-1478

Importance: Transfusion of red blood cells from female donors has been associated with increased mortality in male recipients.

Objective: To quantify the association between red blood cell transfusion from female donors with and without a history of pregnancy and mortality of red blood cell recipients.

Design, Setting, and Participants: Retrospective cohort study of first-time transfusion recipients at 6 major Dutch hospitals enrolled from May 30, 2005, to September 1, 2015; the final follow-up date was September 1, 2015. The primary analysis was the no-donor-mixture cohort (ie, either all red blood cell transfusions exclusively from male donors, or all exclusively from female donors without a history of pregnancy, or all exclusively from female donors with a history of pregnancy). The association between mortality and exposure to transfusions from ever-pregnant or never-pregnant female donors was analyzed using life tables and time-varying Cox proportional hazards models.

Exposures: Red blood cell transfusions from ever-pregnant or never-pregnant female donors, compared with red blood cell transfusions from male donors.

Main Outcomes and Measures: All-cause mortality during follow-up.

Results: The cohort for the primary analyses consisted of 31?118 patients (median age, 65 [interquartile range, 42-77] years; 52% female) who received 59?320 red blood cell transfusions exclusively from 1 of 3 types of donors (88% male; 6% ever-pregnant female; and 6% never-pregnant female). The number of deaths in this cohort was 3969 (13% mortality). For male recipients of red blood cell transfusions, all-cause mortality rates after a red blood cell transfusion from an ever-pregnant female donor vs male

donor were 101 vs 80 deaths per 1000 person-years (time-dependent "per transfusion" hazard ratio [HR] for death, 1.13 [95% CI, 1.01-1.26]). For receipt of transfusion from a never-pregnant female donor vs male donor, mortality rates were 78 vs 80 deaths per 1000 person-years (HR, 0.93 [95% CI, 0.81-1.06]). Among female recipients of red blood cell transfusions, mortality rates for an ever-pregnant female donor vs male donor were 74 vs 62 per 1000 person-years (HR, 0.99 [95% CI, 0.87 to 1.13]); for a never-pregnant female donor vs male donor, mortality rates were 74 vs 62 per 1000 person-years (HR, 1.01 [95% CI, 0.88-1.15]).

Conclusions and Relevance: Among patients who received red blood cell transfusions, receipt of a transfusion from an ever-pregnant female donor, compared with a male donor, was associated with increased all-cause mortality among male recipients but not among female recipients. Transfusions from never-pregnant female donors were not associated with increased mortality among male or female recipients. Further research is needed to replicate these findings, determine their clinical significance, and identify the underlying mechanism.

Impactfactor: 44.405

CAD mutations and uridine-responsive epileptic encephalopathy

Koch J, Mayr JA, Alhaddad B, Rauscher C, Bierau J, Kovacs-Nagy R, **Coene KL**, Bader I, Holzhacker M, Prokisch H, Venselaar H, Wevers RA, Distelmaier F, Polster T, Leiz S, Betzler C, Strom TM, Sperl W, Meitinger T, Wortmann SB, Haack TB

Brain. 2017 Feb 140(2):279-286. Epub 2016 Dec 21

Unexplained global developmental delay and epilepsy in childhood pose a major socioeconomic burden. Progress in defining the molecular bases does not often translate into effective treatment. Notable exceptions include certain inborn errors of metabolism amenable to dietary intervention. CAD encodes a multifunctional enzyme involved in de novo pyrimidine biosynthesis. Alternatively, pyrimidines can be recycled from uridine. Exome sequencing in three families identified biallelic CAD mutations in four children with global developmental delay, epileptic encephalopathy, and anaemia with anisopoikilocytosis. Two died aged 4 and 5 years after a neurodegenerative disease course. Supplementation of the two surviving children with oral uridine led to immediate cessation of seizures in both. A 4-year-old female, previously in a minimally conscious state, began to communicate and walk with assistance after 9 weeks of treatment. A 3-year-old female likewise showed developmental progress. Blood smears normalized and anaemia resolved. We establish CAD as a gene confidently implicated in this neurometabolic disorder, characterized by co-occurrence of global developmental delay, dyserythropoietic anaemia and seizures. While the natural disease course can be lethal in early childhood, our findings support the efficacy of uridine supplementation, rendering CAD deficiency a treatable neurometabolic disorder and therefore a potential condition for future (genetic) newborn screening.

Impactfactor: 10.292

Equal clinical performance of a novel point-of-care cardiac troponin I (cTnI) assay with a commonly used high-sensitivity cTnI assay

Venge P, van Lippen L, Blaschke S, Christ M, Geier F, Giannitsis E, Hagström E, Hausfater P, Khellaf M, Mair J, Pariente D, **Scharnhorst V**, Semjonow V

Clin Chim Acta. 2017 Mar 25;469:119-125

BACKGROUND: Efficient rule-out of acute myocardial infarction (MI) facilitates early disposition of chest pain patients in emergency departments (ED). Point-of-care (POC) cardiac troponin (cTn) may improve patient throughput. We compared the diagnostic accuracy of a novel cTnI test (Minicare cTnI, Philips), with current POC cTnI (I-Stat, Abbott) and high-sensitivity central laboratory cTnI (hs-cTnI; Architect, Abbott) assays.

METHODS: The clinical performance of the assays were compared in samples from 450 patients from a previous clinical evaluation of Minicare cTnI.

RESULTS: Minicare cTnI correlated with Architect hs-cTnI (r2=0.85, p<0.0001) and I-Stat cTnI (r2=0.93, p<0.0001). Areas under the receiver operating characteristics curves were 0.87-0.91 at admission (p=ns) and 0.96-0.97 3h after admission (p=ns). The negative predictive values (NPV) at admission were 95% ((92-97%, 95% CI) for Minicare cTnI and increased to 99% (97-100%) at 2-4h, and similar to Architect hs-cTnI (98%, 96-100%), but higher than I-Stat cTnI (95%, 92-97%; p<0.01). Negative likelihood ratios (LR-) after 2-4h were 0.06 (0.02-0.17, 95% CI) for Minicare cTnI, 0.11 (0.05-0.24) for Architect hs-cTnI (p=0.02) and 0.28 (0.18-0.43) for I-Stat cTnI (p<0.0001). The clinical concordances between Minicare cTnI and

Architect hs-cTnI were 92% (admission) and 95% (2-4h), with lower concordances between Minicare cTnI and I-Stat cTnI (83% and 78%, respectively; p=0.007).
CONCLUSIONS:
The Minicare cTnI POC assay may become useful for prompt and safe ruling-out of AMI in ED patients with suspected AMI using a guideline supported 0/3h sampling protocol.

Impactfactor: 2.873

Improved and more effective algorithms to screen for nutrient deficiencies after bariatric surgery

Bazuin I, Pouwels S, Houterman S, Nienhuijs SW, Smulders JF, **Boer AK**

Eur J Clin Nutr. 2017 Feb 71(2):198-202.

BACKGROUND/OBJECTIVES: Most bariatric guidelines recommend frequent lab monitoring of patients to detect nutrient and vitamin deficiencies as early as possible. The aim of this study was to optimize the cost effectiveness of the nutrient panel, by developing an algorithm, which detects nutrient deficiencies at lower costs.
SUBJECTS/METHODS: In this retrospective study, 2055 patients who had undergone Laparoscopic Roux-Y Gastric Bypass (LRYGB) and Laparoscopic Sleeve Gastrectomy (LSG) surgery at Catharina Hospital Eindhoven between January 2009 and December 2013 were included. Perioperative biochemical measurements (7 days before and 127 days after surgery) and measurements >549 days before surgery were excluded. For analysis, the most recent preoperative and postoperative measurements were selected for each biochemical parameter separately. First, the amount of moderate and severe deficiencies were calculated. Second, we investigated whether each variable (vitamins A, B1, B6, B12, D, folate, ferritin, zinc and magnesium) could predict the presence of deficiency.
RESULTS: In total, 561 (LRYGB) and 831 (LSG) patients had at least preoperative and postoperative values of vitamin A, B1, B6, B12, D, folate, ferritin, zinc or magnesium. The algorithm reduces vitamin D, B12, B6, B1 and ferritin examinations by 15, 11, 28, 28 and 38%, respectively, without missing clinically relevant deficiencies. The corresponding potential cost savings was 14%.
CONCLUSIONS: This study identified substantial cost savings in laboratory test for both LRYGB and LSG procedures. The potential cost reduction of 14% might even be increased to 42% when less frequent moderate deficiencies are not screened anymore, whereas >99.0 of moderate deficiencies will be detected.

Impactfactor: 3.057

Origin of Cardiac Troponin T Elevations in Chronic Kidney Disease

van der Linden N, Cornelis T, Kimenai DM, **Klinkenberg LJ**, Hilderink JM, Lück S, Litjens EJ, Peeters FE, Streng AS, Breidthardt T, van Loon LJ, Bekers O, Kooman JP, Westermark PO, Mueller C, Meex SJ

Circulation. 2017 Sep 12;136(11):1073-1075

Geen abstract beschikbaar

Impactfactor: 19.309

Practical Value of Anti-Xa Activity in the Evaluation of Extracorporeal Circuit Anticoagulation during Haemodialysis: Results of a Cross-Sectional Single-Centre Study

Coene KL, Dekker MJ, Kerskes MC, Hengst M, Schonck MJ, Konings CJ, **Scharnhorst V**

Nephron. 2017;137(3):205-211

BACKGROUND/AIMS: Anticoagulation of the extracorporeal circuit is essential for adequate haemodialysis (HD). Low molecular weight heparins (LMWHs) are safe and sufficient towards achieving this goal. In the Netherlands, dosage is based on bodyweight and adjusted based on clinical events. LMWH levels during dialysis can be quantified through measurement of the anti-Xa activity and a target range of 0.5-1.0 IU/mL has been proposed. We aimed to evaluate the practical value of the anti-Xa activity to guide LMWH dosage in HD patients. Additionally, the value of the activated partial thromboplastin time (APTT) was investigated.
METHODS: All prevalent adult HD patients of our dialysis clinic were included. APTT and anti-Xa activity were measured before, during and after 2 dialysis sessions. Clinical and dialysis characteristics, including LMWH dosage, were derived from digital patient charts.
RESULTS: Our final study cohort consisted of 83 patients. LMWH dosage during dialysis was appropriate for bodyweight in 61% of cases, of which 50% reached an anti-Xa activity within the putative target range of 0.5-1.0 IU/mL. Forty-six percent of patients had an anti-Xa activity >1.0 IU/mL. Anti-Xa levels during and after dialysis were significantly correlated ($r = 0.803$, $p < 0.01$). No thrombotic or

haemorrhagic complications were observed in this study. Correlation of APTT with anti-Xa activity was poor.

CONCLUSION: Anti-Xa activity measurements during dialysis can identify patients in whom LMWH dosage should be lowered in a subsequent dialysis session. Whether such an intervention leads to a decrease in haemorrhagic complications needs to be evaluated in prospective studies.

Impactfactor: 1.939

Real life dabigatran and metabolite concentrations, focused on inter-patient variability and assay differences in patients with atrial fibrillation

Boonen K, Schmitz E, Rozestraten F, **van den Heuvel D, Brunsveld L**, van der Voort P, **van de Kerkhof D**

Clin Chem Lab Med. 2017 Oct 26;55(12):2002-2009

BACKGROUND: Dabigatran is prescribed to increasing numbers of patients with atrial fibrillation (AF). Although routine monitoring is not considered to be useful, measuring drug concentrations can be clinically relevant in specific situations. The aim of this study was the comparison of different functional and non-functional assays for determination of dabigatran concentrations at different timepoints in a real-life patient population with AF. We focused on the differences between assays in identifying patients with low drug concentrations. Furthermore, we studied the effect of glucuronidation on the established concentration as determined with different assays.

METHODS: This study established dabigatran concentration ranges in 40 real-life AF patients by an ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) reference method and compared these with results from coagulation assays (Hemoclot dTT, LD-dTT and ECA). Samples were taken just before and 2 and 4 h after taking the drug.

RESULTS: A wide range of concentrations at different time points was found in this patient group. assays correlate best with UPLC-MS/MS results that include the glucuronidated metabolites, showing that the pharmacologically active glucuronides are also measured in coagulation testing. The LD-dTT has the best agreement with UPLC-MS/MS and combines good sensitivity with high specificity. Several patients show consistently low or high drug concentrations, implying that drug exposure differs between patients.

CONCLUSIONS: Based on the association of dabigatran concentrations with bleeding and thromboembolic risk, we believe that dabigatran monitoring could be beneficial for further optimizing anticoagulation therapy in AF.

Impactfactor: 3.432

Short article: The effect of implementation of a treatment algorithm for infliximab on remission rates and drug costs in inflammatory bowel disease patients

Taks M, Pijls PA, Derijks LJ, Ten Broeke R, Grouls RJ, **Curvers J,** Gilissen LP

Eur J Gastroenterol Hepatol. 2017 Feb;29(2):169-173

INTRODUCTION: The effective, but expensive, drug infliximab is used in patients with inflammatory bowel disease (IBD). Monitoring infliximab trough levels and anti-infliximab antibody (ATI) formation can lead to a more cost-effective use of infliximab therapy. The aim of our study was to investigate the effect of implementation of a treatment algorithm for infliximab in a single-centre IBD cohort, focussing on remission rates and drug costs.

METHODS: IBD patients aged 18 years or older treated with infliximab were asked to participate in this study. Remission rates were assessed using faecal calprotectin levels and a validated questionnaire. Infliximab trough levels and ATIs were determined at baseline and at the third infliximab infusion. According to the advice given by the treatment algorithm, infliximab dosage adjustments were performed at the second infliximab infusion.

RESULTS: Between January and December 2015 a total of 62 IBD patients in our centre were treated with infliximab, of whom 33 (53%) patients agreed to participate in this study. The number of patients in remission was 28 (85%) at baseline and there were 13 dose adaptations suggested by the treatment algorithm for the successive second infusion. Four patients possessed undetectable infliximab levels and positive ATI status at baseline. After the second infusion, there were 29 (88%) patients in remission at the third infusion. All of this resulted in an annual drug cost reduction of &OV0556;47?026 (7.4%).

CONCLUSION: Our developed treatment algorithm of infliximab led to optimization of infliximab therapy in IBD patients by increasing remission rates and reducing drug costs.

Impactfactor: 2.093

Therapeutic drug monitoring (TDM) as a tool in the switch from infliximab innovator to biosimilar in rheumatic patients: results of a 12-month observational prospective cohort study

Schmitz EM , Benoy-De Keuster S, Meier AJ, **Scharnhorst V**, Traksel RA, Broeren MA, Derijks LJ

Clin Rheumatol. 2017 Sep;36(9):2129-2134

The objective of this study is to apply therapeutic drug monitoring (TDM) as an objective tool to monitor the switch from infliximab innovator (INX) to infliximab biosimilar (INB) in our diverse rheumatic cohort in daily clinical practice. All rheumatic patients on INX treatment (Remicade®) and =18 years were switched to INB (Inflectra®) as part of routine care, but in a controlled setting. Patients were monitored by taking blood samples just before the first infusion of INB (T1), and after the second (T2), fourth (T3), and seventh (T4) infusion of INB. T4 reflects the patients' status after ~12 months. Infliximab trough levels, antibodies-to-infliximab (ATI), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and validated disease activity scores (if possible) were measured. Our population consisted of 27 patients with seven different rheumatic diseases who had received INX for 143 (58-161) months (median (IQR)). Half of the patients (52%) received concomitant immunosuppressives. We found widely varying infliximab levels, with only 56% within the proposed therapeutic range of 1-5 µg/mL. One patient had very high ATI levels (>880 au/mL), and two had low ATI levels (=30 au/mL). After switching to INB, seven patients (26%) discontinued the therapy, partially due to subjective reasons. No difference in infliximab levels, CRP levels, and disease activity scores was found between the four time points (p = 0.2460). In conclusion, no pharmacokinetic or clinical differences were found between INX and INB in our diverse rheumatic cohort. TDM is a helpful tool to monitor patients switching from INX to INB.

Impactfactor: 2.365

Treatments for hematologic malignancies in contrast to those for solid cancers are associated with reduced red cell alloimmunization

Evers D, Zwaginga JJ, Tijmensen J, Middelburg RA, de Haas M, de Vooght KM, **van de Kerkhof D**, Visser O, Péquériaux NC, Hudig F, van der Bom JG

Haematologica. 2017 Jan; 102(1):52-59. Epub 2016 Sep 15

Red cell alloimmunization may induce severe hemolytic side effects. Identification of risk-modifying conditions will help tailor preventative strategies. This study aims to quantify the associations of hematologic malignancies and solid cancers with red cell alloimmunization in patients receiving red cell transfusions. We performed a nested multicenter case-control study in a source population of 24,063 patients receiving their first and subsequent red cell transfusions during an 8-year follow-up period. Cases (n=505), defined as patients developing a first transfusion-induced red cell alloantibody, were each compared with 2 non-alloimmunized controls (n=1010) who received a similar number of red cell units. Using multivariate logistic regression analyses, we evaluated the association of various malignancies and treatment regimens with alloimmunization during a delineated 5-week risk period.

The incidence of alloimmunization among patients with acute (myeloid or lymphoid) leukemia and mature (B- or T-cell) lymphoma was significantly reduced compared to patients without these malignancies: adjusted relative risks (RR) with 95% confidence interval (CI) 0.36 (range 0.19-0.68) and 0.30 (range 0.12-0.81).

Associations were primarily explained by immunosuppressive treatments [RR for (any type of) chemotherapy combined with immunotherapy 0.27 (95%CI: 0.09-0.83)].

Alloimmunization risks were similarly diminished in allogeneic or autologous stem cell transplanted patients (RR 0.34, 95%CI: 0.16-0.74), at least during the six months post transplant. Alloimmunization risks of patients with other hematologic diseases or solid cancers, and their associated treatment regimens were similar to risks in the general transfused population. Our findings suggest that, in contrast to malignancies in general, hemato-oncological patients treated with dose-intensive regimens have strongly diminished risk of red cell alloimmunization.

Impactfactor: 7.702

Anesthesiologie

A meta-model for computer executable dynamic clinical safety checklists

Nan S, Van Gorp P, Lu X, Kaymak U, **Korsten H**, Vdovjak R, Duan H

BMC Med Inform Decis Mak. 2017 Dec 12;17(1):170

BACKGROUND: Safety checklist is a type of cognitive tool enforcing short term memory of medical workers with the purpose of reducing medical errors caused by overlook and ignorance. To facilitate the daily use of safety checklists, computerized systems embedded in the clinical workflow and adapted to patient-context are increasingly developed. However, the current hard-coded approach of implementing checklists in these systems increase the cognitive efforts of clinical experts and coding efforts for informaticists. This is due to the lack of a formal representation format that is both understandable by clinical experts and executable by computer programs

METHODS: We developed a dynamic checklist meta-model with a three-step approach. Dynamic checklist modeling requirements were extracted by performing a domain analysis. Then, existing modeling approaches and tools were investigated with the purpose of reusing these languages. Finally, the meta-model was developed by eliciting domain concepts and their hierarchies. The feasibility of using the meta-model was validated by two case studies. The meta-model was mapped to specific modeling languages according to the requirements of hospitals.

RESULTS: Using the proposed meta-model, a comprehensive coronary artery bypass graft peri-operative checklist set and a percutaneous coronary intervention peri-operative checklist set have been developed in a Dutch hospital and a Chinese hospital, respectively. The result shows that it is feasible to use the meta-model to facilitate the modeling and execution of dynamic checklists.

CONCLUSIONS: We proposed a novel meta-model for the dynamic checklist with the purpose of facilitating creating dynamic checklists. The meta-model is a framework of reusing existing modeling languages and tools to model dynamic checklists. The feasibility of using the meta-model is validated by implementing a use case in the system

Impactfactor: 1.643

Comparison of cardiac magnetic resonance imaging and bio-impedance spectroscopy for the assessment of fluid displacement induced by external leg compression

Saporito S, Dovancescu S, **Herold IH**, van den Bosch HC, van Assen HC, Aarts RM, **Korsten HH**, Mischi M

Physiol Meas. 2017 Jan;38(1):15-32. Epub 2016 Dec 12

Heart failure is marked by frequent hospital admissions, often as a consequence of pulmonary congestion. Current gold standard techniques for thoracic fluid measurement require invasive heamodynamic access and therefore they are not suitable for continuous monitoring. Changes in thoracic impedance (TI) may enable non-invasive early detection of congestion and prevention of unplanned hospitalizations. However, the usefulness of TI to assess thoracic fluid status is limited by inter-subject variability and by the lack of reliable normalization methods. Indicator dilution methods allow absolute fluid volume estimation; cardiac magnetic resonance (CMR) has been recently proposed to apply indicator dilution methods in a minimally-invasive manner. In this study, we aim to compare bio-impedance spectroscopy (BIS) and CMR for the assessment of thoracic fluid status, and to determine their ability to detect fluid displacement induced by a leg compression procedure in healthy volunteers. A pressure gradient was applied across each subject's legs for 5?min (100-60 mmHg, distal to proximal). Each subject underwent a continuous TI-BIS measurement during the procedure, and repeated CMR-based indicator dilution measurements on a 1.5 T scanner at baseline, during compression, and after pressure release. The Cole-Cole and the local density random walk models were used for parameter extraction from TI-BIS and indicator dilution measurements, respectively. Intra-thoracic blood volume index (ITBI) derived from CMR, and extracellular fluid resistance (R E) from TI-BIS, were considered as thoracic fluid status measures. Eight healthy volunteers were included in this study. An increase in ITBI of 45.2??±??47.2?ml m-2 was observed after the leg inflation (13.1??±??15.1% w.r.t. baseline, p??<??0.05), while a decrease of??-0.84??±??0.39 O in R E (-1.7??±??0.9% w.r.t. baseline, p??<??0.05) was observed. ITBV and R E normalized by body mass index were strongly inversely correlated (r??=??-0.93, p??<??0.05). In conclusion, an acute fluid displacement to the thoracic circulation was induced in healthy volunteers. Significant changes were observed in the considered thoracic fluid measures derived from BIS and CMR. Good correlation was observed between the two measurement techniques. Further clinical studies will be necessary to prospectively evaluate the value of a combination of the two techniques for prediction of re-hospitalizations after admission for heart failure.

Impactfactor: 2.058

Crisis checklists for in-hospital emergencies: expert consensus, simulation testing and recommendations for a template determined by a multi-institutional and multi-disciplinary learning collaborative

Subbe CP, Kellett J, Barach P, Chaloner C, Cleaver H, Cooksley T, **Korsten E**, Croke E, Davis E, De Bie AJ, Durham L, Hancock C, Hartin J, Savijn T, Welch J. Crisis Checklist Collaborative

BMC Health Serv Res. 2017 May 8; 17(1):334

BACKGROUND: 'Failure to rescue' of hospitalized patients with deteriorating physiology on general wards is caused by a complex array of organisational, technical and cultural failures including a lack of standardized team and individual expected responses and actions. The aim of this study using a learning collaborative method was to develop consensus recomendations on the utility and effectiveness of checklists as training and operational tools to assist in improving the skills of general ward staff on the effective rescue of patients with abnormal physiology.

METHODS: A scoping study of the literature was followed by a multi-institutional and multi-disciplinary international learning collaborative. We sought to achieve a consensus on procedures and clinical simulation technology to determine the requirements, develop and test a safe using a checklist template that is rapidly accessible to assist in emergency management of common events for general ward use.

RESULTS: Safety considerations about deteriorating patients were agreed upon and summarized. A consensus was achieved among an international group of experts on currently available checklist formats performing poorly in simulation testing as first responders in general ward clinical crises. The Crisis Checklist Collaborative ratified a consensus template for a general ward checklist that provides a list of issues for first responders to address (i.e. 'Check In'), a list of prompts regarding common omissions (i.e. 'Stop & Think'), and, a list of items required for the safe "handover" of patients that remain on the general ward (i.e. 'Check Out'). Simulation usability assessment of the template demonstrated feasibility for clinical management of deteriorating patients.

CONCLUSIONS: Emergency checklists custom-designed for general ward patients have the potential to guide the treatment speed and reliability of responses for emergency management of patients with abnormal physiology while minimizing the risk of adverse events. Interventional trials are needed.

Impactfactor: 1.827

Critical care admission following elective surgery was not associated with survival benefit: prospective analysis of data from 27 countries

Kahan BC, Koulenti D, Arvaniti K, Beavis V, Campbell D, Chan M, Moreno R, Pearse RM; International Surgical Outcomes Study (ISOS) group: **Buise M**, **Bouwman RA**

Intensive Care Med. 2017 Jul;43(7):971-979

PURPOSE: As global initiatives increase patient access to surgical treatments, there is a need to define optimal levels of perioperative care. Our aim was to describe the relationship between the provision and use of critical care resources and postoperative mortality.

METHODS: Planned analysis of data collected during an international 7-day cohort study of adults undergoing elective in-patient surgery. We used risk-adjusted mixed-effects logistic regression models to evaluate the association between admission to critical care immediately after surgery and in-hospital mortality. We evaluated hospital-level associations between mortality and critical care admission immediately after surgery, critical care admission to treat life-threatening complications, and hospital provision of critical care beds. We evaluated the effect of national income using interaction tests.

RESULTS: 44,814 patients from 474 hospitals in 27 countries were available for analysis. Death was more frequent amongst patients admitted directly to critical care after surgery (critical care: 103/4317 patients [2%], standard ward: 99/39,566 patients [0.3%]; adjusted OR 3.01 [2.10-5.21]; $p < 0.001$). This association may differ with national income (high income countries OR 2.50 vs. low and middle income countries OR 4.68; $p = 0.07$). At hospital level, there was no association between mortality and critical care admission directly after surgery ($p = 0.26$), critical care admission to treat complications ($p = 0.33$), or provision of critical care beds ($p = 0.70$). Findings of the hospital-level analyses were not affected by national income status. A sensitivity analysis including only high-risk patients yielded similar findings.

CONCLUSIONS: We did not identify any survival benefit from critical care admission following surgery.

Impactfactor: 12.015

Current practice of closed-loop mechanical ventilation modes on intensive care units - a nationwide survey in the Netherlands

Wenstedt EF, De Bie Dekker AJ, Roos AN, Verberne JJ, **Korsten HH**, Schultz MJ, Bindels AJ

Neth J Med. 2017 May; 75(4):145-150

BACKGROUND: The most recent modes for mechanical ventilation are closed-loop modes, which are able to automatically adjust certain respiratory settings. Although closed-loop modes have been investigated in various clinical trials, it is unclear to what extent these modes are actually used in clinical practice. The aim of this study was to determine closed-loop ventilation practice on intensive care units (ICUs) in the Netherlands, and to explore reasons for not applying closed-loop ventilation. Our hypothesis was that closed-loop ventilation is increasingly used.

METHODS: A short survey was conducted among all non-paediatric ICUs in the Netherlands. Use of closed-loop modes was classified as frequently, occasionally or never, if respondents stated they had used these modes in the last week, in the last month/year, or never, respectively.

RESULTS: The response rate of the survey was 82% (72 of 88). Respondents had access to a closed-loop ventilation mode in 58% of the ICUs (42 of 72). Of these ICUs, 43% (18 of 42) frequently applied a closed-loop ventilation mode, while 57% (24 of 42) never or occasionally used it. Reasons for not using these modes were lack of knowledge (40%), insufficient evidence reporting a beneficial effect (35%) and lack of confidence (25%).

CONCLUSION: This study does not support our hypothesis that closed-loop ventilation is increasingly used in the Dutch ICU setting. While industry continues to develop new closed-loop modes, implementation of these modes in clinical practice seems to encounter difficulties. Various barriers could play a role, and these all need attention in future investigations.

Impactfactor: 1.244

Higher Fluid Balance Increases the Risk of Death From Sepsis: Results From a Large International Audit

Sakr Y, Rubatto Birri PN, Kotfis K, Nanchal R, Shah B, Kluge S, Schroeder ME, Marshall JC, Vincent JL; Intensive Care Over Nations Investigators: **Buise M**

Crit Care Med. 2017 Mar;45(3):386-394

OBJECTIVES: Excessive fluid therapy in patients with sepsis may be associated with risks that outweigh any benefit. We investigated the possible influence of early fluid balance on outcome in a large international database of ICU patients with sepsis.

DESIGN: Observational cohort study.

SETTING: Seven hundred and thirty ICUs in 84 countries.

PATIENTS: All adult patients admitted between May 8 and May 18, 2012, except admissions for routine postoperative surveillance. For this analysis, we included only the 1,808 patients with an admission diagnosis of sepsis. Patients were stratified according to quartiles of cumulative fluid balance 24 hours and 3 days after ICU admission.

MEASUREMENTS AND MAIN RESULTS: ICU and hospital mortality rates were 27.6% and 37.3%, respectively. The cumulative fluid balance increased from 1,217?mL (-90 to 2,783?mL) in the first 24 hours after ICU admission to 1,794?mL (-951 to 5,108?mL) on day 3 and decreased thereafter. The cumulative fluid intake was similar in survivors and nonsurvivors, but fluid balance was less positive in survivors because of higher fluid output in these patients. Fluid balances became negative after the third ICU day in survivors but remained positive in nonsurvivors. After adjustment for possible confounders in multivariable analysis, the 24-hour cumulative fluid balance was not associated with an increased hazard of 28-day in-hospital death. However, there was a stepwise increase in the hazard of death with higher quartiles of 3-day cumulative fluid balance in the whole population and after stratification according to the presence of septic shock.

CONCLUSIONS: In this large cohort of patients with sepsis, higher cumulative fluid balance at day 3 but not in the first 24 hours after ICU admission was independently associated with an increase in the hazard of death.

Impactfactor: 7.050

Improving needle tip identification during ultrasound-guided procedures in anaesthetic practice

Scholten HJ, Pourtaherian A, Mihajlovic N, **Korsten HH**, **Bouwman RA**

Anaesthesia. 2017 Jul;72(7):889-904

Ultrasound guidance is becoming standard practice for needle-based interventions in anaesthetic practice, such as vascular access and peripheral nerve blocks. However, difficulties in aligning the needle

and the transducer can lead to incorrect identification of the needle tip, possibly damaging structures not visible on the ultrasound screen. Additional techniques specifically developed to aid alignment of needle and probe or identification of the needle tip are now available. In this scoping review, advantages and limitations of the following categories of those solutions are presented: needle guides; alterations to needle or needle tip; three- and four-dimensional ultrasound; magnetism, electromagnetic or GPS systems; optical tracking; augmented (virtual) reality; robotic assistance; and automated (computerised) needle detection. Most evidence originates from phantom studies, case reports and series, with few randomised clinical trials. Improved first-pass success and reduced performance time are the most frequently cited benefits, whereas the need for additional and often expensive hardware is the greatest limitation to widespread adoption. Novice ultrasound users seem to benefit most and great potential lies in education. Future research should focus on reporting relevant clinical parameters to learn which technique will benefit patients most in terms of success and safety.

Impactfactor: 4.741

Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe

Habre W, Disma N, Virag K, Becke K, Hansen TG, Jöhr M, Leva B, Morton NS, Vermeulen PM, Zielinska M, Boda K, Veyckemans F; APRICOT Group of the European Society of Anaesthesiology Clinical Trial Network: **Bouwman RA**, **Scholten HJ**, **Svircevic-Leijtens V**

Lancet Respir Med. 2017 May;5(5):412-425

BACKGROUND: Little is known about the incidence of severe critical events in children undergoing general anaesthesia in Europe. We aimed to identify the incidence, nature, and outcome of severe critical events in children undergoing anaesthesia, and the associated potential risk factors.

METHODS: The APRICOT study was a prospective observational multicentre cohort study of children from birth to 15 years of age undergoing elective or urgent anaesthesia for diagnostic or surgical procedures. Children were eligible for inclusion during a 2-week period determined prospectively by each centre. There were 261 participating centres across 33 European countries. The primary endpoint was the occurence of perioperative severe critical events requiring immediate intervention. A severe critical event was defined as the occurrence of respiratory, cardiac, allergic, or neurological complications requiring immediate intervention and that led (or could have led) to major disability or death. This study is registered with ClinicalTrials.gov, number NCT01878760.

FINDINGS: Between April 1, 2014, and Jan 31, 2015, 31?127 anaesthetic procedures in 30?874 children with a mean age of 6·35 years (SD 4·50) were included. The incidence of perioperative severe critical events was 5·2% (95% CI 5·0-5·5) with an incidence of respiratory critical events of 3·1% (2·9-3·3). Cardiovascular instability occurred in 1·9% (1·7-2·1), with an immediate poor outcome in 5·4% (3·7-7·5) of these cases. The all-cause 30-day in-hospital mortality rate was 10 in 10?000. This was independent of type of anaesthesia. Age (relative risk 0·88, 95% CI 0·86-0·90; p<0·0001), medical history, and physical condition (1·60, 1·40-1·82; p<0·0001) were the major risk factors for a serious critical event. Multivariate analysis revealed evidence for the beneficial effect of years of experience of the most senior anaesthesia team member (0·99, 0·981-0·997; p<0·0048 for respiratory critical events, and 0·98, 0·97-0·99; p=0·0039 for cardiovascular critical events), rather than the type of health institution or providers.

INTERPRETATION: This study highlights a relatively high rate of severe critical events during the anaesthesia management of children for surgical or diagnostic procedures in Europe, and a large variability in the practice of paediatric anaesthesia. These findings are substantial enough to warrant attention from national, regional, and specialist societies to target education of anaesthesiologists and their teams and implement strategies for quality improvement in paediatric anaesthesia.

Impactfactor: 19.287

Intelligent dynamic clinical checklists improved checklist compliance in the intensive care unit

De Bie AJ, Nan S, Vermeulen LR, Van Gorp PM, **Bouwman RA**, Bindels AJ, **Korsten HH**

Br J Anaesth. 2017 Aug 1;119(2):231-238

Background: Checklists can reduce medical errors. However, the effectiveness of checklists is hampered by lack of acceptance and compliance. Recently, a new type of checklist with dynamic properties has been created to provide more specific checklist items for each individual patient. Our purpose in this simulation-based study was to investigate a newly developed intelligent dynamic clinical checklist (DCC) for the intensive care unit (ICU) ward round.

Methods: Eligible clinicians were invited to participate as volunteers. Highest achievable scores were established for six typical ICU scenarios to determine which items must be checked. The participants 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 requiring a direct intervention. Results: In total, 20 participants were included, who performed 116 scenarios. The median percentage of checked items was 100.0% with the DCC and 73.6% for the scenarios completed with local standard of care (P <0.001). Critical items remained unchecked in 23.1% of the scenarios performed with local standard of care and 0.0% of the scenarios where the DCC was available (P <0.001). The mean satisfaction score of the DCC was 4.13 out of 5.

Conclusions: This simulation study indicates that an intelligent DCC significantly increases compliance with best practice by reducing the percentage of unchecked items during ICU ward rounds, while the user satisfaction rate remains high. Real-life clinical research is required to evaluate this new type of checklist further.

Impactfactor: 6.238

Medical Instrument Detection in 3-Dimensional Ultrasound Data Volumes

Pourtaherian A, **Scholten HJ**, Kusters L, Zinger S, Mihajlovic N, Kolen AF, Zuo F, Ng GC, **Korsten HH**, de With PH

IEEE Trans Med Imaging. 2017 Aug;36(8):1664-1675. Epub 2017 Apr 7

Ultrasound-guided medical interventions are broadly applied in diagnostics and therapy, e.g., regional anesthesia or ablation. A guided intervention using 2-D ultrasound is challenging due to the poor instrument visibility, limited field of view, and the multi-fold coordination of the medical instrument and ultrasound plane. Recent 3-D ultrasound transducers can improve the quality of the image-guided intervention if an automated detection of the needle is used. In this paper, we present a novel method for detecting medical instruments in 3-D ultrasound data that is solely based on image processing techniques and validated on various ex vivo and in vivo data sets. In the proposed procedure, the physician is placing the 3-D transducer at the desired position, and the image processing will automatically detect the best instrument view, so that the physician can entirely focus on the intervention. Our method is based on the classification of instrument voxels using volumetric structure directions and robust approximation of the primary tool axis. A novel normalization method is proposed for the shape and intensity consistency of instruments to improve the detection. Moreover, a novel 3-D Gabor wavelet transformation is introduced and optimally designed for revealing the instrument voxels in the volume, while remaining generic to several medical instruments and transducer types. Experiments on diverse data sets, including in vivo data from patients, show that for a given transducer and an instrument type, high detection accuracies are achieved with position errors smaller than the instrument diameter in the 0.5-1.5-mm range on average.

Impactfactor: 3.942

Monitoring thoracic fluid content using bioelectrical impedance spectroscopy and Cole modeling

Dovancescu S, Saporito S, **Herold IH**, **Korsten HH**, Aarts RM, Misch M

J Electr Bioimp 2017;8:107-15

Heart failure is a chronic disease marked by frequent hospitalizations due to pulmonary fluid congestion. Monitoring the thoracic fluid status may favor the detection of fluid congestion in an early stage and enable targeted preventive measures. Bioelectrical impedance spectroscopy (BIS) has been used in combination with the Cole model for monitoring body composition including fluid status. The model parameters reflect intracellular and extracellular fluid volume as well as cell sizes, types and interactions. Transthoracic BIS may be a suitable approach to monitoring variations in thoracic fluid content. The aim of this study was to identify BIS measures, which can be derived based on the Cole model, that are sensitive to early stages of thoracic fluid accumulation. We simulated this medical condition in healthy subjects by shifting a part of the whole blood from the periphery towards the thorax. The redistribution of blood was achieved non-invasively through leg compression using inflatable leg sleeves. We acquired BIS data before, during and after compression of the legs and examined the effect of thoracic fluid variations on parameters derived based on the Cole model and on geometrical properties of the impedance arc. Indicator dilution measurements obtained through cardiac magnetic resonance imaging were used as a reference for the changes in pulmonary fluid volume.

Eight healthy subjects were included in the study. The Cole model parameters of the study group at baseline were: R0 = 51.4 ± 6.7 O, R8 = 25.0 ± 7.0 O, fc = 49.0 ± 10.5 kHz, a = 0.687 ± 0.027, the

resistances of individual fluid compartments were RE = 51.4 ± 6.7 O, RI = 50.5 ± 22.9 O, the fluid distribution ratio was K = 1.1 ± 0.3, and the radius, area and depression of the arc's center were: R = 15.7 ± 1.3 O, XC = -8.5 ± 1.5 O, A = 134.0 ± 15.6 O2. The effect of leg compression was a relatively small, reversible increase in pulmonary blood volume of 90 ± 57 mL. We observed significant changes in parameters associated with intracellular, extracellular and total fluid volume (R0: -1.5 ± 0.9 %, $p < 0.01$; R8: -2.1 ± 1.1, $p < 0.01$; RI: -2.6 ± 1.6 %, $p < 0.01$), and in the arc's geometrical properties (R: -1.6 ± 1.3 %, $p < 0.05$; XC: -1.7 ± 1.5 %, $p < 0.05$, A: -2.9 ± 1.2 %, $p < 0.01$). K and the parameters associated with tissue structure fc and a remained stable.

Transthoracic BIS is sensitive to small variations in intra-thoracic blood volume, in particular the resistances of fluid compartments and the geometric properties of the impedance arc. Taken together with previous studies, our findings suggest that R0 may be a suitable parameter to monitor congestion. Use of additional parameters such as RI, K, XC, fc and a may enable the discrimination between different types and stages of thoracic fluid accumulation and should be the focus of future research.

Impactfactor: --

Myocardial Microvascular Responsiveness During Acute Cardiac Sympathectomy Induced by Thoracic Epidural Anesthesia

Bulte CS, Boer C, Hartemink KJ, Kamp O, Heymans MW, Loer SA, de Marchi SF, Vogel R, **Bouwman RA**

J Cardiothorac Vasc Anesth. 2017 Feb;31(1):134-141. Epub 2016 May 25

OBJECTIVE: To evaluate the effect of acute cardiac sympathectomy by thoracic epidural anesthesia on myocardial blood flow and microvascular function.

DESIGN: A prospective observational study.

SETTING: The study was conducted in a tertiary teaching hospital.

PARTICIPANTS: Ten patients with a mean age of 48 years (range 22-63 years) scheduled for thoracic surgery.

INTERVENTIONS: Myocardial contrast echocardiography was used to study myocardial blood flow and microvascular responsiveness at rest, during adenosine-induced hyperemia, and after sympathetic stimulation by the cold pressor test. Repeated measurements were performed without and with thoracic epidural anesthesia.

MEASUREMENTS AND MAIN RESULTS: An increased myocardial blood volume was observed with thoracic epidural anesthesia compared to baseline (from 0.08±0.02 to 0.10±0.03 mL/mL; $p = 0.02$). No difference existed in resting myocardial blood flow between baseline conditions and epidural anesthesia (0.85±0.24 v 1.03±0.27 mL/min/g, respectively). Hyperemia during thoracic epidural anesthesia increased myocardial blood flow to 4.31±1.07 mL/min/g ($p = 0.0008$ v baseline) and blood volume to 0.17±0.04 mL/mL ($p = 0.005$ baseline). After sympathetic stimulation, no difference in myocardial blood flow parameters was observed CONCLUSIONS: Acute cardiac sympathectomy by thoracic epidural anesthesia increased the blood volume in the myocardial capillary system. Also, thoracic epidural anesthesia increased hyperemic myocardial blood flow, indicating augmented endothelial-independent vasodilator capacity of the myocardium.

impactfactor: 1.699

[Neurogenic thoracic outlet syndrome] - Neurogeen thoracic-outletsyndroom

Teijink JA, Pesser N, van Grinsven R, **van Suijlekom H**, van Sambeek MR, van Nuenen BF

Ned Tijdschr Geneeskd. 2017;161(0):D1385

Neurogenic thoracic outlet syndrome (nTOS) is a type of thoracic outlet syndrome (TOS) where compression of the brachial plexus is responsible for development of upper-extremity, head and neck symptoms. We present a 16-year-old and a 34-year-old patient with nTOS. Diagnosis in both cases was done by following the recently published reporting standards for (n)TOS. After this multidisciplinary diagnostic work-up we performed a transaxillary thoracic outlet decompression (TOD). Due to lack of literature, difficult nomenclature and complexity of diagnosis and treatment, diagnosis of nTOS is often delayed. Recent experience shows that treatment of nTOS is safe and effective, both in the short term and the long term.

Impactfactor: --

Noninvasive pulmonary transit time: A new parameter for general cardiac performance

de Lepper AG, **Herold IH**, Saporito S, **Bouwman RA**, Mischi M, **Korsten HH**, Reesink K, Houthuizen P

Echocardiography. 2017 Aug;34(8):1138-1145

INTRODUCTION: Pulmonary transit time (PTT) assessed with contrast-enhanced ultrasound (CEUS) is a novel tool to evaluate cardiac function. PTT represents the time for a bolus of contrast to pass from the right to the left ventricle, measured according to the indicator dilution principles using CEUS. We investigated the hypothesis that PTT is a measure of general cardiac performance in patient populations eligible for cardiac resynchronization therapy (CRT).

METHODS: The study population consisted of heart failure patients referred for CRT with NYHA class II-IV, left ventricular ejection fraction (LVEF)=35% and QRS=120 ms. CEUS, ECG, and blood were analyzed, and participants completed a quality of life questionnaire at baseline and 3 months after CRT implantation. Normalized PTT (nPTT) was calculated to compensate for the heart rate. Correlations were assessed with Pearson's or Spearman's coefficients and stratified for rhythm and NYHA class. RESULTS: The study population consisted of 94 patients (67 men) with a mean age of 70±8.9 years. (n)PTT was significantly correlated with left ventricular parameters (rs =-.487, P<.001), right ventricular parameters (r=-.282, P=.004), N-terminal pro-B-type natriuretic peptide (NT-proBNP) (rs =.475, P<.001), and quality of life (rs =.364, P<.001). Stronger significant correlations were found in patients in sinus rhythm.

CONCLUSION: CEUS-derived PTT and nPTT correlate to a fair degree with measures of systolic and diastolic function, NT-pro-BNP, and quality of life. As CEUS-derived PTT can be obtained easily, noninvasively and at the bedside, it is a promising future measure of general cardiac performance.

Impactfactor: 1.314

Preventive methods using lidocaine for reduction of pain associated with propofol intravenous administration: a double blind randomized controlled trial

Dortangs EJ, Niesten MW, **van Loon FH**, van Zundert AA

Acta Anaesth. Belg., 2017, 68, 13-18

Introduction: The aim of this randomized controlled trial (RCT) was to identify, among the commonly used ones, the most effective method of preventing pain upon the intravenous administration of propofol (PIP).

Methods : A total of 440, 18-80 year old, ASA 1 or 2 patients were randomized into four groups. All patients received an intravenous 2 mL pre-emptive intravenous injection and a 2 mL addition to the propofol solution

(Propofol-Lipuro®). Patients in study group A received pre-treatment with normal saline (NS), and NS in the propofol solution. Group B received pre-emptive NS and 2% lidocaine as the propofol addition. Group C received pre-emptive 2% lidocaine and NS, while group D received 1% lidocaine twice. PIP was scored on a four point Ambesh scale (at induction) and on an eleven-point Numeric Rating Score (NRS) (for postoperative recall).

Results : Group B and D had significantly lower pain incidences and severity scores than the control group A.

Conclusions : Adding 2 mL of lidocaine to propofol 1% significantly reduces PIP in healthy patients undergoing general anesthesia.

Impactfactor: --

Procedural sedation in the emergency department by Dutch emergency physicians: a prospective multicentre observational study of 1711 adults

Smits GJ, Kuypers MI, Mignot LA, Reijners EP, Oskam E, Van Doorn K, Thijssen WA, **Korsten EH**

Emerg Med J. 2017 Apr;34(4):237-242. Epub 2016 Oct 21

OBJECTIVE: To describe our experience performing ED procedural sedation in a country where emergency medicine (EM) is a relatively new specialty.

METHODS: This is a prospective observational study of adult patients undergoing procedural sedation by emergency physicians (EPs) or EM residents in eight hospitals in the Netherlands. Data were collected on a standardised form, including patient characteristics, sedative and analgesic used, procedural success, adverse events (classified according to World SIVA) and rescue interventions.

RESULTS: 1711 adult cases were included from 2006 to 2013. Propofol, midazolam and esketamine (S+ enantiomer of ketamine) were the most used sedatives (63%, 29% and 8%). We had adverse event data on all patients. The overall adverse event rate was 11%, mostly hypoxia or apnoea. There was no

difference in adverse event rate between EPs and EM residents. However, there was a significantly higher success rate of the procedure when EPs did the procedural sedation (92% vs 84%). No moderate (unplanned hospital admission or escalation of care) or sentinel SIVA outcomes occurred (pulmonary aspiration syndrome, death or permanent neurological deficit).

CONCLUSION: Adverse events during procedural sedation occurred in 11% of patients. There were no moderate or sentinel outcomes. All events could be managed by the sedating physician. In a country where EM is a relatively new specialty, procedural sedation appears to be safe when performed by EPs or trained EM residents and has comparable adverse event rates to international studies.

Impactfactor: 1.861

Reducing Caloric Intake Prevents Ischemic Injury and Myocardial Dysfunction and Affects Anesthetic Cardioprotection in Type 2 Diabetic Rats

van den Brom CE, Boer C, van den Akker RF, Loer SA, **Bouwman RA**

J Diabetes Res. 2017;2017:4126820

Background. Type 2 diabetes mellitus (T2DM) increases the risk of myocardial ischemia, followed by increased perioperative risk of cardiovascular morbidity. We investigated whether reducing caloric intake reduces ischemic injury and myocardial dysfunction and affects the protective effects of the volatile anesthetic sevoflurane in diet-induced T2DM rats. Methods. Rats received a western (WD) or control diet (CD). Caloric intake was reduced by reversing WD-fed rats to CD. Myocardial function was determined with echocardiography. After 8 weeks of diet feeding, myocardial infarction was induced and the effect of sevoflurane was studied on myocardial function and ischemia/reperfusion injury. Results. WD-feeding resulted in a mild T2DM phenotype and myocardial dysfunction. Sevoflurane further impaired systolic function in WD-fed rats. Unexpectedly, WD-feeding reduced infarct size compared to CD-feeding. Sevoflurane reduced infarct size in CD-fed rats; however it enlarged infarct size in WD-fed rats. Caloric reduction restored myocardial dysfunction and the protective effect of sevoflurane against ischemia compared to WD-fed rats, whereas the protective effects of WD-feeding persisted. Conclusion. Caloric reduction restored the T2DM phenotype and myocardial function, while the cardioprotective properties of WD-feeding or sevoflurane persisted. Our data suggest that reducing caloric intake in T2DM might be a possible intervention to reduce perioperative risk of cardiovascular morbidity.

Impactfactor: 2.717

Short-Term Changes in Cardiovascular Hemodynamics in Response to Bariatric Surgery and Weight Loss Using the Nexfin® Non-invasive Continuous Monitoring Device: a Pilot Study

Pouwels S, **Lascaris B**, Nienhuijs SW, **Bouwman AR**, **Buise MP**

Obes Surg. 2017 Jul;27(7):1835-1841

BACKGROUND: Compared to healthy individuals, obese have significantly higher systolic and diastolic blood pressure, mean arterial pressure, heart rate, and cardiac output. The aim of this study was to evaluate cardiovascular hemodynamic changes before and 3 months after bariatric surgery. METHODS: Patients scheduled for bariatric surgery between the 29th of September 2016 and 24th of March 2016 were included and compared with 24 healthy individuals. Hemodynamic measurements were performed preoperatively and 3 months after surgery, using the Nexfin® non-invasive continuous hemodynamic monitoring device (Edwards Lifesciences/BMEYE B.V., Amsterdam, the Netherlands). RESULTS: Eighty subjects were included in this study, respectively, 56 obese patients scheduled for bariatric surgery and 24 healthy individuals. Baseline hemodynamic measurements showed significant differences in cardiac output (6.5 ± 1.6 versus 5.7 ± 1.6 l/min, p = 0.046), mean arterial pressure (107 ± 19 versus 89 ± 11 mmHg, p = 0.001), systolic (134 ± 24 versus 116 ± 18 mmHg, p = 0.001) and diastolic blood pressure (89 ± 17 versus 74 ± 10 mmHg, p = 0.001), and heart rate (87 ± 12 versus 76 ± 14 bpm, p = 0.02) between obese and healthy subjects. Three months after surgery, significant changes occurred in mean arterial pressure (89 ± 17 mmHg, p = 0.001), systolic (117 ± 24 mmHg, p = 0.001) and diastolic blood pressure (71 ± 15 mmHg, p = 0.001), stroke volume (82.2 ± 22.4 ml, p = 0.03), and heart rate (79 ± 17 bpm, p = 0.02) CONCLUSIONS: Three months after bariatric surgery, significant improvements occur in hemodynamic variables except cardiac output and cardiac index, in the patient group.

Impactfactor: 3.947

The Influence of End-of-Life Care on Organ Donor Potential

Witjes M, Kotsopoulos A, **Herold IH**, Otterspoor L, Simons KS, van Vliet J, de Blauw M, Festen B, Eijkenboom JJ, Jansen NE, van der Hoeven JG, Abdo WF

Am J Transplant. 2017 Jul 17(7):1922-1927. Epub 2017 May 2

Many patients with acute devastating brain injury die outside intensive care units and could go unrecognized as potential organ donors. We conducted a prospective observational study in seven hospitals in the Netherlands to define the number of unrecognized potential organ donors outside intensive care units, and to identify the effect that end-of-life care has on organ donor potential. Records of all patients who died between January 2013 and March 2014 were reviewed. Patients were included if they died within 72 h after hospital admission outside the intensive care unit due to devastating brain injury, and fulfilled the criteria for organ donation. Physicians of included patients were interviewed using a standardized questionnaire regarding logistics and medical decisions related to end-of-life care. Of the 5170 patients screened, we found 72 additional potential organ donors outside intensive care units. Initiation of end-of-life care in acute settings and lack of knowledge and experience in organ donation practices outside intensive care units can result in under-recognition of potential donors equivalent to 11-34% of the total pool of organ donors. Collaboration with the intensive care unit and adjusting the end-of-life path in these patients is required to increase the likelihood of organ donation.

Impactfactor: 6.165

Use of failure-to-rescue to identify international variation in postoperative care in low-, middle- and high-income countries: a 7-day cohort study of elective surgery

Ahmad T, **Bouwman RA**, Grigoras , Aldecoa C, Hofer C, Hoeft A, Holt P, Fleisher LA, Buhre W, Pearse RM; International Surgical Outcomes Study (ISOS) group

Br J Anaesth. 2017 Aug 1;119(2):258-266

Background: The incidence and impact of postoperative complications are poorly described. Failure-to-rescue, the rate of death following complications, is an important quality measure for perioperative care but has not been investigated across multiple health care systems.

Methods: We analysed data collected during the International Surgical Outcomes Study, an international 7-day cohort study of adults undergoing elective inpatient surgery. Hospitals were ranked by quintiles according to surgical procedural volume (Q1 lowest to Q5 highest). For each quintile we assessed in-hospital complications rates, mortality, and failure-to-rescue. We repeated this analysis ranking hospitals by risk-adjusted complication rates (Q1 lowest to Q5 highest).

Results: A total of 44 814 patients from 474 hospitals in 27 low-, middle-, and high-income countries were available for analysis. Of these, 7508 (17%) developed one or more postoperative complication, with 207 deaths in hospital (0.5%), giving an overall failure-to-rescue rate of 2.8%. When hospitals were ranked in quintiles by procedural volume, we identified a three-fold variation in mortality (Q1: 0.6% vs Q5: 0.2%) and a two-fold variation in failure-to-rescue (Q1: 3.6% vs Q5: 1.7%). Ranking hospitals in quintiles by risk-adjusted complication rate further confirmed the presence of important variations in failure-to-rescue, indicating differences between hospitals in the risk of death among patients after they develop complications.

Conclusions: Comparison of failure-to-rescue rates across health care systems suggests the presence of preventable postoperative deaths. Using such metrics, developing nations could benefit from a data-driven approach to quality improvement, which has proved effective in high-income countries.

Impactfactor: 6.238

Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery

Haanschoten MC, Kreeftenberg HG, **Bouwman RA,** van Straten AH, Buhre WF, Soliman Hamad MA

J Cardiothorac Vasc Anesth. 2017 Feb;31(1):45-53. Epub 2016 Apr 22

OBJECTIVES: In the present study, the authors investigated the predictive value of postoperative peak arterial lactate levels for early and late mortality after cardiac surgery.

DESIGN: Retrospective analysis of prospectively collected data.

SETTING: Single-center study in an academic hospital.

PARTICIPANTS: Adult patients who underwent cardiac surgery between 2004 and 2014 (n = 16,376).

INTERVENTIONS: Different cardiac surgical procedures.

MEASUREMENTS AND RESULTS: Patients were classified according to the peak arterial lactate level (PALL) within 3 days postoperatively. Logistic regression analysis and Cox regression analysis were performed to identify postoperative peak arterial lactate level as a predictor for early and late mortality

respectively. In 8460 patients (51.7%), lactate was not measured postoperatively because these patients were managed according to the fast-track protocol. These patients constituted group 1 in our population but were excluded from the regression analysis. The remaining patients (n = 7,916; 48.3%) were divided according to the postoperative peak arterial lactate level (PALL): PALL<5 mmol/L (group 2), PALL 5 to 10 mmol/L (group 3), and PALL of>10 mmol/L (group 4). Early mortality was 3.7%, 20.4%, and 62.9% in groups 2, 3, and 4 respectively (p<0.0001). This mortality rate was significantly higher than that of group 1 (1.6%); p<0.0001. Multivariate regression analyses revealed postoperative peak arterial lactate as a significant predictor of 30-day mortality (odds ratio = 1.44 [1.39-1.48], p<0.001) as well as for late mortality (hazard ratio = 1.05 [1.01-1.10], p<0.025).

CONCLUSIONS: Postoperative peak arterial lactate level in patients undergoing cardiac surgery is an independent predictor for both early and late mortality.

Impactfactor: 1.699

Validation of the NexfinÂ® non-invasive continuous blood pressure monitoring validated against Riva-Rocci/Korotkoff in a bariatric patient population

Pouwels S, **Lascaris B,** Nienhuijs SW, **Arthur Bouwman RA**, **Buise MP**

J Clin Anesth. 2017 Jun; 39:89-95. Epub 2017 Mar 31

STUDY OBJECTIVE:The present study aimed to validate the Nexfin® monitor and to assess the accuracy compared to classical sphygmomanometry (Riva-Rocci/Korotkoff (RRK)) blood pressure (BP) measurements in patients with obesity scheduled for bariatric surgery.

DESIGN: Validation study.

SETTING: Outpatient clinic for bariatric surgery.

PATIENTS: 33 patients scheduled for bariatric surgery.

MEASUREMENTS: The validation process was done according to the protocols developed by the European Society of Hypertension from 2010. The Nexfin® monitor (Edwards Lifesciences/BMEYE B.V., Amsterdam, The Netherlands) calculates beat-to-beat blood pressure from finger pulse wave analysis. Measurements of systolic and diastolic BP were obtained using classical sphygmomanometry and the Nexfin® alternatingly.

MAIN RESULTS: In total 99 pairs of BP measurements were used. The device failed pass phase 1 as 65 systolic readings fell within 5mmHg (73 required). And 61, 76 and 90 diastolic readings fell within 5, 10 and 15mmHg respectively. Finally, it failed to pass phase 2 as 23 patients for systolic and 25 for diastolic had at least 2/3 of their comparisons falling within 5mmHg (24 required) but 10 subjects for systolic and 8 for diastolic had all three comparisons more than 5mmHg different from the RRK readings (zero allowed). Mean differences were 7.8±6.9mmHg for SBP and 8.0±7.2mmHg for DBP. CONCLUSION: Using the revised protocol, the Nexfin® device was not able to pass validation. However using the original protocol, the Nexfin® device passed phase 1 and 2.1 of the validation process and failed to pass phase 2.2.

Impactfactor: 1.677

What Do Anesthesiologists Know about p Values, Confidence Intervals, and Correlations: A Pilot Survey

Schober P, Bossers SM, **Dong PV,** Boer C, Schwarte LA

Anesthesiol Res Pract. 2017;2017:4201289.Epub 2017 Oct 12

Background: Statistical methods form the basis for clinical decision-making in evidence-based anesthesia. Data on the knowledge of anesthesiologists about statistics are lacking. This pilot study aims to provide a first impression of the anesthesiologists' understanding of commonly used concepts in statistics.

Methods: A cross-sectional pilot survey was performed at a major international anesthesia conference. The questionnaire consisted of three basic multiple-choice questions on the topics "p value," "confidence interval," and "correlation." Results of the questions are reported as percentage of correct answers (95% confidence interval).

Results: 65 questionnaires were analyzed. Forty participants were male, and mean age was 40 (standard deviation: 10) years. The question addressing the p value was correctly answered by 15% (95% CI: 8 to 27%) of respondents. The question concerning the 95% confidence interval was answered correctly by 28% (95% CI: 18 to 40%) of participants. For the question about correlation, a correct answer was given by 52% (95% CI: 40 to 64%). None of the participants answered all questions correctly, and 19 participants provided a wrong answer to all questions.

Conclusions: Anesthesiologists seem to demonstrate a poor understanding of statistical key concepts.

Further studies are needed to address statistical knowledge gaps among anesthesiologists more comprehensively.

Impactfactor: --

Apotheek

A 25% higher vancomycin maintenance dose is required in neutropenic hematologic patients

Bury D, ter Heine R, van de Garde EM, **Grouls RJ, Deenen MJ**

Nederlands Platform voor Farmaceutisch Onderzoek 2017;2:a1666

Impactfactor: --

Dose evaluation of lamivudine in human immunodeficiency virus-infected children aged 5 months to 18 years based on a population pharmacokinetic analysis

Janssen EJ, **Bastiaans DE**, Välitalo PA, van Rossum AM, Jacqz-Aigrain E, Lyall H, Knibbe CA, Burger DM

Br J Clin Pharmacol. 2017 Jun;83(6):1287-1297

AIM: The objectives of this study were to characterize age-related changes in lamivudine pharmacokinetics in children and evaluate lamivudine exposure, followed by dose recommendations for subgroups in which target steady state area under the daily plasma concentration-time curve (AUC0-24h) is not reached.

METHODS: Population pharmacokinetic modelling was performed in NONMEM using data from two model-building datasets and two external datasets [n = 180 (age 0.4-18 years, body weight 3.4-60.5 kg); 2061 samples (median 12 per child); daily oral dose 60-300 mg (3.9-17.6 mg kg-1)]. Steady state AUC0-24h was calculated per individual (adult target 8.9 mg·h l-1).

RESULTS: A two-compartment model with sequential zero order and first order absorption best described the data. Apparent clearance and central volume of distribution (% RSE) were 13.2 l h-1 (4.2%) and 38.9 l (7.0%) for a median individual of 16.6 kg, respectively. Bodyweight was identified as covariate on apparent clearance and volume of distribution using power functions (exponents 0.506 (20.2%) and 0.489 (32.3%), respectively). The external evaluation supported the predictive ability of the final model. In 94.5% and 35.8% of the children with a body weight >14 kg and <14 kg, respectively, the target AUC0-24h was reached.

CONCLUSION: Bodyweight best predicted the developmental changes in apparent lamivudine clearance and volume of distribution. For children aged 5 months-18 years with a body weight <14 kg, the dose should be increased from 8 to 10 mg kg-1 day-1 if the adult target for AUC0-24h is aimed for. In order to identify whether bodyweight influences bioavailability, clearance and/or volume of distribution, future analysis including data on intravenously administered lamivudine is needed.

Impactfactor: *3.493*

Following trends in steam sterilizer performance by quantitative monitoring of non-condensable gases

van Wezel RA, van Gastel A, de Ranitz A, van Doornmalen Gomez Hoyos JP

J Hosp Infect. 2017 Dec;97(4):357-362

Standards require a daily steam penetration test before starting production with a steam sterilizer. In many cases the results of steam penetration tests are not used for improvements or optimization of processes. This study aimed to detect whether trend analysis with an objective and quantifying steam penetration test has added value for the end-user. The databases of an objective quantifying steam penetration test, from the hospital and the manufacturer, are coupled and analysed. In this study, the databases included five steam sterilizers and approximately a four-year period. Based on the analysis, the process of the sterilizers was optimized. The results of the steam penetration tests became more stable over longer periods. This may result in lengthened periods between maintenance and validation. The analysis demonstrates that an objective, quantifying steam penetration test delivers more insights and knowledge of the functioning of the steam sterilization process. This knowledge may be used to optimize the process and reduce costs for the end-user.

Impactfactor: *3.126*

In vivo and in vitro palatability testing of a new paediatric formulation of valaciclovir

Bastiaans DE, Immohr LI, Zeinstra GG, Strik-Albers R, Pein-Hackelbusch M, van der Flier M, de Haan AFJ, Boelens JJ, Lankester AC, Burger DM, Warris A

Br J Clin Pharmacol. 2017 Dec;83(12):2789-2797

AIMS: The palatability of a new paediatric formulation of valaciclovir was assessed in children and their parents: non-inferiority of the new paediatric formulation (test formulation) compared to the reference formulation was investigated.

METHODS: In vivo palatability testing was performed in a randomized, two-period, multicentre, cross-over study. Children and their parents scored the liking of the new paediatric valaciclovir formulation

and the reference formulation on a 100 mm visual analogue scale (VAS). To support formulation development and palatability testing, electronic tongue measurements were applied.
RESULTS: The electronic tongue measurement indicated taste-masking capabilities for three different formulations in the developmental phase. A glycerol-based formulation was further tested and compared to the reference formulation prepared out of crushed and suspended tablets. The mean difference (95% CI) in VAS scores between both formulations, as indicated by the children (n = 20), was 2.4 (-8.5, 13) mm, in favour of the new paediatric valaciclovir formulation. The mean (95% CI) difference in VAS scores indicated by the parents (n = 20) was -0.9 (-12, 9.8) mm.
CONCLUSION: The palatability of the new paediatric valaciclovir formulation was considered non-inferior to the reference formulation prepared out of crushed tablets. We were able to optimize the study design and number of children to be included in the palatability testing by using electronic tongue measurements.

**Ten tijde van het onderzoek werkzaam bij Radboud Ziekenhuis.*
Impactfactor: 3.493

Letter regarding Zhao et al. entitled DPYD gene polymorphisms are associated with risk and chemotherapy prognosis in pediatric patients with acute lymphoblastic leukemia
Deenen MJ, Henricks LM, Sonke GS, Schellens JH, Meulendijks D
Tumour Biol. 2017 Jun;39(6):1010428317701629.

Zhao et al. investigated the association between germline genetic polymorphisms in DPYD, the gene encoding dihydropyrimidine dehydrogenase, and (1) the risk of developing pediatric acute lymphoblastic leukemia and (2) outcome of acute lymphoblastic leukemia following the treatment with 5-fluorouracil plus oxaliplatin (FOLFOX). The authors found that the common DPYD variant c.85T>C (rs1801265, DPYD*9A) was significantly associated with (1) risk of developing pediatric acute lymphoblastic leukemia, (2) complete response rate, (3) event-free survival, and (4) treatment-related toxicity. The authors conclude that patients carrying the c.85T>C C allele have an increased risk of developing acute lymphoblastic leukemia and have inferior outcome, and that DPYD c.85T>C can be used as a guide for individualized treatment and the decision to utilize 5-fluorouracil in acute lymphoblastic leukemia patients. In our view, the published article gives rise to multiple critical issues regarding the study's rationale and the methodology used, which strongly question the validity of the authors' conclusions.
Comment on: DPYD gene polymorphisms are associated with risk and chemotherapy prognosis in pediatric patients with acute lymphoblastic leukemia [Tumour Biol. 2016]

Impactfactor: 3.650

Naar een optimaal beheer van medicatie bij nierpatiënten : zelf doen waar het kan, overnemen waar het moet
Kerskes MC, Hengst M.
Pil 2017 (4):34-6.

Nierpatiënten zijn kwetsbare patiënten. In deze groep zien we veel multimorbiditeit, meerdere behandelaren en polyfarmacie. In de praktijk blijkt de medicatiebewaking bij deze groep patiënten vaak suboptimaal te zijn door het ontbreken van relevante informatie (zoals nierfunctie of dialysevorm) en hun actuele medicatiegebruik. Tevens blijkt dat niet alle nierpatiënten even therapietrouw zijn. Het Catharina Ziekenhuis in Eindhoven heeft samen met de Nierstichting, Nierpatiëntenvereniging en het Instituut voor Verantwoord Medicijngebruik een checklist ontwikkeld, waarmee het medicatiebeheer van nierpatiënten gestructureerd in kaart kan worden gebracht en mogelijkheden voor verbetering worden aangedragen.

Impactfactor: --

Pharmacogenetic analysis of irreversible severe cisplatin-induced nephropathy: a case report of a 27-year-old woman
de Jong C, Sanders S, Creemers GJ, Burylo AM, **Taks M,** Schellens JH, **Deenen MJ**
Br J Clin Pharmacol. 2017 Sep;83(9):2120-2122

In this report we describe a young patient diagnosed with bulky FIGO stage IIIb squamous cell cervix carcinoma with severe and irreversible nephropathy after three weekly low-doses of cisplatin. Besides several known risk factors such as hypomagnesemia and hypoalbuminemia, the patient also proved to be homozygously polymorphic for two polymorphisms within the COMT gene (c.615 + 310C>T and

c.616-367C>T). As COMT polymorphism has been associated with cisplatin-induced ototoxicity, its effect on nephrotoxicity of cisplatin should be the subject of further investigation.

Impactfactor: 3.493

Pharmacogenetic variants associated with outcome in patients with advanced gastric cancer treated with fluoropyrimidine and platinum-based triplet combinations: a pooled analysis of three prospective studies

Meulendijks D, Rozeman EA, Cats A, Sikorska K, Joerger M, **Deenen MJ**, Beijnen JH, Schellens JH

Pharmacogenomics J. 2017 Oct 17(5):441-451. doi: 10.1038/tpj.2016.81. Epub 2016 Dec 20

The main treatment for advanced gastric cancer is fluoropyrimidine and platinum-based chemotherapy. We investigated the clinical validitiy of 19 candidate pharmacogenetic variants in ENOSF1 (enolase superfamily member 1), TYMS, CDA, MTHFR, TYMP, DPYD, ERCC1, ERCC2, GSTP1, GSTT1, GSTM1, CYP3A4 and CYP3A5 in relation to overall survival (OS), progression-free survival, objective response rate (ORR) and toxicity in 185 patients receiving triplet chemotherapy. The formal significance threshold was P<0.0026. TYMS VNTR (variable number of 28-bp tandem repeats) 3?R/3?R genotype was formally associated with inferior ORR (odds ratio (OR) 0.3, P=0.0025), whereas ENOSF1 rs2612091 G/G was nominally associated with OS after adjustment for TYMS 3?R/3?R (hazard ratio (HR) 1.5, P=0.041). In a subgroup analysis of patients with locally advanced disease (n=33), ENOSF1 rs2612091 was strongly associated with OS (HR 6.5, P=0.001). CYP3A4*22/CYP3A5*3 genotype was nominally associated with grade 3/4 toxicity in patients receiving docetaxel-containing chemotherapy (P=0.0175). This is the first study suggesting that ENOSF1 rs2612091 is prognostic or predictive of OS in gastric cancer. This finding requires prospective validation.

Impactfactor: 2.184

Practical Value of Anti-Xa Activity in the Evaluation of Extracorporeal Circuit Anticoagulation during Haemodialysis: Results of a Cross-Sectional Single-Centre Study

Coene KL, Dekker MJ, **Kerskes MC**, Hengst M, Schonck MJ, Konings CJ, Scharnhorst V

Nephron. 2017;137(3):205-211

BACKGROUND/AIMS: Anticoagulation of the extracorporeal circuit is essential for adequate haemodialysis (HD). Low molecular weight heparins (LMWHs) are safe and sufficient towards achieving this goal. In the Netherlands, dosage is based on bodyweight and adjusted based on clinical events. LMWH levels during dialysis can be quantified through measurement of the anti-Xa activity and a target range of 0.5-1.0 IU/mL has been proposed. We aimed to evaluate the practical value of the anti-Xa activity to guide LMWH dosage in HD patients. Additionally, the value of the activated partial thromboplastin time (APTT) was investigated.

METHODS: All prevalent adult HD patients of our dialysis clinic were included. APTT and anti-Xa activity were measured before, during and after 2 dialysis sessions. Clinical and dialysis characteristics, including LMWH dosage, were derived from digital patient charts.

RESULTS: Our final study cohort consisted of 83 patients. LMWH dosage during dialysis was appropriate for bodyweight in 61% of cases, of which 50% reached an anti-Xa activity within the putative target range of 0.5-1.0 IU/mL. Forty-six percent of patients had an anti-Xa activity >1.0 IU/mL. Anti-Xa levels during and after dialysis were significantly correlated ($r = 0.803$, $p < 0.01$). No thrombotic or haemorrhagic complications were observed in this study. Correlation of APTT with anti-Xa activity was poor.

CONCLUSION: Anti-Xa activity measurements during dialysis can identify patients in whom LMWH dosage should be lowered in a subsequent dialysis session. Whether such an intervention leads to a decrease in haemorrhagic complications needs to be evaluated in prospective studies.

Impactfactor: 1.939

Pretreatment serum uracil concentration as a predictor of severe and fatal fluoropyrimidine-associated toxicity

Meulendijks D, Henricks LM, Jacobs BA, Aliev A, **Deenen MJ,** de Vries N, Rosing H, van Werkhoven E, de Boer A, Beijnen JH, Mandigers CM, Soesan M, Cats A, Schellens JH

Br J Cancer. 2017 May 23;116(11):1415-1424

BACKGROUND: We investigated the predictive value of dihydropyrimidine dehydrogenase (DPD) phenotype, measured as pretreatment serum uracil and dihydrouracil concentrations, for severe as well as fatal fluoropyrimidine-associated toxicity in 550 patients treated previously with fluoropyrimidines during a prospective multicenter study.

METHODS: Pretreatment serum concentrations of uracil and dihydrouracil were measured using a validated LC-MS/MS method. The primary endpoint of this analysis was global (any) severe fluoropyrimidine-associated toxicity, that is, grade ?3 toxicity according to the NCI CTC-AE v3.0, occurring during the first cycle of treatment. The predictive value of uracil and the uracil/dihydrouracil ratio for early severe fluoropyrimidine-associated toxicity were compared. Pharmacogenetic variants in DPYD (c.2846A>T, c.1679T>G, c.1129-5923C>G, and c.1601G>A) and TYMS (TYMS 5'-UTR VNTR and TYMS 3'-UTR 6-bp ins/del) were measured and tested for associations with severe fluoropyrimidine-associated toxicity to compare predictive value with DPD phenotype. The Benjamini-Hochberg false discovery rate method was used to control for type I errors at level q<0.050 (corresponding to P<0.010).

RESULTS: Uracil was superior to the dihydrouracil/uracil ratio as a predictor of severe toxicity. High pretreatment uracil concentrations (>16?ng?ml-1) were strongly associated with global severe toxicity (OR 5.3, P=0.009), severe gastrointestinal toxicity (OR 33.7, P<0.0001), toxicity-related hospitalisation (OR 16.9, P<0.0001), as well as fatal treatment-related toxicity (OR 44.8, P=0.001). None of the DPYD variants alone, or TYMS variants alone, were associated with severe toxicity.

CONCLUSIONS: High pretreatment uracil concentration was strongly predictive of severe, including fatal, fluoropyrimidine-associated toxicity, and is a highly promising phenotypic marker to identify patients at risk of severe fluoropyrimidine-associated toxicity.

Impactfactor: 6.176

Recommendation on testing for dihydropyrimidine dehydrogenase deficiency in the ESMO consensus guidelines for the management of patients with metastatic colorectal cancer

Deenen MJ, Meulendijks D

Ann Oncol. 2017 Jan 1; 28(1):184

Geen abstract beschikbaar

Impactfactor: 11.855

Short article: The effect of implementation of a treatment algorithm for infliximab on remission rates and drug costs in inflammatory bowel disease patients

Taks M, Pijls PA, Derijks LJ, **Ten Broeke R**, **Grouls RJ**, Curvers J, Gilissen LP

Eur J Gastroenterol Hepatol. 2017 Feb;29(2):169-173

INTRODUCTION: The effective, but expensive, drug infliximab is used in patients with inflammatory bowel disease (IBD). Monitoring infliximab trough levels and anti-infliximab antibody (ATI) formation can lead to a more cost-effective use of infliximab therapy. The aim of our study was to investigate the effect of implementation of a treatment algorithm for infliximab in a single-centre IBD cohort, focussing on remission rates and drug costs.

METHODS: IBD patients aged 18 years or older treated with infliximab were asked to participate in this study. Remission rates were assessed using faecal calprotectin levels and a validated questionnaire. Infliximab trough levels and ATIs were determined at baseline and at the third infliximab infusion. According to the advice given by the treatment algorithm, infliximab dosage adjustments were performed at the second infliximab infusion.

RESULTS: Between January and December 2015 a total of 62 IBD patients in our centre were treated with infliximab, of whom 33 (53%) patients agreed to participate in this study. The number of patients in remission was 28 (85%) at baseline and there were 13 dose adaptations suggested by the treatment algorithm for the successive second infusion. Four patients possessed undetectable infliximab levels and positive ATI status at baseline. After the second infusion, there were 29 (88%) patients in remission at the third infusion. All of this resulted in an annual drug cost reduction of &OV0556;47?026 (7.4%).

CONCLUSION: Our developed treatment algorithm of infliximab led to optimization of infliximab therapy in IBD patients by increasing remission rates and reducing drug costs.

Impactfactor: 1.968

Sustained Viral Suppression in HIV-infected Children on Once-daily Lopinavir/Ritonavir in Clinical Practice

Gondrie IP, **Bastiaans DE,** Fraaij PL, Driessen GJ, van der Knaap LC, Visser EG, van Jaarsveld P, de Groot R, Hartwig NG, Burger DM, van Rossum AM

Pediatr Infect Dis J. 2017 Oct;36(10):976-980

BACKGROUND: The use of lopinavir/ritonavir once-daily (LPV/r QD) has not been approved for children. Good short-term clinical, virologic and immunologic outcomes have been observed in children on LPV/r QD.

METHODS: We evaluated the long-term effectiveness of a LPV/r QD containing regimen in HIV-1-infected children in clinical practice. Selected children (0-18 years of age) with an undetectable HIV-1 RNA viral load (<50 copies/mL) for at least 6 months on a twice-daily LPV/r-containing regimen switched to LPV/r QD. The main outcome measures were the percentage of patients with an undetectable HIV-1 viral load each subsequent year after switch to LPV/r QD (on treatment and last observation carried forward), and virologic failure during follow-up (>400 copies/mL twice within 6 months). Also, the exposure to LPV on the initial once-daily dosing regimen was determined.
RESULTS: Forty children (median age: 6.5 years; range: 1.0-17) were included. Median follow-up was 6.3 years (range: 1.0-10.3). During yearly follow-up, the percentage of children with an undetectable viral load varied between 82% and 100% (on treatment) and 83% and 93% (last observation carried forward). Five children (12.5%) met the criteria for failure. CD4+ and CD8+ counts remained stable at normal values. Geometric mean LPV area under the plasma concentration-time curve (linear up-log down method) over a dosing interval from time 0 to 24 hours after dosing was 169.3?mg x h/L, and last observed drug concentration was 1.35?mg/L. Adverse events were encountered in 8 patients, were mainly gastrointestinal, and in these cases, no reason to stop treatment.
CONCLUSION: A once-daily LPV/r-containing regimen in HIV-1-infected children with intensive clinical and therapeutic drug monitoring is well tolerated and has good long-term clinical, virologic and immunologic outcomes.
Impactfactor: 2.486

Cardiologie

A novel synchronised diastolic injection method to reduce contrast volume during aortography for aortic regurgitation assessment: in vitro experiment of a transcatheter heart valve model

Miyazaki Y, Abdelghani M, de Boer ES, Aben JP, van Sloun M, Suchecki T, **van 't Veer M**, Collet C, Asano T, Katagiri Y, Tenekecioglu E, Soliman OII, Onuma Y, de Winter R, **Tonino P**, van de Vosse FN, Rutten MC, Serruys PW

EuroIntervention. 2017 Dec 20;13(11):1288-1295

AIMS: In the minimalist transcatheter aortic valve implantation (TAVI) era, the usage of transoesophageal echocardiography has become restricted. Conversely, aortography has gained clinical ground in quantifying prosthetic valve regurgitation (PVR) during the procedure. In a mock circulation system, we sought to compare the contrast volume required and the accuracy of aortographic videodensitometric PVR assessment using a synchronised diastolic and standard (non-synchronised) injection aortography.

METHODS AND RESULTS: Synchronised diastolic injection triggered by the signal stemming from the mock circulation was compared with standard non-synchronised injection. A transcatheter heart valve was implanted and was deformed step by step by advancing a screw perpendicularly to the cage of the valve in order to create increasing PVR. Quantitative measurement of PVR was derived from time-density curves of both a reference area (aortic root) and a region of interest (left ventricle) developed by a videodensitometric software. The volume of contrast required for the synchronised diastolic injection was significantly less than in the non-synchronised injection (8.1 [7.9-8.5] ml vs. 19.4 [19.2-19.9] ml, p<0.001). The correlation between the two methods was substantial (Spearman's coefficient rho ranging from 0.991 to 0.968). Intraobserver intra-class correlation coefficient for both methods of injection was 0.999 (95% CI: 0.996-1.000) for the synchronised diastolic and 0.999 (95% CI: 0.996-1.000) for the non-synchronised injection group. The mean difference in the rating was 0.17% and limits of agreement were ±1.64% for both groups.

CONCLUSIONS: A short synchronised diastolic injection enables contrast volume reduction during aortography without compromising the accuracy of the quantitative assessment of PVR using videodensitometry.

Impactfactor: 5.193

Accuracy of Fractional Flow Reserve Measurements in Clinical Practice: Observations From a Core Laboratory Analysis

Matsumura M, Johnson NP, Fearon WF, Mintz GS, Stone GW, Oldroyd KG, De Bruyne B, **Pijls NH**, Maehara A, Jeremias A

JACC Cardiovasc Interv. 2017 Jul 24;10(14):1392-1401

OBJECTIVES: The aim of this study was to compare site-reported measurements of fractional flow reserve (FFR) with FFR analysis by an independent core laboratory (CL).

BACKGROUND: FFR is an index of coronary stenosis severity that has been validated in multiple trials and is widely used in clinical practice. However, the incidence of suboptimal FFR measurements is unknown.

METHODS:

Patients undergoing FFR assessment within the CONTRAST (Can Contrast Injection Better Approximate FFR Compared to Pure Resting Physiology) study had paired, repeated measurements of multiple physiological metrics per local practice. An independent central physiology CL analyzed blinded pressure tracings off-line in a standardized fashion for comparison.

RESULTS: A total of 763 patients were included in the study; 4,946 distal coronary artery pressure/aortic pressure (nonhyperemic) and FFR tracings were analyzed by the CL (mean 6.5 tracings per patient). Pull-back data were available for 616 patients (80.7%), of whom 108 (17.5%) had signal drift, defined as distal coronary artery pressure/aortic pressure (nonhyperemic) <0.97 or >1.03. Among the remaining 4,217 tracings without evidence of signal drift, 222 (5.3%) were noted to have ventricularization of the aortic waveform, and 168 (4.0%) had aortic waveform distortion. Excluding cases with signal drift and waveform distortion, there was excellent agreement between CL-calculated and site-reported FFR, with a mean difference of 0.003 ± 0.02. Predictors of distorted waveforms were smaller guiding catheter size (odds ratio: 6.30; 95% confidence interval: 3.22 to 12.32; p < 0.001) and intracoronary adenosine use (odds ratio: 0.13; 95% confidence interval: 0.05 to 0.33; p < 0.001).

CONCLUSIONS: This FFR CL analysis showed that almost 10% of tracings demonstrated waveform artifacts, and an additional 17.5% had signal drift. Among adequate tracings, there was a close

correlation between site-reported and CL-analyzed FFR values. Attention to detail is critical for FFR studies to ensure adequate technique and optimal results.

Impactfactor: 8.841

Acute cardioversion vs a wait-and-see approach for recent-onset symptomatic atrial fibrillation in the emergency department: Rationale and design of the randomized ACWAS trial

Dudink E, Essers B, Holvoet W, Weijs B, Luermans J, Ramanna H, Liem A, van Opstal J, **Dekker L**, van Dijk V, Lenderink T, Kamp O, Kulker L, Rienstra M, Kietselaer B, Alings M, Widdershoven J, Meeder J, Prins M, van Gelder I, Crijns H

Am Heart J. 2017 Jan;183:49-53

BACKGROUND: Current standard of care for patients with recent-onset atrial fibrillation (AF) in the emergency department aims at urgent restoration of sinus rhythm, although paroxysmal AF is a condition that resolves spontaneously within 24 hours in more than 70% of the cases. A wait-and-see approach with rate-control medication only and when needed cardioversion within 48 hours of onset of symptoms is hypothesized to be noninferior, safe, and cost-effective as compared with current standard of care and to lead to a higher quality of life.

DESIGN: The ACWAS trial (NCT02248753) is an investigator-initiated, randomized, controlled, 2-arm noninferiority trial that compares a wait-and-see approach to the standard of care. Consenting adults with recent-onset symptomatic AF in the emergency department without urgent need for cardioversion are eligible for participation. A total of 437 patients will be randomized to either standard care (pharmacologic or electrical cardioversion) or the wait-and-see approach, consisting of symptom reduction through rate control medication until spontaneous conversion is achieved, with the possibility of cardioversion within 48 hours after onset of symptoms. Primary end point is the presence of sinus rhythm on 12-lead electrocardiogram at 4 weeks; main secondary outcomes are adverse events, total medical and societal costs, quality of life, and cost-effectiveness for 1 year.

CONCLUSIONS: The ACWAS trial aims at providing evidence for the use of a wait-and-see approach for patients with recent-onset symptomatic AF in the emergency department.

Impactfactor: 4.436

Adequate sensing of ventricular fibrillation?

Oomen AW, van Gelder BM, Bracke FA

Neth Heart J. 2017 Sep 25(9):528-529

Geen abstract beschikbaar

Impactfactor: 1.894

Agreement of the Resting Distal to Aortic Coronary Pressure With the Instantaneous Wave-Free Ratio

Kobayashi Y, Johnson NP, **Zimmermann FM**, Witt N, Berry C, Jeremias A, Koo BK, Esposito G, Rioufol G, Park SJ, Nishi T, Choi DH, Oldroyd KG, Barbato E, **Pijls NH**, De Bruyne B, Fearon WF, CONTRAST Study Investigators

J Am Coll Cardiol. 2017 Oct 24;70(17):2105-2113

BACKGROUND: Recently, 2 randomized controlled trials showed that the instantaneous wave-free ratio (iFR), a resting coronary physiological index, is noninferior to fractional flow reserve for guiding revascularization. The resting distal to aortic coronary pressure (Pd/Pa) measured at rest is another adenosine-free index widely available in the cardiac catheterization laboratory; however, little is known about the agreement of Pd/Pa using iFR as a reference standard.

OBJECTIVES: The goal of this study was to investigate the agreement of Pd/Pa with iFR.

METHODS: A total of 763 patients were prospectively enrolled from 12 institutions. iFR and Pd/Pa were measured under resting conditions. Using iFR =0.89 as a reference standard, the agreement of Pd/Pa and its best cutoff value were assessed.

RESULTS: According to the independent core laboratory analysis, iFR and Pd/Pa were analyzable in 627 and 733 patients (82.2% vs. 96.1%; $p < 0.001$), respectively. The median iFR and Pd/Pa were 0.90 (interquartile range: 0.85 to 0.94) and 0.92 (interquartile range: 0.88 to 0.95), and the 2 indices were highly correlated ($R2 = 0.93$; $p < 0.001$; iFR = 1.31 * Pd/Pa -0.31). According to the receiver-operating characteristic curve analysis, Pd/Pa showed excellent agreement (area under the curve: 0.98; 95% confidence interval: 0.97 to 0.99; $p < 0.001$) with a best cutoff value of Pd/Pa =0.91. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 93.0%, 91.4%, 94.4%, 93.3%, and 92.7%, respectively. These results were similar in patients with acute coronary syndrome and stable angina.

CONCLUSIONS: Pd/Pa was analyzable in a significantly higher number of patients than iFR. Pd/Pa showed excellent agreement with iFR, suggesting that it could be applied clinically in a similar fashion. (Can Contrast Injection Better Approximate FFR Compared to Pure Resting Physiology? [CONTRAST]; NCT02184117).

Impactfactor: 19.896

An unusual cause of left main coronary artery obstruction

Triantafyllis AS, Rega F, Dubois C, Desmet W

Acta Cardiol. 2017 Dec;72(6):687

Geen abstract beschikbaar

Ten tijde van publicatie verbonden aan: Department of Cardiovascular Medicine, University Hospitals Leuven, Leuven, Belgium.

Impactfactor: 0.808

Analysis of suboptimal stent deployment using intravascular ultrasound and coronary pressure pullback measurement

Tanaka N, **Pijls NH**, Yamashita J, Kimura Y, Ogawa M, Murata N, Sakoda K, Hoshino K, Hokama Y, Yamashina A

J Cardiol. 2017 Apr;69(4):613-618. doi: 10.1016/j.jjcc.2016.09.005. Epub 2016 Nov 19

BACKGROUND: There are some cases in whom a sufficient improvement in fractional flow reserve (FFR) could not be achieved even if anatomical results indicated satisfactory stent deployment. We investigated the relation of abnormal findings between intravascular ultrasound (IVUS) and coronary pressure pullback measurement (CP-PB).

METHODS: IVUS and CP-PB were investigated after stent deployment in 60 vessels in 53 patients. CP-PB criterion for adequate stent deployment was defined as a ratio of coronary pressure at the stent distal edge to the proximal edge (Psd/Psp) that is greater than 0.95.

RESULTS: Residual pressure gradient across the stent which was indicated by Psd/Psp=0.95 was present in 11 (18%), and four of them were caused by insufficient stent expansion (incomplete apposition and asymmetric dilation), and five of them were caused by issues with stent edge (edge dissection and incomplete coverage of the plaques). Insufficient FFR recovery which was recorded at distal part of target vessel was present in 10 (17%), and the main causes corresponded to inadequate stent deployment in half of the lesions, and presence of residual lesion at a non-stent segment in the other half. There were six lesions in whom Psd/Psp was =0.95 but FFR was =0.80. Disagreement between IVUS and CP-PB findings was seen in 12 (20%).

CONCLUSIONS: Residual pressure gradient across the stent can reflect not only an insufficient stent expansion but also issues with stent edges. The decision of optimum stent deployment as assessed by IVUS and CP-PB was mismatched in 20% of cases, therefore careful attention should be paid to decoding the CP-PB findings.

Impactfactor: 2.732

Appropriate or inappropriate ICD shock; what is the post-shock rhythm?

van Gelder BM, Ter Burg B, Bracke FA

Neth Heart J. 2017 Nov; 25(11):647-648

Geen abstract beschikbaar

Impactfactor: 1.894

Characteristics and Long-Term Prognosis of Patients ≤35 Years of Age with ST Segment Elevation Myocardial Infarction and "Normal or Near Normal" Coronary Arteries

Rallidis LS, Gialeraki A, **Triantafyllis AS***, Tsirebolos G, Liakos G, Moutsatsou P, Iliodromitis E

Am J Cardiol. 2017 Sep 1;120(5):740-746

There are scarce data regarding risk factors and prognosis of patients with premature ST segment elevation myocardial infarction (STEMI) and "normal or near normal" coronary arteries (N/NNCAs). We compared the characteristics and long-term prognosis of patients with premature STEMI and N/NNCAs with their counterparts with significant coronary artery disease (CAD). We recruited 330 patients who had STEMI ≤35 years of age and 167 age- and gender-matched controls. All patients underwent coronary angiography. Coronary arteries with no lesions or lesions causing <30% reduction in lumen diameter were defined as N/NNCAs, whereas narrowings causing ≥50% diameter reduction formed the significant CAD group. Lipid profile, homocysteine levels, and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism were determined. Sixty patients (18%) had N/NNCAs. Patients with N/NNCAs had lower

low-density lipoprotein-cholesterol and higher high-density lipoprotein-cholesterol levels, higher homocysteine levels, and higher prevalence of MTHFR TT genotype (34.6 vs 18%, p = 0.008) compared with patients with significant CAD. After a median follow-up of 8 years, cardiovascular events occurred in 105 (36%) of 291 patients with available follow-up data. Significant CAD was associated with higher risk for recurrent cardiovascular events after adjustment for traditional risk factors (hazard ratio 2.095, 95% confidence interval 1.088 to 3.664, p = 0.022) and additional adjustment for the left ventricular ejection fraction, reperfusion therapy, and persistent smoking (hazard ratio 1.869, 95% confidence interval 1.007 to 3.468, p = 0.041). In conclusion, patients with premature STEMI and N/NNCAs have fewer lipid abnormalities, higher homocysteine levels and prevalence of MTHFR TT genotype, and better long-term prognosis compared with their counterparts with significant CAD.

**Ten tijde van publicatie verbonden aan: Department of Cardiovascular Medicine, University Hospitals Leuven, Leuven, Belgium.*

Impactfactor: 3.398

Classical determinants of coronary artery disease as predictors of complexity of coronary lesions, assessed with the SYNTAX score

Montero-Cabezas JM, Karalis I, Wolterbeek R, Kraaijeveld AO, Hoefer IE, Pasterkamp G, **Pijls NH**, Doevendans PA, Walterberger J, Kuiper J, van Zonneveld AJ, Jukema JW

Neth Heart J. 2017 Sep;25(9):490-497

BACKGROUND: We need new biomarkers that can predict cardiovascular disease to improve both diagnosis and therapeutic strategies. The CIRCULATING CELLS study was designed to study the role of several cellular mediators of atherosclerosis as biomarkers of coronary artery disease (CAD). An objective and reproducible method for the quantification of CAD extension is required to establish relationships with these potential biomarkers. We sought to analyse the correlation of the SYNTAX score with known CAD risk factors to test it as a valid marker of CAD extension.

METHODS AND RESULTS: A subgroup of 279 patients (67.4% males) were included in our analysis. Main exclusion criteria were a history of previous percutaneous coronary intervention or surgical revascularisation that prevent an accurate assessment of the SS. Diabetes mellitus, smoking, renal insufficiency, body mass index and a history of CAD and myocardial infarction were all positively and strongly associated with a higher SYNTAX score after adjustment for the non-modifiable biological factors (age and sex). In the multivariate model, age and male sex, along with smoking and renal insufficiency, remain statistical significantly associated with the SYNTAX score.

CONCLUSION: In a selected cohort of revascularisation-naive patients with CAD undergoing coronary angiography, non-modifiable cardiovascular risk factors such as advanced age, male sex, as well as smoking and renal failure were independently associated with CAD complexity assessed by the SYNTAX score. The SYNTAX score may be a valid marker of CAD extension to establish relationships with potential novel biomarkers of coronary atherosclerosis.

Impactfactor: 1.894

Comparison of Different Diastolic Resting Indexes to iFR: Are They All Equal?

Van't Veer M, **Pijls NH**, Hennigan B, Watkins S, Ali ZA, De Bruyne B, **Zimmermann FM**, **van Nunen LX**, Barbato E, Berry C, Oldroyd KG

J Am Coll Cardiol. 2017 Dec 26;70(25):3088-3096

BACKGROUND: Pressure measurement for the duration of the wave-free period (WFP) is considered essential for resting-state physiological assessment of coronary stenosis severity using the instantaneous wave-free ratio (iFR).

OBJECTIVES: The aim of this study was to compare other diastolic resting indexes to iFR.

METHODS: In the population of the VERIFY2 (Pd/Pa vs iFR in an Unselected Population Referred for Invasive Angiography) study, iFR calculated by proprietary software (Volcano Harvest, Volcano Corporation, Rancho Cordova, California) was compared with the ratio of resting distal coronary pressure and aortic pressure during the complete duration of diastole (dPR), 25% to 75% of diastole (dPR25-75), and midpoint of diastole (dPRmid), along with Matlab calculated iFR (iFRmatlab) and iFR-like indexes shortening the length of the WFP by 50 and 100 ms (iFR-50ms and iFR-100ms), respectively. Mutual differences, Spearman correlations, area under the curve values from receiver-operating characteristic analyses, and diagnostic performance with respect to iFR and fractional flow reserve (FFR) were calculated for all indexes.

RESULTS: Median iFR in 197 patients with 257 vessels was 0.91 with an interquartile range of 0.87 to 0.95. The mutual differences (± SD) with iFR were 0.006 ± 0.011 (dPR), 0.001 ± 0.007 (dPR25-75), 0.001 ± 0.008 (dPRmid), 0.005 ± 0.009 (iFRmatlab), 0.003 ± 0.008 (iFR-50ms), and 0.001 ± 0.009 (iFR-100ms). Correlations for all indexes with iFR were >0.99 ($p < 0.001$ for all). Area under the curve values for predicting iFR were >0.99 for all indexes as well. Diagnostic accuracy compared with FFR was 76% to 77% for all indexes including iFR.

CONCLUSIONS: All diastolic resting indexes tested were identical to iFR, both numerically and with respect to their agreement with FFR. A numerically equal value to iFR can be determined without restriction to the WFP. Cutoff values, guidelines, and clinical recommendations for iFR can therefore be extended to these other indexes. (Pd/Pa vs iFR in an Unselected Population Referred for Invasive Angiography [VERIFY2]; NCT02377310).

Impactfactor: 19.896

Current MitraClip experience, safety and feasibility in the Netherlands

Rahhab Z, Kortlandt FA, Velu JF, Schurer RAJ, Delgado V, **Tonino P**, Boven AJ, Van den Branden BJ, Kraaijeveld AO, Voskuil M, Hoorntje J, van Wely M, van Houwelingen K, Bleeker GB, Rensing B, Kardys I, Baan J Jr, Van der Heyden JAS, Van Mieghem NM

Neth Heart J. 2017 Jun 25(6):394-400

PURPOSE: Data on MitraClip procedural safety and efficacy in the Netherlands are scarce. We aim to provide an overview of the Dutch MitraClip experience.

METHODS: We pooled anonymised demographic and procedural data of 1151 consecutive MitraClip patients, from 13 Dutch hospitals. Data was collected by product specialists in collaboration with local operators. Effect on mitral regurgitation was intra-procedurally assessed by transoesophageal echocardiography. Technical success and device success were defined according to modified definitions of the Mitral Valve Academic Research Consortium (MVARC).

RESULTS: Median age was 76 (interquartile range 69-82) years and 59% were males. Patients presented with =moderate mitral regurgitation and a predominance of functional mitral regurgitation (72%). Overall, 611 (53%) patients were treated with one Clip, 486 (42%) with =2 Clips and 54 (5%) received no Clip. The number of patients with =2 Clips increased from 22% in 2009 to 52% in 2016. Device success and technical success were 91 and 95%, respectively, and were consistent over the years. Significant reduction of mitral regurgitation by MitraClip was achieved in 94% of patients and was observed more often in patients with functional mitral regurgitation (95% vs. 91%, p = 0.025). Device time declined from 145?min in 2009 to 55?min in 2016.

CONCLUSION: MitraClip experience in the Netherlands is growing with excellent technical success and device success. Over the years, device time decreased and more patients were treated with =2 Clips.

Impactfactor: 1.894

Diabetes does not impact the diagnostic performance of contrast-based fractional flow reserve: insights from the CONTRAST study

Gargiulo G, Stabile E, Ferrone M, Barbato E, **Zimmermann FM** , Adjedj J, Hennigan B, Matsumura M, Johnson NP, Fearon WF, Jeremias A, Trimarco B, Esposito G CONTRST Study Investigators

Cardiovasc Diabetol. 2017 Jan 13 16(1):7

BACKGROUND: Adenosine-free coronary pressure wire metrics have been proposed to test the functional significance of coronary artery lesions, but it is unexplored whether their diagnostic performance might be altered in patients with diabetes.

METHODS: We performed a post-hoc analysis of the CONTRAST study, which prospectively enrolled an international cohort of patients undergoing routine fractional flow reserve (FFR) assessment for standard indications. Paired, repeated measurements of all physiology metrics (Pd/Pa, iFR, contrast-based FFR, and FFR) were made. A central core laboratory analyzed blinded pressure tracings in a standardized fashion.

RESULTS: Of 763 subjects enrolled at 12 international centers, 219 (29%) had diabetes. The two groups were well-balanced for age, clinical presentation (stable or unstable), coronary vessel studied, volume and type of intracoronary contrast, and volume of intracoronary adenosine. A binary threshold of cFFR = 0.83 produced an accuracy superior to both Pd/Pa and iFR when compared with FFR = 0.80 in the absence of significant interaction with diabetes status; indeed, accuracy in subgroups of patients with or without diabetes was similar for cFFR (86.7 vs 85.4% respectively; p = 0.76), iFR (84.2 vs 80.0%, p = 0.29) and Pd/Pa (81.3 vs 78.9%, p = 0.55). There was no significant heterogeneity between patients with or

without diabetes in terms of sensitivity and specificity of all metrics. The area under the receiver operating characteristic (ROC) curve was largest for cFFR compared with Pd/Pa and iFR which were equivalent (cFFR 0.961 and 0.928; Pd/Pa 0.916 and 0.870; iFR 0.911 and 0.861 in diabetic and non-diabetic patients respectively).

CONCLUSIONS: cFFR provides superior diagnostic performance compared with Pd/Pa or iFR for predicting FFR irrespective of diabetes.

Impactfactor: 4.752

Dutch outcome in implantable cardioverter-defibrillator therapy (DO-IT): registry design and baseline characteristics of a prospective observational cohort study to predict appropriate indication for implantable cardioverter-defibrillator

van Barreveld M, Dijkgraaf MG, Hulleman M, Boersma LVA, Delnoy PP, Meine M, Tuinenburg AE, Theuns DA, **van der Voort PH**, Kimman GP, Buskens E, Tijssen JP, Bruinsma N, Verstraelen TE, Zwinderman AH, van Dessel PH, Wilde AA; DO-IT investigators

Neth Heart J. 2017 Oct;25(10):574-580

BACKGROUND: Implantable cardioverter-defibrillators (ICDs) are widely used for the prevention of sudden cardiac death. At present, both clinical benefit and cost-effectiveness of ICD therapy in primary prevention patients are topics of discussion, as only a minority of these patients will eventually receive appropriate ICD therapy.

METHODS/DESIGN: The DO-IT Registry is a nationwide prospective cohort with a target enrolment of 1,500 primary prevention ICD patients with reduced left ventricular function in a setting of structural heart disease. The primary outcome measures are death and appropriate ICD therapy for ventricular tachyarrhythmias. Secondary outcome measures are inappropriate ICD therapy, death of any cause, hospitalisation for ICD related complications and for cardiovascular reasons. As of December 2016, data on demographic, clinical, and ICD characteristics of 1,468 patients have been collected. Follow-up will continue up to 24 months after inclusion of the last patient. During follow-up, clinical and ICD data are collected based on the normal follow-up of these patients, assuming ICD interrogations take place every six months and clinical follow-up is once a year. At baseline, the mean age was 66 (standard deviation [SD] 10) years and 27% were women.

CONCLUSION: The DO-IT Registry represents a real-world nationwide cohort of patients receiving ICDs for primary prevention of sudden cardiac death with reduced left ventricular function in a setting of structural heart disease. The registry investigates the efficacy of the current practice and aims to develop prediction rules to identify subgroups who will not (sufficiently) benefit from ICD implantation and to provide results regarding costs and budget impact of targeted supply of primary preventions ICDs.

Impactfactor:1.894

Effect of functional electrical stimulation on cardiovascular outcomes in patients with chronic heart failure

Kadoglou NP, Mandila C, Karavidas A, Farmakis D, Matzaraki V, Varounis C, Arapi S, Perpinia A, Parissis J

Eur J Prev Cardiol. 2017 May 24(8):833-839

Background/design Functional electrical stimulation of lower limb muscles is an alternative method of training in patients with chronic heart failure (CHF). Although it improves exercise capacity in CHF, we performed a randomised, placebo-controlled study to investigate its effects on long-term clinical outcomes. Methods We randomly assigned 120 patients, aged 71 ± 8 years, with stable CHF (New York Heart Association (NYHA) class II/III (63%/37%), mean left ventricular ejection fraction 28 ± 5%), to either a 6-week functional electrical stimulation training programme or placebo. Patients were followed for up to 19 months for death and/or hospitalisation due to CHF decompensation. Results At baseline, there were no significant differences in demographic parameters, CHF severity and medications between groups. During a median follow-up of 383 days, 14 patients died (11 cardiac, three non-cardiac deaths), while 40 patients were hospitalised for CHF decompensation. Mortality did not differ between groups (log rank test P = 0.680), while the heart failure-related hospitalisation rate was significantly lower in the functional electrical stimulation group (hazard ratio (HR) 0.40, 95% confidence interval (CI) 0.21-0.78, P = 0.007). The latter difference remained significant after adjustment for prognostic factors: age, gender, baseline NYHA class and left ventricular ejection fraction (HR 0.22, 95% CI 0.10-0.46, P < 0.001). Compared to placebo, functional electrical stimulation training was associated with a lower occurrence of the composite endpoint (death or heart failure-related hospitalisation) after adjustment for the above-mentioned prognostic factors (HR 0.21, 95% CI 0.103-0.435, P < 0.001). However, that effect was

mostly driven by the favourable change in hospitalisation rates. Conclusions In CHF patients, 6 weeks functional electrical stimulation training reduced the risk of heart failure-related hospitalisations, without affecting the mortality rate. The beneficial long-term effects of this alternative method of training require further investigation.

Impactfactor: 3.606

Effect of Using the HEART Score in Patients With Chest Pain in the Emergency Department: A Stepped-Wedge, Cluster Randomized Trial

Poldervaart JM, Reitsma JB, Backus BE, Koffijberg H, Veldkamp RF, Ten Haaf ME, Appelman Y, Mannaerts HFJ, **van Dantzig JM, van den Heuvel M, El Farissi M**, Rensing BJW, Ernst NM, Dekker IM, den Hartog FR, Oosterhof T, Lagerweij GR, Buijs EM, van Hessen MW, Landman MA, van Kimmenade RR, Cozijnsen L, Bucx JJ, van Ofwegen-Hanekamp CE, Cramer MJ, Six AJ, Doevendans PA, Hoes AW

Ann Intern Med. 2017 May 16 166(10):689-697. Erratum in: Ann Intern Med. 2017 Jul 18 167(2):144

Background: The HEART (History, Electrocardiogram, Age, Risk factors, and initial Troponin) score is an easy-to-apply instrument to stratify patients with chest pain according to their short-term risk for major adverse cardiac events (MACEs), but its effect on daily practice is unknown.

Objective: To measure the effect of use of the HEART score on patient outcomes and use of health care resources.

Design: Stepped-wedge, cluster randomized trial. (ClinicalTrials.gov: NCT01756846).

Setting: Emergency departments in 9 Dutch hospitals.

Patients: Unselected patients with chest pain presenting at emergency departments in 2013 and 2014.

Intervention: All hospitals started with usual care. Every 6 weeks, 1 hospital was randomly assigned to switch to "HEART care," during which physicians calculated the HEART score to guide patient management.

Measurements: For safety, a noninferiority margin of a 3.0% absolute increase in MACEs within 6 weeks was set. Other outcomes included use of health care resources, quality of life, and cost-effectiveness.

Results: A total of 3648 patients were included (1827 receiving usual care and 1821 receiving HEART care). Six-week incidence of MACEs during HEART care was 1.3% lower than during usual care (upper limit of the 1-sided 95% CI, 2.1% [within the noninferiority margin of 3.0%]). In low-risk patients, incidence of MACEs was 2.0% (95% CI, 1.2% to 3.3%). No statistically significant differences in early discharge, readmissions, recurrent emergency department visits, outpatient visits, or visits to general practitioners were observed.

Limitation: Physicians were hesitant to refrain from admission and diagnostic tests in patients classified as low risk by the HEART score.

Conclusion: Using the HEART score during initial assessment of patients with chest pain is safe, but the effect on health care resources is limited, possibly due to nonadherence to management recommendations.

Impactfactor: 17.202

Evaluation of bifurcation stenting techniques at Catharina Hospital, Eindhoven in 2013

Leus SJ, van Hagen E, Zimmermann FM, van Nunen LX, van 't Veer M, Koolen J, Pijls NH

Neth Heart J. 2017 Jan;25(1):40-46

AIMS:

Percutaneous coronary intervention (PCI) of bifurcation lesions can be performed using various techniques. The aim of this study was to analyse the outcome of various techniques of bifurcation stenting in all patients undergoing bifurcation stenting at one large intervention centre in 2013, taking into account that more complex lesions might more often warrant a two-stent technique.

METHODS AND RESULTS:

This retrospective study included 260 consecutive patients who underwent non-primary PCI of a bifurcation lesion at the Catharina Hospital, Eindhoven, in 2013. Patients were classified into two groups: one-stent technique (provisional stenting), and two-stent techniques (culotte, crush and T-stenting). The primary endpoint was the rate of restenosis at 1 year. The secondary endpoints were procedural complications (side branch occlusion, periprocedural infarction, and death) and major adverse cardiac events (MACE) at 1 year. Periprocedural complications occurred in 15 patients (5.8?%) with no difference between the groups (p = 0.27). After 1 year, restenosis occurred in 3.2?% of the patients in the one-stent technique group and 7.3?% in the two-stent technique group (p = 0.20). MACE at 1 year did not differ between the groups at 11.9?% and 12.2?% respectively (p = 1.00).

CONCLUSIONS:

This study shows that there is no significant difference between restenosis rate, or any other outcome parameter, with the different techniques of bifurcation stenting. Since provisional stenting is the simplest, most straightforward and cheapest approach, if technically feasible this technique has our preference as the initial approach, and an upgrade can be considered if the result is insufficient.

Impactfactor: 1.894

Fractional flow reserve and pressure-bounded coronary flow reserve to predict outcomes in coronary artery disease

Ahn JM, **Zimmermann FM**, Johnson NP, Shin ES, Koo BK, Lee PH, Park DW, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, **Pijls NH**, Park SJ

Eur Heart J. 2017 Jul 1 38(25):1980-1989

Aims: Fractional flow reserve (FFR) has proven to its prognostic and therapeutic value. However, the additive prognostic value of coronary flow reserve (CFR) remains unclear. This study sought to investigate the clinical utility of combined FFR and CFR measurements to predict outcomes.

Methods and results: Using the prospective, multicentre Interventional Cardiology Research Incooperation Society-FFR registry, a total of 2088 lesions from 1837 patients were included in this substudy. Based on baseline and hyperaemic pressure gradients, we computed physiologic limits of CFR [the so called pressure-bounded (pb) CFR] and classified lesions as low (<2) or high (=2). The primary endpoint was major adverse cardiac events (MACE, a composite of cardiac death, myocardial infarction, and revascularization) analysed on a per-patient basis. During a median follow-up of 1.9 years (inter-quartile range: 1.0-3.0 years), MACE occurred in 5.7% of patients with FFR?=0.80 vs. 2.8% of patients with FFR?>0.80 [adjusted hazard ratio (aHR): 2.15, 95% confidence interval (CI): 1.19-3.89; P?=?0.011. In contrast, the incidence of MACE did not differ between patients with pb-CFR?<?2 vs. pb-CFR?=?2 (4.2% vs. 4.2%; aHR: 0.98, CI: 0.60 to 1.58; P?=?0.92). Incorporation of FFR significantly improved model prediction of MACE (global ?2 38.8-48.1, P?=?0.002). However, pb-CFR demonstrated no incremental utility to classify outcomes (global ?2 48.1-48.2, P?>?0.99).

Conclusions: In this large, prospective registry of over 2000 coronary lesions, FFR was strongly associated with clinical outcomes. In contrast, a significant association between pb-CFR and clinical events could not be determined and adding knowledge of pb-CFR did not improve prognostication over FFR alone.

Impactfactor: 20.212

Giant coronary aneurysm exposed on routine echocardiogram

Zelis JM, Andriessen FP, Elenbaas TW, Peels KH

Eur Heart J. 2017 Nov 14;38(43):3240

Geen abstract beschikbaar

Impactfactor: 20.212

Incidence, risk factors, and predictors of infective endocarditis in adult congenital heart disease: focus on the use of prosthetic material

Kuijpers JM, Koolbergen DR, Groenink M, **Peels KC**, Reichert CLA, Post MC, Bosker HA, Wajon EM, Zwinderman AH, Mulder BJM, Bouma BJ

Eur Heart J. 2017 Jul 7 38(26):2048-2056

Aims: Adult congenital heart disease (ACHD) predisposes to infective endocarditis (IE). Surgical advancements have changed the ACHD population, whereas associated prosthetic material may constitute additional IE targets. We aimed to prospectively determine contemporary incidence, risk factors, and predictors of IE in a nationwide ACHD cohort, focusing on the presence of prosthetics.

Methods and results: We identified 14 224 patients prospectively followed in the CONCOR ACHD registry (50.5% female, median age 33.6years). IE incidence was determined using Poisson regression, risk factors and predictors using Cox regression. Overall incidence was 1.33 cases/1000 person-years (124 cases in 93 562 person-years). For risk-factor analysis, presence of prosthetics was forced-as separate time-updated variables for specific prosthetics-into a model with baseline characteristics univariably associated with IE. Valve-containing prosthetics were independently associated with greater risk both short- and long term after implantation [0-6 months: hazard ratio (HR)?=?17.29; 7.34-40.70, 6-12 months: HR?=?15.91; 6.76-37.45, beyond 12 months: HR?=?5.26; 3.52-7.86], non-valve-containing prosthetics, including valve repair, only in the first 6 months after implantation (HR?=?3.34; 1.33-8.41),

not thereafter. A prediction model was derived and validated using bootstrapping techniques. Independent predictors of IE were baseline valve-containing prosthetics, main congenital heart defect, multiple defects, previous IE, and sex. The model had fair discriminative ability and provided accurate predictions up to 10 years.

Conclusions: This study provides IE incidence estimates, and determinants of IE risk in a nationwide ACHD cohort. Our findings, essentially informing IE prevention guidelines, indicate valve-containing prosthetics as a main determinant of IE risk whereas other prosthetics, including valve-repair, are not associated with increased risk long term after implantation.

Impactfactor: 20.212

Influence of Contrast Media Dose and Osmolality on the Diagnostic Performance of Contrast Fractional Flow Reserve

Nishi T, Johnson NP, De Bruyne B, Berry C, Gould KL, Jeremias A, Oldroyd KG, Kobayashi Y, Choi DH, **Pijls NH**, Fearon WF; CONTRAST Study Investigators

Circ Cardiovasc Interv. 2017 Oct;10(10). pii: e004985

BACKGROUND: Contrast fractional flow reserve (cFFR) is a method for assessing functional significance of coronary stenoses, which is more accurate than resting indices and does not require adenosine. However, contrast media volume and osmolality may affect the degree of hyperemia and therefore diagnostic performance.

METHODS AND RESULTS: cFFR, instantaneous wave-free ratio, distal pressure/aortic pressure at rest, and FFR were measured in 763 patients from 12 centers. We compared the diagnostic performance of cFFR between patients receiving low or iso-osmolality contrast (n=574 versus 189) and low or high contrast volume (n=341 versus 422) using FFR=0.80 as a reference standard. The sensitivity, specificity, and overall accuracy of cFFR for the low versus iso-osmolality groups were 73%, 93%, and 85% versus 87%, 90%, and 89%, and for the low versus high contrast volume groups were 69%, 99%, and 83% versus 82%, 93%, and 88%. By receiver operating characteristics (ROC) analysis, cFFR provided better diagnostic performance than resting indices regardless of contrast osmolality and volume (P<0.001 for all groups). There was no significant difference between the area under the curve of cFFR in the low- and iso-osmolality groups (0.938 versus 0.957; P=0.40) and in the low- and high-volume groups (0.939 versus 0.949; P=0.61). Multivariable logistic regression analysis showed that neither contrast osmolality nor volume affected the overall accuracy of cFFR; however, both affected the sensitivity and specificity.

CONCLUSIONS: The overall accuracy of cFFR is greater than instantaneous wave-free ratio and distal pressure/aortic pressure and not significantly affected by contrast volume and osmolality. However, contrast volume and osmolality do affect the sensitivity and specificity of cFFR.

Impactfactor: 6.598

Influenza infection and heart failure-vaccination may change heart failure prognosis?

Kadoglou NP, Bracke F, Simmers T, Tsiodras S, Parissis J

Heart Fail Rev. 2017 May; 22(3):329-336

The interaction of influenza infection with the pathogenesis of acute heart failure (AHF) and the worsening of chronic heart failure (CHF) is rather complex. The deleterious effects of influenza infection on AHF/CHF can be attenuated by specific immunization. Our review aimed to summarize the efficacy, effectiveness, safety, and dosage of anti-influenza vaccination in HF. In this literature review, we searched MEDLINE and EMBASE from January 1st 1966 to December 31st, 2016, for studies examining the association between AHF/CHF, influenza infections, and anti-influenza immunizations. We used broad criteria to increase the sensitivity of the search. HF was a prerequisite for our search. The search fields used included "heart failure," "vaccination," "influenza," "immunization" along with variants of these terms. No restrictions on the type of study design were applied. The most common clinical scenario is exacerbation of pre-existing CHF by influenza infection. Scarce evidence supports a potential positive association of influenza infection with AHF. Vaccinated patients with pre-existing CHF have reduced all-cause morbidity and mortality, but effects are not consistently documented. Immunization with higher antigen quantity may confer additional protection, but such aggressive approach has not been generally advocated. Further studies are needed to delineate the role of influenza infection on AHF/CHF pathogenesis and maintenance. Annual anti-influenza vaccination appears to be an effective measure for secondary prevention in HF. Better immunization strategies and more efficacious vaccines are urgently necessary.

Impactfactor: 3.481

Instantaneous Wave-free Ratio versus Fractional Flow Reserve
Pijls NH, De Bruyne
N Engl J Med. 2017 Oct 19;377(16):1596
Comment on
Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. [N Engl J Med. 2017]
Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI. [N Engl J Med. 2017]
Impactfactor: 72.406

Intracoronary Hypothermia Before Reperfusion to Reduce Reperfusion Injury in Acute Myocardial Infarction: A Novel Hypothesis and Technique
Otterspoor LC, van Nunen LX, van 't Veer M, Johnson NP, **Pijls NH**
Ther Hypothermia Temp Manag. 2017 Dec; 7(4):199-205.Epub 2017 May 18

Because current reperfusion strategies in acute myocardial infarction (AMI) seem to be exhausted in terms of additional mortality benefit, there remains a need for new methods to attenuate reperfusion injury and, thereby, further reduce myocardial infarct size and improve long-term survival. Therapeutic hypothermia (32-35°C) diminishes reperfusion injury and reduces infarct size in a variety of animal models of AMI if provided before reperfusion. In human studies this reduction has not been confirmed so far, most likely because systemic cooling acts slowly, and therefore, the target temperature is not reached in time or at all in a substantial number of patients. Furthermore, systemic cooling can cause adverse effects such as severe shivering, volume overload, and an enhanced adrenergic state. In most randomized clinical trials, however, subgroups of patients with anterior myocardial infarction that reached the target temperature before reperfusion did show a reduction in infarct size. To transform therapeutic hypothermia into a clinically feasible treatment for AMI, its method must be modified. An ideal technique should be quick enough to achieve sufficient myocardial hypothermia before reperfusion, without significant delay and without the adverse effects of systemic cooling. In this review, we propose a novel, potentially feasible method of selective intracoronary hypothermia to overcome the problems encountered with prior techniques.

Impactfactor: 1.787

Intracoronary hypothermia for acute myocardial infarction in the isolated beating pig heart
Otterspoor LC, **van Nunen LX**, Rosalina TT, **Veer MV**, Tuijl SV, Stijnen M, Rutten MC, van de Vosse FN, **Pijls NH.**
Am J Transl Res. 2017 Feb 15;9(2):558-568. eCollection 2017

Hypothermia may attenuate reperfusion injury and thereby improve acute myocardial infarction therapy. Systemic cooling trials failed to reduce infarct size, perhaps because the target temperature was not reached fast enough. The use of selective intracoronary hypothermia combined with intracoronary temperature monitoring allows for titrating to target temperature and optimizing the cooling rate. We aimed to the test the feasibility of intracoronary cooling for controlled, selective myocardial hypothermia in an isolated beating pig heart. In five porcine hearts the left anterior descending artery (LAD) was occluded by an over-the-wire balloon (OTWB). After occlusion, saline at 22°C was infused through the OTWB lumen for 5 minutes into the infarct area at a rate of 30 ml/min. Thereafter the balloon was deflated but infusion continued with saline at 4°C for 5 minutes. Distal coronary temperature was continuously monitored by a pressure/temperature guidewire. Myocardial temperature at several locations in the infarct and control areas was recorded using needle thermistors. In the occlusion phase, coronary temperature decreased by 11.4°C (range 9.4-12.5°C). Myocardial temperature throughout the infarct area decreased by 5.1°C (range 1.8-8.1°C) within three minutes. During the reperfusion phase, coronary temperature decreased by 6.2°C (range 4.1-10.3°C) and myocardial temperature decreased by 4.5°C (range 1.5-7.4°C). Myocardial temperature outside the infarct area was not affected. In the isolated beating pig heart with acute occlusion of the LAD, we were able to rapidly "induce, maintain, and control" a stable intracoronary and myocardial target temperature of at least 4°C below body temperature without side effects and using standard PCI equipment, justifying further studies of this technique in humans.

Impactfactor: --

Letter by Zimmermann et al Regarding Article, Excess Cardiovascular Risk in Women Relative to Men Referred for Coronary Angiography Is Associated With Severely Impaired Coronary Flow Reserve, Not Obstructive Disease

Zimmermann FM, Zelis JM, Van't Veer M.

Circulation. 2017 Jul 11;136(2):239-240

geen abstract beschikbaar

Impactfactor: 19.309

Long-term serial non-invasive multislice computed tomography angiography with functional evaluation after coronary implantation of a bioresorbable everolimus-eluting scaffold: the ABSORB cohort B MSCT substudy

Onuma Y, Collet C, van Geuns RJ, de Bruyne B, Christiansen E, **Koolen J**, Smits P, Chevalier B, McClean D, Dudek D, Windecker S, Meredith I, Nieman K, Veldhof S, Ormiston J, Serruys PW, ABSORB Investigators

Eur Heart J Cardiovasc Imaging. 2017 May 1 18(8):870-879

Aims:

Multimodality invasive imaging of the first-in-man cohort demonstrated at 5 years stable lumen dimensions and a low rate of major adverse cardiac events (MACE). However, the long-term non-invasive assessment of this device remains to be documented. The objective was to describe the 72-month multislice computed tomography (MSCT) angiographic and functional findings after the implantation of the second iteration of the fully resorbable everolimus-eluting polymeric scaffold.

Methods and results:

In the ABSORB Cohort B trial patients with non-complex de novo lesions were treated with second iteration bioresobable vascular scaffold (BVS). MSCT angiography was performed as an optional investigation at 18 months; patients were reconsented for a second investigation at 72 months. MSCT data were analysed at independent core laboratories for quantitative analysis of lumen dimensions and for calculation of fractional flow reserve derived from computed tomography (FFRCT). From the overall Cohort B (101 patients), 53 patients underwent MSCT imaging at 72 months. The MACE rate was 1.9% (1/53). At 72 months, the median minimal lumen area (MLA) was 4.05?mm2 (interquartile range [IQR]: 3.15-4.90) and the mean percentage area stenosis was 18% (IQR: 4.75-31.25), one scaffold was totally occluded. In 39 patients with paired MSCT analysis, the MLA significantly increased from the first to the second follow-up (??=?0.80?mm2, P?=?0.002). The change in the median FFRCT scaffold gradient between time points was zero.

Conclusion:

The long-term serial non-invasive MSCT evaluation with FFRCT assessment after bioresorbable scaffold implantation confirmed in-scaffold late lumen enlargement with the persistence of normalization of the FFRCT.

Impactfactor: 5.990

Long-term vagal stimulation for heart failure: Eighteen month results from the NEural Cardiac TherApy foR Heart Failure (NECTAR-HF) trial

De Ferrari GM, Stolen C, Tuinenburg AE, Wright DJ, Brugada J, Butter C, Klein H, Neuzil P, **Botman CJ**, Castel MA, D'Onofrio A, de Borst GJ, Solomon S, Stein KM, Schubert B, Stalsberg K, Wold N, Ruble S, Zannad F

Int J Cardiol. 2017 Oct 1;244:229-234

BACKGROUND:

The NECTAR-HF study evaluated safety and feasibility of vagal nerve stimulation (VNS) for the treatment of heart failure patients. The first six-month randomized phase of the study did not show improvement in left ventricular remodelling in response to VNS. This study reports the 18-month results and provides novel findings aiming to understand the lack of efficacy of VNS, including a new technique assessing the effects of VNS.

METHODS: Ninety-six patients were randomized 2:1 to active or inactive VNS for 6months, thereafter VNS was activated for all patients. The primary safety endpoint was 18-month all-cause mortality.

RESULTS:

Ninety-one patients continued in the long-term evaluation with active VNS. The on-therapy survival estimate at 18months was 95% with a 95% one-sided lower confidence limit of 91%, (better than the predefined criterion). Left ventricular systolic volume decreased in the crossover group (VNS OFF?ON; 144±37 to 139±40, p<0.05) after VNS activation; LVESD (5.02±0.77 to 4.96±0.82, p>0.05) and LVEF (33.2±4.9 to 33.3±6.5, p>0.05) did not change. A new technique to detect subtle heart rate changes

during Holter recordings, i.e. "heat maps", revealed that VNS evoked heart rate response in only 13/106 studies (12%) at 6 and 12months with active VNS.
CONCLUSIONS:
Although a favourable long-term safety profile was found, improvements in the efficacy endpoints were not seen with VNS. A new technique for detecting acute heart rate responses to VNS suggests that the recruitment of nerve fibres responsible for heart rate changes were substantially lower in NECTAR-HF than in pre-clinical models.

Impactfactor: 6.189

Mapping for Acute Transvenous Phrenic Nerve Stimulation Study (MAPS Study)

Dekker LR, Gerritse B, Scheiner A, Kornet L.

Pacing Clin Electrophysiol. 2017 Mar 40(3):294-300

BACKGROUND:
Central sleep apnea syndrome, correlated with the occurrence of heart failure, is characterized by periods of insufficient ventilation during sleep. This acute study in 15 patients aims to map the venous system and determine if diaphragmatic movement can be achieved by phrenic nerve stimulation at various locations within the venous system.
METHODS:
Subjects underwent a scheduled catheter ablation procedure. During the procedural waiting time, one multielectrode electrophysiology catheter was subsequently placed at the superior and inferior vena cava and the junctions of the left jugular and left brachiocephalic vein and right jugular and right brachiocephalic vein, for phrenic nerve stimulation (1-2 seconds ON/2-3 seconds OFF, 40 Hz, pulse width 210 μs). Diaphragmatic movement was assessed manually and by a breathing mask. During a follow-up assessment between 2 and 4 weeks postprocedure, occurrence of adverse events was assessed.
RESULTS:
In all patients diaphragmatic movement was induced at one or more locations using a median threshold of at least 2 V and maximally 7.5 V (i.e., e 3.3 mA, 14.2 mA). The lowest median current to obtain diaphragmatic stimulation without discomfort was found for the right brachiocephalic vein (4.7 mA). In 12/15 patients diaphragmatic movement could be induced without any discomfort, but in three patients hiccups occurred.
CONCLUSION:
Diaphragmatic stimulation from the brachiocephalic and caval veins is feasible. Potential side effects should be eliminated by adapting the stimulation pattern. This information could be used to design a catheter, combining cardiac pacing with enhancing diaphragm movement during a sleep apnea episode.

Impactfactor: 1.486

Non-invasive FFRCT revealing severe inducible ischaemia in an anomalous right coronary artery

Zimmermann FM, Kobayashi Y, Mullen WL, Fearon WF

Eur Heart J. 2017 Sep 1;38(33):2569

Geen abstract beschikbaar

Impactfactor: 20.212

Noninvasive pulmonary transit time: A new parameter for general cardiac performance

de Lepper AG, Herold IH, Saporito S, Bouwman RA, Mischi M, Korsten HH, Reesink K, **Houthuizen P**

Echocardiography. 2017 Aug;34(8):1138-1145

INTRODUCTION: Pulmonary transit time (PTT) assessed with contrast-enhanced ultrasound (CEUS) is a novel tool
to evaluate cardiac function. PTT represents the time for a bolus of contrast to pass from the right to the left ventricle, measured according to the indicator dilution principles using CEUS. We investigated the hypothesis that PTT is a measure of general cardiac performance in patient populations eligible for cardiac resynchronization therapy (CRT).
METHODS:
The study population consisted of heart failure patients referred for CRT with NYHA class II-IV, left ventricular ejection fraction (LVEF)=35% and QRS=120 ms. CEUS, ECG, and blood were analyzed, and participants completed a quality of life questionnaire at baseline and 3 months after CRT implantation. Normalized PTT (nPTT) was calculated to compensate for the heart rate. Correlations were assessed with Pearson's or Spearman's coefficients and stratified for rhythm and NYHA class.

RESULTS:

The study population consisted of 94 patients (67 men) with a mean age of 70±8.9 years. (n)PTT was significantly correlated with left ventricular parameters (rs =-.487, P<.001), right ventricular parameters (r=-.282, P=.004), N-terminal pro-B-type natriuretic peptide (NT-proBNP) (rs =.475, P<.001), and quality of life (rs =.364, P<.001). Stronger significant correlations were found in patients in sinus rhythm.

CONCLUSION:

CEUS-derived PTT and nPTT correlate to a fair degree with measures of systolic and diastolic function, NT-pro-BNP, and quality of life. As CEUS-derived PTT can be obtained easily, noninvasively and at the bedside, it is a promising future measure of general cardiac performance.

Impactfactor: 1.314

Optical coherence tomography findings: insights from the "randomised multicentre trial investigating angiographic outcomes of hybrid sirolimus-eluting stents with biodegradable polymer compared with everolimus-eluting stents with durable polymer in chronic total occlusions" (PRISON IV) trial

Teeuwen K*, Spoormans EM, Bennett J, Dubois C, Desmet W, Ughi GJ, Belmans A, Kelder JC, Tijssen JGP, Agostoni P, Suttorp MJ, Adriaenssens T

EuroIntervention. 2017 Aug 4;13(5):e522-e530

AIMS:

The PRISON IV trial investigated the next-generation sirolimus-eluting stent (SES) with ultra-thin struts and biodegradable polymer against the second-generation everolimus-eluting stent (EES) with thin struts and durable polymer in patients with successfully recanalised chronic total occlusions (CTO). In this study, we examined the secondary optical coherence tomography endpoints.

METHODS AND RESULTS:

The main PRISON IV trial randomised 330 patients to either SES or EES. At nine months, 281 (85%) patients underwent repeat angiography. Of these, 60 consecutive patients received optical coherence tomography divided over both stent groups. The mean number of struts analysed was 750±337 and 633±358 in SES and EES patients, respectively (p=0.07). The minimal lumen area, minimal stent area, maximal neointima area and neointimal thickness were comparable between the groups (4.8±2.1 and 4.4±1.5 mm2; 5.3±1.8 and 5.3±1.4 mm2; 2.5±2.0 and 2.2±1.5 mm2; 0.7±1.7 and 0.4±0.2 mm). The percentage of uncovered struts was higher with EES (6.2±7.5% and 11.9±13.4%, p=0.04), whereas the percentage of malapposed struts and mean number of coronary evaginations were significantly higher with SES (2.9±4.0% and 1.2±2.4%, p=0.02; 18.5±17.7 and 5.3±3.1, p=0.004).

CONCLUSIONS:

The optical coherence tomography findings of this substudy demonstrated improved strut coverage with ultra-thin strut SES with bioresorbable polymer compared to thin-strut EES with durable polymer in CTO. On the other hand, SES showed a higher rate of stent strut malappositon and coronary evaginations. The clinical relevance of these findings remains to be demonstrated

** ten tijde van publicatie werkzaam bij:* Department of Cardiology, St. Antonius Hospital, Nieuwegein.

Impactfactor: 5.193

Predicting the infarct-related artery in STEMI from the surface ECG: independent validation of proposed criteria

Eerdekens R, Chavez JF, Fox JM, Flaherty JD**, Dekker LR,** Johnson NP

EuroIntervention. 2017 Oct 20; 13(8):953-961

AIMS:

This study independently evaluated the diagnostic performance of electrocardiographic (ECG) criteria to predict the infarct-related artery (IRA) in patients with an acute ST-segment elevation myocardial infarction (STEMI). While a number of ECG criteria have been proposed to predict the IRA in STEMI, many of these "rules" came from modestly sized populations and did not undergo external validation. Therefore, we aimed to evaluate popular criteria from the literature in an independent cohort.

METHODS AND RESULTS:

All acute STEMI cases over a 10-year period from a single hospital were retrospectively identified. We excluded patients with a missing pre-intervention ECG, irretrievable angiographic films, prior coronary artery bypass grafting, left bundle branch block, ventricular pacing, or not meeting strict STEMI criteria. After review of the angiograms for the IRA, cases with either no or multiple culprits were excluded. We included 480 subjects meeting STEMI criteria in inferior leads (192, 40%), anterior leads (184, 38%), both anterior and inferior leads (88, 18%), isolated lateral leads (nine, 2%), or a posterior pattern (seven, 1%).

Notably, every pattern except isolated lateral STEMI included an IRA in both the right and left coronary arteries.

CONCLUSIONS:

Existing ECG criteria to predict the IRA in STEMI have modest diagnostic performance when externally validated, and lower than in the original reports. Distinguishing the level of obstruction in the left anterior descending artery remains especially challenging. Hence, their use should be pragmatic when selecting an initial catheter for treating STEMI, since discordances will occur when compared to the actual angiogram.

Impactfactor: 5.193

Prognostic Value of Fractional Flow Reserve Measured Immediately After Drug-Eluting Stent Implantation

Piroth Z, Toth GG, **Tonino PA**, Barbato E, Aghlmandi S, Curzen N, Rioufol G, **Pijls NH**, Fearon WF, Jüni P, De Bruyne B

Circ Cardiovasc Interv. 2017 Aug;10(8). pii: e005233

BACKGROUND:

The predictive value of fractional flow reserve (FFR) measured immediately after percutaneous coronary intervention (PCI) with drug-eluting stent placement has not been prospectively investigated. We investigated the potential of post-PCI FFR measurements to predict clinical outcome in patients from FAME 1 and 2 trials (Fractional Flow Reserve or Angiography for Multivessel Evaluation).

METHODS AND RESULTS:

All patients of FAME 1 and FAME 2 who had post-PCI FFR measurement were included. The primary outcome was vessel-oriented composite end point at 2 years, defined as vessel-related cardiovascular death, vessel-related spontaneous myocardial infarction, and ischemia-driven target vessel revascularization. Eight hundred thirty-eight vessels in 639 patients were analyzed. Baseline FFR values did not differ between vessels with versus without vessel-oriented composite end point (0.66±0.11 versus 0.63±0.14, respectively; P=0.207). Post-PCI FFR was significantly lower in vessels with vessel-oriented composite end point (0.88±0.06 versus 0.90±0.06, respectively; P=0.019). Comparing the 2-year outcome of lower and upper tertiles of post-PCI FFR significant difference was found favoring upper tertile in terms of overall vessel-oriented composite end point (9.2% versus 3.8%, respectively; hazard ratio, 1.46; 95% confidence interval, 1.02-2.08; P=0.037) and target vessel revascularization (7.0% versus 2.4%, respectively; hazard ratio, 1.59; 95% confidence interval, 1.03-2.46; P=0.037). When adjusted to sex, hypertension, diabetes mellitus, target vessel, serial stenosis, and baseline percentage diameter stenosis, a strong trend was preserved in terms of target vessel revascularization (harzard ratio, 1.55; 95% confidence interval, 0.97-2.46; P=0.066), favoring the upper tertile. Post-PCI FFR of 0.92 was found to have the highest diagnostic accuracy; however, the positive likelihood ratio remained low (<1.4).

CONCLUSIONS:

A higher post-PCI FFR value is associated with a better vessel-related outcome. However, its predictive value is too low to advocate its use as a surrogate clinical end point.

Predicting the infarct-related artery in STEMI from the surface ECG: independent validation of proposed criterIa

Impactfactor: 6.598

Randomized Multicenter Trial Investigating Angiographic Outcomes of Hybrid Sirolimus-Eluting Stents With Biodegradable Polymer Compared With Everolimus-Eluting Stents With Durable Polymer in Chronic Total Occlusions: The PRISON IV Trial

Teeuwen K*, van der Schaaf RJ, Adriaenssens T, **Koolen JJ**, Smits PC, Henriques JP, Vermeersch PH, Tjon Joe Gin RM, Schölzel BE, Kelder JC, Tijssen JG, Agostoni P, Suttorp MJ

JACC Cardiovasc Interv. 2017 Jan 23;10(2):133-143

OBJECTIVES: The aim of this study was to investigate the efficacy and safety of the hybrid ultrathin-strut sirolimus-eluting stent (SES) with biodegradable polymer compared with the thin-strut everolimus-eluting stent (EES) with durable polymer in successfully recanalized chronic total occlusions (CTOs).

BACKGROUND: The introduction of drug-eluting stents revolutionized the treatment of CTOs. However, limited data are available on new-generation drug-eluting stents with biodegradable polymer in CTOs.

METHODS: In this multicenter trial, patients were randomized, after successful CTO recanalization, to either SES or EES. The primary noninferiority endpoint was in-segment late lumen loss (noninferiority margin 0.2 mm). Secondary endpoints included in-stent late lumen loss and clinical endpoints.

RESULTS: Overall, 330 patients were included. At 9 months, angiography was available in 281 patients (85%). Duration of occlusion =3 months was 92.5%, with mean stent length of 52.4 ± 28.1 mm versus 52.3 ± 26.5 mm in the SES and EES groups. The primary noninferiority endpoint, in-segment late lumen loss, was not met for SES versus EES (0.13 ± 0.63 mm vs. 0.02 ± 0.47 mm; p = 0.08, 2-sided; difference 0.11 mm; 95% confidence interval: -0.01 to 0.25 mm; pnoninferiority = 0.11, 1-sided). In-stent late lumen loss was comparable between SES and EES (0.12 ± 0.59 mm vs. 0.07 ± 0.46 mm; p = 0.52). The incidence of in-stent and in-segment binary restenosis was significantly higher with SES compared with EES (8.0% vs. 2.1%; p = 0.028), with comparable rates of reocclusions (2.2% vs. 1.4%; p = 0.68). Clinically indicated target lesion and target vessel revascularization (9.2% vs. 4.0% [p = 0.08] and 9.2% vs. 6.0% [p = 0.33]), target vessel failure (9.9% vs. 6.6%; p = 0.35), and definite or probable stent thrombosis (0.7% vs. 0.7%; p = 1.00) were comparable between the SES and EES groups.

CONCLUSIONS: This randomized trial failed to show noninferiority of hybrid SES relative to EES in terms of in-segment late lumen loss in successfully recanalized CTOs. Furthermore, a statistically significantly higher rate of binary restenosis was found with SES.

** Ten tijde van publicatie werkzaam bij: Department of Cardiology, St. Antonius Hospital, Nieuwegein.*
Impactfactor: 8.841

Rationale of a novel study design for the BIOFLOW V study, a prospective, randomized multicenter study to assess the safety and efficacy of the Orsiro sirolimus-eluting coronary stent system using a Bayesian approach

Doros G, Massaro JM, Kandzari DE, Waksman R, **Koolen JJ**, Cutlip DE, Mauri L
Am Heart J. 2017 Nov;193:35-45

BACKGROUND:

Traditional study design submitted to the Food and Drug Administration to test newer drug-eluting stents (DES) for marketing approval is the prospective randomized controlled trial. However, several DES have extensive clinical data from trials conducted outside the United States that have led to utilization of a novel design using the Bayesian approach. This design was proposed for testing DES with bioresorbable polymer compared with DES most commonly in use today that use durable polymers for drug elution.

STUDY DESIGN AND OBJECTIVES:

This prospective, multicenter, randomized, controlled trial is designed to assess the safety and efficacy of the Orsiro bioresorbable polymer sirolimus-eluting stent (BP SES). Up to 1,334 subjects with up to 3 de novo or restenotic coronary artery lesions who qualify for percutaneous coronary intervention with stenting will be randomized 2:1 to the BP SES versus the Xience durable polymer everolimus-eluting stent (DP EES). Data from this trial will be combined with data from 2 similarly designed trials that also randomize subjects to BP SES and DP EES (BIOFLOW II, N=452 and BIOFLOW IV, N=579) by using a Bayesian approach. The primary end point is target lesion failure at 12 months post index procedure, defined as cardiac death, target vessel myocardial infarction, or clinically driven target lesion revascularization, and the primary analysis is a test of noninferiority of the BP SES versus DP EES on the primary end point according to a noninferiority delta of 3.85%. Secondary end points include stent thrombosis and the individual components of target lesion failure. Subjects will be followed for 5 years after randomization.

CONCLUSIONS:

The BIOFLOW V trial offers an opportunity to assess clinical outcomes in patients treated with coronary revascularization using the Orsiro BP SES relative to a commonly used DP EES. The use of a Bayesian analysis combines a large randomized cohort of patients 2 two smaller contributing randomized trials to augment the efficiency of the comparison.

Impactfactor: 4.436

Real life dabigatran and metabolite concentrations, focused on inter-patient variability and assay differences in patients with atrial fibrillation

Boonen K, Schmitz E, **Rozestraten F**, van den Heuvel D, Brunsveld L, **van der Voort P***, van de Kerkhof D*
Clin Chem Lab Med. 2017 Oct 26;55(12):2002-2009.

BACKGROUND:

Dabigatran is prescribed to increasing numbers of patients with atrial fibrillation (AF). Although routine monitoring is not considered to be useful, measuring drug concentrations can be clinically relevant in specific situations. The aim of this study was the comparison of different functional and non-functional assays for determination of dabigatran concentrations at different timepoints in a real-life patient population with AF. We focused on the differences between assays in identifying patients with low drug

concentrations. Furthermore, we studied the effect of glucuronidation on the established concentration as determined with different assays.
METHODS:
This study established dabigatran concentration ranges in 40 real-life AF patients by an ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) reference method and compared these with results from coagulation assays (Hemoclot dTT, LD-dTT and ECA). Samples were taken just before and 2 and 4 h after taking the drug.
RESULTS:
A wide range of concentrations at different time points was found in this patient group. Coagulation assays correlate best with UPLC-MS/MS results that include the glucuronidated metabolites, showing that the pharmacologically active glucuronides are also measured in coagulation testing. The LD-dTT has the best agreement with UPLC-MS/MS and combines good sensitivity with high specificity. Several patients show consistently low or high drug concentrations, implying that drug exposure differs between patients.
CONCLUSIONS:
Based on the association of dabigatran concentrations with bleeding and thromboembolic risk, we believe that dabigatran monitoring could be beneficial for further optimizing anticoagulation therapy in AF.

Impactfactor: 3.432

Recommendations for the use of bioresorbable vascular scaffolds in percutaneous coronary interventions : 2017 revision

Everaert B, Wykrzykowska JJ, **Koolen J**, van der Harst P, den Heijer P, Henriques JP, van der Schaaf R, de Smet B, Hofma SH, Diletti R, Weevers A, Hoorntje J, Smits P, van Geuns RJ

Neth Heart J. 2017 Jul;25(7-8):419-428

BACKGROUND: To eliminate some of the potential late limitations of permanent metallic stents, the bioresorbable coronary stents or 'bioresorbable vascular scaffolds' (BVS) have been developed.
METHODS: We reviewed all currently available clinical data on BVS implantation.
RESULTS: Since the 2015 position statement on the appropriateness of BVS in percutaneous coronary interventions, several large randomised trials have been presented. These have demonstrated that achieving adequate 1 and 2 year outcomes with these first-generation BVS is not straightforward. These first adequately powered studies in non-complex lesions showed worse results if standard implantation techniques were used for these relatively thick scaffolds. Post-hoc analyses hypothesise that outcomes similar to current drug-eluting stents are still possible if aggressive lesion preparation, adequate sizing and high-pressure postdilatation are implemented rigorously. As long as this has not been confirmed in prospective studies the usage should be restricted to experienced centres with continuous outcome monitoring. For more complex lesions, results are even more disappointing and usage should be discouraged. When developed, newer generation scaffolds with thinner struts or faster resorption rates are expected to improve outcomes. In the meantime prolonged dual antiplatelet therapy (DAPT, beyond one year) is recommended in an individualised approach for patients treated with current generation BVS.
CONCLUSION: The new 2017 recommendations downgrade and limit the use of the current BVS to experienced centres within dedicated registries using the updated implantation protocol and advise the prolonged usage of DAPT. In line with these recommendations the manufacturer does not supply devices to the hospitals without such registries in place.

Impactfactor: 1.894

Response by Piroth et al to Letter Regarding Article, Prognostic Value of Fractional Flow Reserve Measured Immediately After Drug-Eluting Stent Implantation

Piroth Z, Toth GG, **Tonino PAL**, Barbato E, Aghlmandi S, Curzen N, Rioufol G, **Pijls NH**, Fearon WF, Juni P, De Bruyne B

Circ Cardiovasc Interv. 2017 Oct;10(10). pii: e005973

geen abstract beschikbaar

Impactfactor: 6.598

Safety and feasibility of selective intracoronary hypothermia in acute myocardial infarction

Otterspoor LC, Van 't Veer M, Van Nunen LX, Brueren GR, Tonino PA, Wijnbergen IF, Helmes H, Zimmermann FM, Van Hagen E, Johnson NP, Pijls NH

EuroIntervention. 2017 Dec 8;13(12):e1475-e1482

AIMS:

Hypothermia reduces reperfusion injury and infarct size in animal models of acute myocardial infarction if started before reperfusion. Human studies have not confirmed benefit, probably due to insufficient myocardial cooling and adverse systemic effects. This study sought to assess the safety and feasibility of a novel method for selective, sensor-monitored intracoronary hypothermia.

METHODS AND RESULTS:

Ten patients undergoing primary percutaneous coronary intervention (PPCI) were included. Saline at room temperature was administered distal to the culprit lesion through an inflated overthe- wire balloon (OTWB) in order to cool the endangered myocardium for 10 minutes (occlusion phase). Next, the OTWB was deflated and cooling continued with saline at 4°C for another 10 minutes (reperfusion phase). A sensor-tipped temperature wire in the distal coronary artery allowed titration of the infusion rate to achieve the desired coronary temperature (6°C below body temperature). Target coronary temperature was achieved within 27 seconds (median; IQR 21-46). Except for two patients with inferior wall infarction experiencing transient conduction disturbances, no side effects occurred. Systemic temperature remained unchanged. Finally, PPCI was performed as per routine.

CONCLUSIONS:

Selective hypothermia of the infarct area by intracoronary infusion of saline provides a novel method to reduce coronary temperature quickly and guarantee local myocardial hypothermia. In anterior wall myocardial infarctions, the protocol appeared safe, without serious haemodynamic or systemic side effects. In inferior wall myocardial infarctions, transient conduction abnormalities of short duration occurred. Potentially, selective intracoronary delivery of hypothermia could attenuate reperfusion injury caused by traditional PPCI.

Impactfactor: 5.193

Saline-Induced Coronary Hyperemia: Mechanisms and Effects on Left Ventricular Function

De Bruyne B, Adjedj J, Xaplanteris P, Ferrara A, Mo Y, Penicka M, Floré V, Pellicano M, Toth G, Barbato E, Duncker DJ, **Pijls NH**

Circ Cardiovasc Interv. 2017 Apr 10(4). pii: e004719

BACKGROUND: During thermodilution-based assessment of volumetric coronary blood flow, we observed that intracoronary infusion of saline increased coronary flow. This study aims to quantify the extent and unravel the mechanisms of saline-induced hyperemia.

METHODS AND RESULTS: Thirty-three patients were studied; in 24 patients, intracoronary Doppler flow velocity measurements were performed at rest, after intracoronary adenosine, and during increasing infusion rates of saline at room temperature through a dedicated catheter with 4 lateral side holes. In 9 patients, global longitudinal strain and flow propagation velocity were assessed by transthoracic echocardiography during a prolonged intracoronary saline infusion. Taking adenosine-induced maximal hyperemia as reference, intracoronary infusion of saline at rates of 5, 10, 15, and 20 mL/min induced 6%, 46%, 111%, and 112% of maximal hyperemia, respectively. There was a close agreement of maximal saline- and adenosine-induced coronary flow reserve (intraclass correlation coefficient, 0.922; P<0.001). The same infusion rates given through 1 end hole (n=6) or in the contralateral artery (n=6) did not induce a significant increase in flow velocity. Intracoronary saline given on top of an intravenous infusion of adenosine did not further increase flow. Intracoronary saline infusion did not affect blood pressure, systolic, or diastolic left ventricular function. Heart rate decreased by 15% during saline infusion (P=0.021).

CONCLUSIONS: Intracoronary infusion of saline at room temperature through a dedicated catheter for coronary thermodilution induces steady-state maximal hyperemia at a flow rate =15 mL/min. These findings open new possibilities to measure maximal absolute coronary blood flow and minimal microcirculatory resistance.

Impactfactor: 6.598

Salt intake and blood pressure response to percutaneous renal denervation in resistant hypertension

de Beus E, de Jager RL, Beeftink MM, Sanders MF, Spiering W, Vonken EJ, Voskuil M, Bots ML, Blankestijn PJ; SYMPATHY study group: **Tonino WA, Brueren BR,** Konings CJ

J Clin Hypertens (Greenwich). 2017 Nov;19(11):1125-1133

The effect of lowering sympathetic nerve activity by renal denervation (RDN) is highly variable. With the exception of office systolic blood pressure (BP), predictors of the BP-lowering effect have not been identified. Because dietary sodium intake influences sympathetic drive, and, conversely, sympathetic activity influences salt sensitivity in hypertension, we investigated 24-hour urinary sodium excretion in participants of the SYMPATHY trial. SYMPATHY investigated RDN in patients with resistant hypertension. Both 24-hour ambulatory and office BP measurements were end points. No relationship was found for baseline sodium excretion and change in BP 6 months after RDN in multivariable-adjusted regression analysis. Change in the salt intake-measured BP relationships at 6 months vs baseline was used as a measure for salt sensitivity. BP was 8 mm Hg lower with similar salt intake after RDN, suggesting a decrease in salt sensitivity. However, the change was similar in the control group, and thus not attributable to RDN.

Impactfactor: 3.242

Serial 5-Year Evaluation of Side Branches Jailed by Bioresorbable Vascular Scaffolds Using 3-Dimensional Optical Coherence Tomography: Insights From the ABSORB Cohort B Trial (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions)

Onuma Y, Grundeken MJ, Nakatani S, Asano T, Sotomi Y, Foin N, Ng J, Okamura T, Wykrzykowska JJ, de Winter RJ, van Geuns RJ, **Koolen J**, Christiansen E, Whitbourn R, McClean D, Smits P, Windecker S, Ormiston JA, Serruys PWCirc Cardiovasc Interv. 2017 Sep;10(9). pii: e004393

BACKGROUND:

The long-term fate of Absorb bioresorbable vascular scaffold (Abbott Vascular, Santa Clara, CA) struts jailing side branch ostia has not been clarified. We therefore evaluate serially (post-procedure and at 6 months, 1, 2, 3, and 5 years) the appearance and fate of jailed Absorb bioresorbable vascular scaffold struts.

METHODS AND RESULTS:

We performed 3-dimensional optical coherence tomographic analysis of the ABSORB Cohort B trial (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions) up to 5 years using a novel, validated cut-plane analysis method. We included 29 patients with a total of 85 side branch ostia. From the 12 ostia which could be assessed in true serial fashion, 7 showed a pattern of initial decrease in the ostial area free from struts, followed by an increase in strut-free ostial area toward the end of the 5 years of follow-up. In a repeated-measures analysis with time as fixed variable and ostial area free from struts as dependent variable, we showed a numeric decrease in the estimated ostial area free from struts from 0.75 mm2 (baseline) to 0.68 mm2 (first follow-up visit at 6 months or 1 year) and 0.63 mm2 (second follow-up visit at 2 or 3 years). However, from the second visit to the 5-year follow-up visit, there was a statistically significant increase from 0.63 to 0.89 mm2 (P=0.001). Struts overlying an ostium divided the ostium into compartments, and the number of these compartments decreased over time.

CONCLUSIONS:

This study showed that in most cases, the side branch ostial area free from struts initially decreased. However, with full scaffold bioresorption, the ostial area free from scaffold increased between 2 to 3 years and 5 years in the vast majority of patients.

Impactfactor: 6.598

Serial Assessment of Tissue Precursors andÂ Progression of Coronary Calcification Analyzed by Fusion of IVUS and OCT: 5-Year Follow-Up of Scaffolded and Nonscaffolded Arteries

Zeng Y, Tateishi H, Cavalcante R, Tenekecioglu E, Suwannasom P, Sotomi Y, Collet C, Nie S, Jonker H, Dijkstra J, Radu MD, Räber L, McClean DR, van Geuns RJ, Christiansen EH, Fahrni T, **Koolen J**, Onuma Y, Bruining N, Serruys PW.

JACC Cardiovasc Imaging. 2017 Oct 10(10 Pt A):1151-1161. Epub 2017 Mar 15

OBJECTIVES:

The aim of this study was to assess calcium growth with fused grayscale intravascular ultrasound (IVUS), IVUS-virtual histology, and optical coherence tomography (OCT) from baseline to 5-year follow-up in patients treated with bioresorbable vascular scaffolds.
BACKGROUND:
IVUS and OCT have individual strengths in assessing plaque composition and volume. Fusion of images obtained using these methods could potentially aid in coronary plaque assessment.
METHODS:
Anatomic landmarks and endoluminal radiopaque markers were used to fuse OCT and IVUS images and match baseline and follow-up.
RESULTS:
Seventy-two IVUS-virtual histology and OCT paired matched cross-sectional in- and out-scaffold segments were fused at baseline and follow-up. In total, 46 calcified plaques at follow-up were detected using the fusion method (33 in-scaffold, 13 out-scaffold), showing either calcium progression (52.2%) or de novo calcifications (47.8%). On OCT, calcification volume increased from baseline to follow-up by 2.3 ± 2.4 mm3 (p = 0.001). The baseline virtual histologic tissue precursors of dense calcium at follow-up were necrotic core in 73.9% and fibrous or fibrofatty plaque in 10.9%. In 15.2%, calcium was already present at baseline. Precursors on OCT were lipid pool in 71.2%, fibrous plaque in 4.3%, and fibrocalcific plaque in 23.9%.
CONCLUSIONS:
The use of OCT and IVUS fusion imaging shows similar calcium growth in- and out-scaffold segments. Necrotic core is the most frequent precursor of calcification. The scaffold resorption process creates a tissue layer that re-caps the calcified plaques.

Impactfactor: 10.189

Stenting of bifurcation lesions

Pijls NH, Leus SJ, Zimmermann FM, van Nunen LX, Van't Veer M, Koolen J, van Hagen E

Neth Heart J. 2017 Apr;25(4):290-291

Geen abstract beschikbaar

Impactfactor: 1.894

The association of ferritin with cardiovascular and all-cause mortality in community-dwellers: The English longitudinal study of ageing

Kadoglou NP, Biddulph JP, Rafnsson SB, Trivella M, Nihoyannopoulos P, Demakakos P

PLoS One. 2017 Jun 7;12(6):e0178994

BACKGROUND:
Ferritin constitutes a sensitive iron-storage index and multi-functional protein. Evidence on its association with mortality in general population is scarce and conflicting. We investigated the sex-specific associations of ferritin levels with all-cause and cardiovascular mortality in a population-based cohort.
METHODS:
Data came from the English Longitudinal Study of Ageing and the national mortality registry. The sample comprised 5,471 participants aged =52 years. Blood concentration of ferritin was measured at baseline in 2004-05. Sex-specific Cox proportional hazards models were estimated with adjustment for age, major chronic diseases, marital status, educational attainment, total net household wealth, anemia, inflammatory markers, body mass index, smoking, and physical activity. Stratified analyses by chronic disease status were also performed.
RESULTS:
We categorized ferritin in sex-specific quartiles. In men, we used, the following categorization: lowest (2-69ng/ml), second lowest (70-118ng/ml), second highest (reference category) (119-193ng/ml) and highest (194-598ng/ml) ferritin quartiles. In women, ferritin was categorized as follows: lowest (2-44ng/ml), second lowest (45-73ng/ml), second highest (reference category) (74-115ng/ml) and highest (116-341ng/ml) ferritin quartiles. 841 deaths of which 262 cardiovascular disease-related were recorded over a mean follow-up time of 7.7 years. Risk for all-cause mortality was found increased in men with hyperferritinemia (194-598ng/ml) and no history of major chronic diseases compared with the reference group [fully-adjusted HR: 1.49 (95%CI 1.03-2.16)]. Among women, those in the lowest ferritin quartile (2-44ng/ml) had increased risk for all-cause mortality [fully-adjusted HR: 1.59 (95%CI 1.18-2.13)] compared with the reference group after adjustment for all covariates. Regarding cardiovascular mortality, we

observed a positive association with ferritin levels in men, which was blunted after adjustment for inflammatory markers and lifestyle parameters. Men with no major chronic diseases who were in the highest ferritin quartile had a significantly increased risk of cardiovascular mortality. No association between ferritin levels and cardiovascular mortality was detected in women.

CONCLUSION:

Circulating ferritin levels showed sex-specific prognostic patterns. High ferritin levels in men with no major chronic disease and low ferritin levels in all women were associated with increased all-cause mortality after adjusting for covariates. High ferritin levels in men with no major chronic diseases were also independently associated with an increased risk of cardiovascular mortality. Future research is needed to clarify the prognostic role of ferritin.

Impactfactor: 2.806

The Influence of End-of-Life Care on Organ Donor Potential

Witjes M, Kotsopoulos A, Herold IH, **Otterspoor L**, Simons KS, van Vliet J, de Blauw M, Festen B, Eijkenboom JJ, Jansen NE, van der Hoeven JG, Abdo WF

Am J Transplant. 2017 Jul 17(7):1922-1927. Epub 2017 May 2

Many patients with acute devastating brain injury die outside intensive care units and could go unrecognized as potential organ donors. We conducted a prospective observational study in seven hospitals in the Netherlands to define the number of unrecognized potential organ donors outside intensive care units, and to identify the effect that end-of-life care has on organ donor potential. Records of all patients who died between January 2013 and March 2014 were reviewed. Patients were included if they died within 72 h after hospital admission outside the intensive care unit due to devastating brain injury, and fulfilled the criteria for organ donation. Physicians of included patients were interviewed using a standardized questionnaire regarding logistics and medical decisions related to end-of-life care. Of the 5170 patients screened, we found 72 additional potential organ donors outside intensive care units. Initiation of end-of-life care in acute settings and lack of knowledge and experience in organ donation practices outside intensive care units can result in under-recognition of potential donors equivalent to 11-34% of the total pool of organ donors. Collaboration with the intensive care unit and adjusting the end-of-life path in these patients is required to increase the likelihood of organ donation.

Impactfactor: 6.165

Third generation drug eluting stent (DES) with biodegradable polymer in diabetic patients: 5 years follow-up

Wiemer M, Stoikovic S, Samol A, Dimitriadis Z, Ruiz-Nodar JM, Birkemeyer R, Monsegu J Finet G, Hildick-Smith D, Tresukosol D, Novo EG, **Koolen JJ**, Barbato E, Danzi GB; NOBORI 2 investigators

Cardiovasc Diabetol. 2017 Feb 10;16(1):23

OBJECTIVE: To report the long-term safety and efficacy data of a third generation drug eluting stent (DES) with biodegradable polymer in the complex patient population of diabetes mellitus after a follow-up period of 5 years.

BACKGROUND: After percutaneous coronary intervention patients with diabetes mellitus are under higher risk of death, restenosis and stent thrombosis (ST) compared to non-diabetic patients.

METHODS: In 126 centers worldwide 3067 patients were enrolled in the NOBORI 2 registry, 888 patients suffered from diabetes mellitus (DM), 213 of them (14%) being insulin dependent (IDDM). Five years follow-up has been completed in this study.

RESULTS: At 5 years, 89.3% of the patients were available for follow-up. The reported target lesion failure (TLF) rates at 5 years were 12.39% in DM group and 7.34% in non-DM group; ($p < 0.0001$). In the DM group, the TLF rate in patients with IDDM was significantly higher than in the non-IDDM subgroup (17.84 vs. 10.67%; $p < 0.01$). The rate of ST at 5 years was not different among diabetic versus non-diabetic patients or IDDM versus NIDDM. Only 10 (<0.4%) very late stent thrombotic events beyond 12 months occurred.

CONCLUSIONS: The Nobori DES performed well in patients with DM. As expected patients with DM, particularly those with IDDM, had worse outcomes. However, the very low rate of very late stent thrombosis in IDDM patients might have significant clinical value in the treatment of these patients.

Impactfactor: 4.752

Three-Vessel Assessment of Coronary Microvascular Dysfunction in Patients With Clinical Suspicion of Ischemia: Prospective Observational Study With the Index of Microcirculatory Resistance

Kobayashi Y, Lee JM, Fearon WF, Lee JH, Nishi T, Choi DH, **Zimmermann FM**, Jung JH, Lee HJ, Doh JH, Nam CW, Shin ES, Koo BK

Circ Cardiovasc Interv. 2017 Nov;10(11). pii: e005445

BACKGROUND:

Difficulty directly visualizing the coronary microvasculature as opposed to the epicardial coronary artery makes its assessment challenging. The goal of this study is to measure the index of microcirculatory resistance (IMR) in all 3 major coronary vessels to identify the clinical and angiographic predictors of an abnormal IMR.

METHODS AND RESULTS:

Ninety-three patients who underwent coronary physiological assessment in all 3 major coronary vessels were prospectively enrolled (59.8±9.4 years with 77.4% men). IMR was corrected using Yong's formula and coronary microvascular dysfunction (CMD) was defined using vessel-specific cutoffs. A global IMR was calculated as the sum of the IMR in all 3 major epicardial vessels. Angiographic epicardial disease severity was assessed with vessel-specific and overall SYNTAX score. Median IMR and fractional flow reserve was 17.2 (Q1-Q3: 13.3-22.9) and 0.92 (0.85-0.97). The majority of patients (59.1%) had no CMD, 23.7% had 1-vessel CMD, 14.0% had 2-vessel CMD, and 3.2% had 3-vessel CMD. CMD was observed at a similar rate in the territories supplied by all 3 major coronary vessels (left anterior descending coronary artery 28.0%, left circumflex artery 19.4%, and right coronary artery 23.7%; P=0.39). Fractional flow reserve had a weak, positive correlation with IMR (?=0.16; P<0.01). The SYNTAX score had no significant correlation with IMR, both at a patient level (?=-0.002; P=0.99) and a vessel-specific level (?=-0.06; P=0.36). By multivariable ordinal logistic regression analysis, no variable was left as an independent predictor of an abnormal IMR.

CONCLUSIONS:

Clinical factors and epicardial coronary disease severity are not predictors of the extent of CMD.

Impactfactor: 6.598

To the Editor - Cardiac resynchronization therapy in coronary sinus atresia delivered using leadless endocardial pacing.

van Gelder BM, Bracke FA

HeartRhythm Case Rep. 2017 Jan 21; 3(3):194. eCollection 2017 Mar

AIMS:

This study independently evaluated the diagnostic performance of electrocardiographic (ECG) criteria to predict the infarct-related artery (IRA) in patients with an acute ST-segment elevation myocardial infarction (STEMI). While a number of ECG criteria have been proposed to predict the IRA in STEMI, many of these "rules" came from modestly sized populations and did not undergo external validation. Therefore, we aimed to evaluate popular criteria from the literature in an independent cohort.

METHODS AND RESULTS:

All acute STEMI cases over a 10-year period from a single hospital were retrospectively identified. We excluded patients with a missing pre-intervention ECG, irretrievable angiographic films, prior coronary artery bypass grafting, left bundle branch block, ventricular pacing, or not meeting strict STEMI criteria. After review of the angiograms for the IRA, cases with either no or multiple culprits were excluded. We included 480 subjects meeting STEMI criteria in inferior leads (192, 40%), anterior leads (184, 38%), both anterior and inferior leads (88, 18%), isolated lateral leads (nine, 2%), or a posterior pattern (seven, 1%). Notably, every pattern except isolated lateral STEMI included an IRA in both the right and left coronary arteries.

CONCLUSIONS:

Existing ECG criteria to predict the IRA in STEMI have modest diagnostic performance when externally validated, and lower than in the original reports. Distinguishing the level of obstruction in the left anterior descending artery remains especially challenging. Hence, their use should be pragmatic when selecting an initial catheter for treating STEMI, since discordances will occur when compared to the actual angiogram.

Impactfactor: --

Ultrasound functional imaging in an ex vivo beating porcine heart platform

Petterson NJ, Fixsen LS, Rutten MC, **Pijls NH**, van de Vosse FN, Lopata RG

Phys Med Biol. 2017 Nov 14;62(23):9112-9126

In recent years, novel ultrasound functional imaging (UFI) techniques have been introduced to assess cardiac function by measuring, e.g. cardiac output (CO) and/or myocardial strain. Verification and reproducibility assessment in a realistic setting remain major issues. Simulations and phantoms are often unrealistic, whereas in vivo measurements often lack crucial hemodynamic parameters or ground truth data, or suffer from the large physiological and clinical variation between patients when attempting clinical validation. Controlled validation in certain pathologies is cumbersome and often requires the use of lab animals. In this study, an isolated beating pig heart setup was adapted and used for performance assessment of UFI techniques such as volume assessment and ultrasound strain imaging. The potential of performing verification and reproducibility studies was demonstrated. For proof-of-principle, validation of UFI in pathological hearts was examined. Ex vivo porcine hearts (n??=??6, slaughterhouse waste) were resuscitated and attached to a mock circulatory system. Radio frequency ultrasound data of the left ventricle were acquired in five short axis views and one long axis view. Based on these slices, the CO was measured, where verification was performed using flow sensor measurements in the aorta. Strain imaging was performed providing radial, circumferential and longitudinal strain to assess reproducibility and inter-subject variability under steady conditions. Finally, strains in healthy hearts were compared to a heart with an implanted left ventricular assist device, simulating a failing, supported heart. Good agreement between ultrasound and flow sensor based CO measurements was found. Strains were highly reproducible (intraclass correlation coefficients??>0.8). Differences were found due to biological variation and condition of the hearts. Strain magnitude and patterns in the assisted heart were available for different pump action, revealing large changes compared to the normal condition. The setup provides a valuable benchmarking platform for UFI techniques. Future studies will include work on different pathologies and other means of measurement verification.

Impactfactor: 2.742

Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial

Kandzari DE, Mauri L, **Koolen JJ**, Massaro JM, Doros G, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE, Waksman R; BIOFLOW V Investigators

Lancet. 2017 Oct 21;390(10105):1843-1852

BACKGROUND:

The development of coronary drug-eluting stents has included use of new metal alloys, changes in stent architecture, and use of bioresorbable polymers. Whether these advancements improve clinical safety and efficacy has not been shown in previous randomised trials. We aimed to examine the clinical outcomes of a bioresorbable polymer sirolimus-eluting stent compared with a durable polymer everolimus-eluting stent in a broad patient population undergoing percutaneous coronary intervention.

METHODS:

BIOFLOW V was an international, randomised trial done in patients undergoing elective and urgent percutaneous coronary intervention in 90 hospitals in 13 countries (Australia, Belgium, Canada, Denmark, Germany, Hungary, Israel, the Netherlands, New Zealand, South Korea, Spain, Switzerland, and the USA). Eligible patients were those aged 18 years or older with ischaemic heart disease undergoing planned stent implantation in de-novo, native coronary lesions. Patients were randomly assigned (2:1) to either an ultrathin strut (60 µm) bioresorbable polymer sirolimus-eluting stent or to a durable polymer everolimus-eluting stent. Randomisation was via a central web-based data capture system (mixed blocks of 3 and 6), and stratified by study site. The primary endpoint was 12-month target lesion failure. The primary non-inferiority comparison combined these data from two additional randomised trials of bioresorbable polymer sirolimus-eluting stent and durable polymer everolimus-eluting stent with Bayesian methods. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT02389946.

FINDINGS:

Between May 8, 2015, and March 31, 2016, 4772 patients were recruited into the study. 1334 patients met inclusion criteria and were randomly assigned to treatment with bioresorbable polymer sirolimus-eluting stents (n=884) or durable polymer everolimus-eluting stents (n=450). 52 (6%) of 883 patients in the bioresorbable polymer sirolimus-eluting stent group and 41 (10%) of 427 patients in the durable polymer everolimus-eluting stent group met the 12-month primary endpoint of target lesion failure

(95% CI -6·84 to -0·29, p=0·0399), with differences in target vessel myocardial infarction (39 [5%] of 831 patients vs 35 [8%] of 424 patients, p=0·0155). The posterior probability that the bioresorbable polymer sirolimus-eluting stent is non-inferior to the durable polymer everolimus-eluting stent was 100% (Bayesian analysis, difference in target lesion failure frequency -2·6% [95% credible interval -5·5 to 0·1], non-inferiority margin 3·85%, n=2208).

INTERPRETATION:

The outperformance of the ultrathin, bioresorbable polymer sirolimus-eluting stent over the durable polymer everolimus-eluting stent in a complex patient population undergoing percutaneous coronary intervention suggests a new direction in improving next generation drug-eluting stent technology.

Impactfactor: 57.000

Unusually aggressive immature neo-intimal hyperplasia causing in-stent restenosis

McCutcheon K, **Triantafyllis AS***, Bennett J, Adriaenssens T

Cardiovasc J Afr. 2017 Nov/Dec 23;28(6):404-405

This image illustrates a very unusual pattern of early and aggressive immature neo-intimal hyperplasia in a 52-year-old man with unstable angina, two months after deployment of a drug-eluting stent in the proximal left anterior descending artery.

**Ten tijde van publicatie verbonden aan: Department of Cardiovascular Medicine, University Hospitals Leuven, Leuven, Belgium*

Impactfactor: --

Web-based distress management for implantable cardioverter defibrillator patients: A randomized controlled trial

Habibovic M, Denollet J, Cuijpers P, **van der Voort PH**, Herrman JP, Bouwels L, Valk SD, Alings M, Theuns DA, Pedersen SS

Health Psychol. 2017 Apr 36(4):392-401. Epub 2017 Feb 13

OBJECTIVE:

Sudden cardiac arrest caused by cardiac arrhythmias is 1 of the leading causes of death worldwide. Implantable cardioverter defibrillators (ICDs) are considered as standard care for patients with increased risk of arrhythmias. However, 1 in 4 ICD patients experiences psychological distress post-ICD implantation. The WEB-based distress management program for ICD patients (WEBCARE) was developed to mitigate anxiety and depression and enhance health-related quality of life in ICD patients. This study investigates the 6- and 12-months outcomes.

METHOD:

A total of 289 consecutive ICD patients from 6 referral hospitals in the Netherlands were randomized to either the WEBCARE (n = 146) or usual care (n = 143) group. Patients in the WEBCARE group received an online, 12-weeks fixed, 6 lesson behavioral treatment based on problem solving therapy. Patients in the usual care group receive care as usual.

RESULTS:

Current findings show no significant difference on anxiety, depression or quality of life between the WEBCARE and Usual Care group at 6- and 12-months postimplantation.

CONCLUSIONS:

In this clinical trial of a Web-based behavioral intervention for ICD patients, the Web-based treatment was not superior to usual care on the long-term regarding patient reported outcomes. Future studies are warranted to examine the applicability of blended-care models and focus on further personalizing the program in order to increase adherence and improve outcomes.

Impactfactor: 3.458

What can intracoronary pressure measurements tell us about flow reserve? Pressure-Bounded coronary flow reserve and example application to the randomized DEFER trial

Zimmermann FM, **Pijls NH**, De Bruyne B, Bech GJ, van Schaardenburgh P, Kirkeeide RL, Gould KL, Johnson NP

Catheter Cardiovasc Interv. 2017 Nov 15 90(6):917-925. Epub 2017 Mar 15

OBJECTIVE:

We propose a novel technique called pressure-bounded coronary flow reserve (pb-CFR) and demonstrate its application to the randomized DEFER trial.

BACKGROUND:

Intracoronary flow reserve assessment remains underutilized relative to pressure measurements partly due to less robust tools.
METHODS:
While rest and hyperemic intracoronary pressure measurements cannot quantify CFR exactly, they do provide upper and lower bounds. We validated pb-CFR invasively against traditional CFR, then applied it to high fractional flow reserve (FFR?=?0.75) lesions in DEFER randomized to revascularization or medical therapy.
RESULTS:
pb-CFR showed an 84.4% accuracy to predict invasive CFR?<?2 or CFR?=?2 in 107 lesions. In its proof of concept application to DEFER lesions with FFR?=?0.75, the 28 with pb-CFR?<?2 compared to 28 with pb-CFR?=?2 had a non-significant reduction in freedom from angina (61% vs. 71% at 5 years, P?=?0.57) and a non-significantly higher rate of major adverse cardiac events (MACE, 25% vs. 15%, P?=?0.34). Lesions with FFR?=?0.75 but pb-CFR?<?2 showed no difference in freedom from angina (61% vs. 50%, P?=?0.54) or MACE (25% vs. 38%, P?=?0.27) between the 28 randomized to medical therapy and the 16 randomized to revascularization.
CONCLUSIONS:
pb-CFR offers a new method for studying FFR/CFR discordances using regular pressure wire measurements. As an example application, DEFER suggested that low pb-CFR with high FFR may be a risk marker for more angina and worse outcomes, but that this risk cannot be modified by revascularization.
Impactfactor: 2.602

Cardiothoracale Chirurgie

Emergency left arial appendage clipping after percutaneous pulmonary vein isolation in a patient with a partial anomalous pulmonary venous connection

Verberkmoes NJ, Akca F

HeartRhythm Case Rep. 2017 Jun 8;3(8):400-401.

Geen abstract beschikbaar

Impactfactor: 4.825

Giant coronary aneurysm exposed on routine echocardiogram

Zelis JM, Andriessen FP, **Elenbaas TW**, Peels KH

Eur Heart J. 2017 Nov 14;38(43):3240

Geen abstract beschikbaar

Impactfactor: 20.212

Is there an alternative treatment for patients intolerant to antiplatelet therapy if percutaneous left atrial appendage closure is considered?

Akca F, Verberkmoes NJ, Verstraeten SE, van Laar C, van Putte BP, **van Straten AH**

Neth Heart J. 2017 Sep 25(9):510-515

INTRODUCTION:

Left atrial appendage (LAA) closure has become of major interest for patients with atrial fibrillation intolerant to oral anticoagulation therapy (OAC). Patients with a contraindication to both OAC and antiplatelet therapy are not eligible for percutaneous LAA closure. We aimed to find an alternative treatment for these specific patients.

METHODS:

From March 2014 until December 2015 five patients were referred for percutaneous LAA closure. Alternative treatment was necessary due to an absolute contraindication to OAC and antiplatelet therapy (n = 4) or after previous failed percutaneous device implantation (n = 1). A stand-alone full thoracoscopic closure of the LAA using the Atriclip PRO device (AtriCure Inc., Dayton, OH, USA) was performed under guidance of transoesophageal echocardiography (TEE). After three months all patients underwent a computed tomography scan. Mean follow-up was 7.2 months [range 4.5-9.8 months].

RESULTS:

All procedures were achieved without the occurrence of complications. Complete LAA closure was obtained in all patients without any residual flow confirmed by TEE. Postoperative computed tomography confirmed persisting adequate clip positioning with complete LAA closure and absence of intracardial thrombi. During follow-up no thromboembolic events occurred.

CONCLUSION:

For atrial fibrillation patients with an absolute contraindication to OAC and antiplatelet therapy a stand-alone, minimally invasive thoracoscopic closure of the LAA is a safe and feasible alternative treatment. This might be a solution to avoid serious bleeding complications while eliminating the thromboembolic risk originating from the LAA in patients who are not eligible for percutaneous LAA closure.

Impactfactor: 1.894

Mismatch between the origin of premature ventricular complexes and the noncompacted myocardium in patients with noncompaction cardiomyopathy patients: involvement of the conduction system?

Van Malderen S, Wijchers S, **Akca F**, Caliskan K, Szili-Torok T

Ann Noninvasive Electrocardiol. 2017 Mar;22(2):e12394

BACKGROUND:

Noncompaction cardiomyopathy (NCCM) is considered to be the result of an arrest in the normal myocardial embryogenesis. The histological, developmental, and electrophysiological explanation of ventricular arrhythmias in NCCM is still unknown. The aim of this study was to determine the origin of premature ventricular contractions (PVCs) in NCCM and to identify any predominant arrhythmic foci.

METHODS:

Retrospective data from our NCCM registry including 101 patients were analyzed. A total number of 2069 electrocardiograms (ECGs) were studied to determine the origin of PVCs. Echocardiographic data were analyzed in patients with PVCs in all 12 leads. Segments affected by noncompaction (NC) were compared with the origin of PVCs.

RESULTS:

PVCs were documented in 250 ECGs from 55 (54%) patients. Thirty-five ECGs recorded PVCs on all 12 leads and the origin of 20 types of PVCs could be determined. Ninety-five percent of PVCs did not originate from left ventricular NC myocardial areas and two PVCs (10%) had a true myocardial origin. All other PVCs originated from structures such as the outflow tracts (8/20), the fascicles (7/20), especially the posteromedial fascicle (6/20), and the mitral and tricuspid annulus (3/20).

CONCLUSIONS:

Our data suggest that PVCs in NCCM mainly originate from the conduction system and related myocardium.

Impactfactor: 1.852

One-Year Outcomes of Transcatheter Aortic Valve Implantation Using the Direct Aortic Approach

Bruschi G, Branny M, Schiltgen M, Ettori F, Marcheix B, Amrane H, Bushnaq H, **Tan ME**, Trivedi U, Branny P, Klugmann S, Coletti G, Dumonteil N, Porta F, Nordell A, Moat N

Ann Thorac Surg. 2017 May; 103(5):1434-1440. . Epub 2016 Oct 25

BACKGROUND: The direct aortic (DA) approach allows for transcatheter aortic valve implantation (TAVI) in patients with difficult peripheral vascular anatomy. The CoreValve ADVANCE Direct Aortic (ADVANCE DA) study was performed to assess the outcomes of DA TAVI with the CoreValve System (Medtronic, Minneapolis, MN) in routine practice.

METHODS: Patients were selected for the DA approach by local cardiac surgical teams, and TAVI was performed with patients under general anesthesia. Safety events were adjudicated according to the Valve Academic Research Consortium-2 definitions by an independent clinical events committee. All imaging data, including that from multislice computed tomography and follow-up echocardiography, were analyzed by an independent core laboratory. RESULTS: From September 2012 to February 2014, 100 patients were enrolled (52.0% male, age 81.9 ± 5.9 years, The Society of Thoracic Surgeons Score 5.9 ± 3.2%) at 9 centers in Europe. Peripheral vascular disease was present in 51.0% of patients, and 38.0% had diabetes. Of the 100 patients enrolled, 92 underwent TAVI. At 30 days after TAVI, 98.1% were free of moderate or severe paravalvular leak. At 1 year, 16 patients had died (Kaplan-Meier rate 17.9%), 1 (1.1%) patient had had a stroke, classified as nondisabling, and 15 (17.0%) patients had received a permanent pacemaker. Most patients experienced improved quality of life as measured by the Kansas City Cardiomyopathy Questionnaire overall summary score (mean change from baseline to 1 year, 39.6 ± 26.3; $p < 0.01$).

CONCLUSIONS: The DA approach provides a feasible alternative for patients with challenging anatomic features that may otherwise preclude use of the TAVI procedure.

Impactfactor: 3.700

Quadricuspid aortic valve replacement

Arumugam S, Lam KY, Akca F, van Straten BH

J Card Surg. 2017 Sep;32(9):579-580

Geen abstract beschikbaar

Impactfactor: 0.518

Sutureless aortic valve replacement in a calcified homograft combined with mitral valve replacement

Akca F, Lam K, Özdemir I, Tan E

J Cardiothorac Surg. 2017 Sep 7;12(1):82

BACKGROUND: Aortic valve replacement in a patient with an aortic homograft can be very challenging, especially when concomitant mitral valve surgery needs to be performed.

CASE PRESENTATION: We report a case of implantation of a sutureless aortic valve bioprosthesis combined with mitral valve replacement in a patient with a severely calcified aortic homograft where conventional valve replacement was technically unfeasible.

CONCLUSIONS: We believe that sutureless AVR is a viable option especially for young patients with a high surgical risk where conventional valve replacement cannot be achieved.

Impactfactor: 1.101

Use of an intraoperative checklist to decrease the incidence of re-exploration for postoperative bleeding after cardiac surgery

van Boxtel AG, van Veghel D, **Soliman Hamad MA**, Schulz DN, Stepaniak PS, **van Straten AH**

Interact Cardiovasc Thorac Surg. 2017 Oct 1;25(4):555-558

OBJECTIVES: We have implemented an intraoperative checklist aiming to reduce the incidence of re-exploration for bleeding after cardiac surgery. The present report addresses the results of adopting such a checklist regarding the incidence of postoperative bleeding.

METHODS: The checklist was implemented by presenting it in several staff meetings of the Catharina Heart Center. Copies of the checklist were presented in every operating room. Data were collected by the Catharina Heart Center, aligned with the 'Meetbaar Beter' data manual and validated by 'Meetbaar Beter' through their data quality system. The incidence of re-exploration for bleeding was analysed in a variable life-adjusted display curve. The patient population operated after the implementation of the checklist was compared with a recent historical population before its implementation.

RESULTS: From January 2013 through April 2016, 4817 cardiac surgical procedures were performed in our institution. Before May 2015, 3210 procedures were performed (Group 1), complicated by 112 re-exploration for bleeding (3.5%). The 'reoperation for bleeding checklist' was implemented on 1 May 2015. After this date, the number of re-explorations for bleeding decreased to 29 (1.8%) of the 1607 cardiac surgical procedures (Group 2) (P?<?0.05).

CONCLUSIONS: An intraoperative checklist is feasible to implement, low cost, quick and simple to measure with a significant reduction in the incidence of re-exploration for bleeding. This report shows an example of the positive effects of transparency in publishing outcomes' data in cardiac surgery.

Impactfactor: 1.857

Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery

Haanschoten MC, Kreeftenberg HG, Arthur Bouwman R, **van Straten AH**, Buhre WF, **Soliman Hamad MA**

J Cardiothorac Vasc Anesth. 2017 Feb;31(1):45-53

OBJECTIVES:

In the present study, the authors investigated the predictive value of postoperative peak arterial lactate levels for early and late mortality after cardiac surgery.

DESIGN: Retrospective analysis of prospectively collected data.

SETTING: Single-center study in an academic hospital.

PARTICIPANTS: Adult patients who underwent cardiac surgery between 2004 and 2014 (n = 16,376).

INTERVENTIONS: Different cardiac surgical procedures.

MEASUREMENTS AND RESULTS:

Patients were classified according to the peak arterial lactate level (PALL) within 3 days postoperatively. Logistic regression analysis and Cox regression analysis were performed to identify postoperative peak arterial lactate level as a predictor for early and late mortality respectively. In 8460 patients (51.7%), lactate was not measured postoperatively because these patients were managed according to the fast-track protocol. These patients constituted group 1 in our population but were excluded from the regression analysis. The remaining patients (n = 7,916; 48.3%) were divided according to the postoperative peak arterial lactate level (PALL): PALL<5 mmol/L (group 2), PALL 5 to 10 mmol/L (group 3), and PALL of>10 mmol/L (group 4). Early mortality was 3.7%, 20.4%, and 62.9% in groups 2, 3, and 4 respectively (p<0.0001). This mortality rate was significantly higher than that of group 1 (1.6%); p<0.0001. Multivariate regression analyses revealed postoperative peak arterial lactate as a significant predictor of 30-day mortality (odds ratio = 1.44 [1.39-1.48], p<0.001) as well as for late mortality (hazard ratio = 1.05 [1.01-1.10], p<0.025).

CONCLUSIONS:

Postoperative peak arterial lactate level in patients undergoing cardiac surgery is an independent predictor for both early and late mortality.

Impactfactor: 1.519

Chirurgie

A multicenter prospective study of patients undergoing open ventral hernia repair with intraperitoneal positioning using the monofilament polyester composite ventral patch: interim results of the PANACEA study

Berrevoet F, Doerhoff C, Muysoms F, Hopson S, Muzi MG, **Nienhuijs S**, Kullman E, Tollens T, Schwartz MR, LeBlanc K, Velanovich V, Jørgensen LN

Med Devices (Auckl). 2017 May 12;10:81-88

PURPOSE:

This study assessed the recurrence rate and other safety and efficacy parameters following ventral hernia repair with a polyester composite prosthesis (Parietex™ Composite Ventral Patch [PCO-VP]).

PATIENTS AND METHODS:

A single-arm, multicenter prospective study of 126 patients undergoing open ventral hernia repair with the PCO-VP was performed. Patient outcomes were assessed at discharge and at 10 days, 1, 6, 12, and 24 months postoperative.

RESULTS:

All patients had hernioplasty for umbilical (n = 110, 87.3%) or epigastric hernia (n = 16, 12.7%). Mean hernia diameter was 1.8 ± 0.8 cm. Mean operative time was 36.2 ±15.6 minutes, with a mean mesh positioning time of 8.1 ± 3.4 minutes. Surgeons reported satisfaction with mesh ease of use in 95% of surgeries. The cumulative hernia recurrence rate at 1 year was 2.8% (3/106). Numeric Rating Scale (NRS) pain scores showed improvement from 2.1 ± 2.0 at preoperative baseline to 0.5 ± 0.7 at 1 month postoperative ($P < 0.001$), and this low pain level was maintained at 12 months postsurgery ($P < 0.001$). The mean global Carolina's Comfort Scale® (CCS) score improved postoperatively from 3.8 ± 6.2 at 1 month to 1.6 ± 3.5 at 6 months ($P < 0.001$). One patient was unsatisfied with the procedure.

CONCLUSION:

This 1-year interim analysis using PCO-VP for primary umbilical and epigastric defects shows promising results in terms of mesh ease of use, postoperative pain, and patient satisfaction. Recurrence rate is low, but, as laparoscopic evaluation shows a need for patch repositioning in some cases, an accurate surgical technique remains of utmost importance.

Impactfactor: --

A Multicentre Trial of Patient specific Rehearsal Prior to EVAR: Impact on Procedural Planning and Team Performance

Desender L, Van Herzeele I, Lachat M, Duchateau J, Bicknell C, **Teijink J**, Heyligers J, Vermassen F; PAVLOV Study Group: **Sambeek M van**

Eur J Vasc Endovasc Surg. 2017 Mar;53(3):354-361

OBJECTIVE: Patient specific rehearsal (PsR) prior to endovascular aneurysm repair (EVAR) enables the endovascular team to practice and evaluate the procedure prior to treating the real patient. This multicentre trial aimed to evaluate the utility of PsR prior to EVAR as a pre-operative planning and briefing tool.

MATERIAL AND METHODS: Patients with an aneurysm suitable for EVAR were randomised to pre-operative or post-operative PsR. Before and after the PsR, the lead implanter completed a questionnaire to identify any deviation from the initial treatment plan. All team members completed a questionnaire evaluating realism, technical issues, and human factor aspects pertinent to PsR. Technical and human factor skills, and technical and clinical success rates were compared between the randomised groups.

RESULTS: 100 patients were enrolled between September 2012 and June 2014. The plan to visualise proximal and distal landing zones was adapted in 27/50 (54%) and 38/50 (76%) cases, respectively. The choice of the main body, contralateral limb, or iliac extensions was adjusted in 8/50 (16%), 17/50 (34%), and 14/50 (28%) cases, respectively. At least one of the abovementioned parameters was changed in 44/50 (88%) cases. For 100 EVAR cases, 199 subjective questionnaires post-PsR were completed. PsR was considered to be useful for selecting the optimal C-arm angulation (median 4, IQR 4-5) and was recognised as a helpful tool for team preparation (median 4, IQR 4-4), to improve communication (median 4, IQR 3-4), and encourage confidence (median 4, IQR 3-4). Technical and human factor skills and technical and initial clinical success rates were similar between the randomisation groups.

CONCLUSION: PsR prior to EVAR has a significant impact on the treatment plan and may be useful as a pre-operative planning and briefing tool. Subjective ratings indicate that this technology may facilitate planning of optimal C-arm angulation and improve non-technical skills.

Impactfactor: *4.061*

Addition of Video-Assisted Thoracoscopic Surgery to the Treatment of Flail Chest

Schots JP, Vissers YL, Hulsewé KW, Meesters B, Hustinx PA, Pijnenburg A, Siebenga J, de Loos ER

Ann Thorac Surg. 2017 Mar;103(3):940-944

BACKGROUND:

Video-assisted thoracoscopic surgery (VATS) is increasingly used in chest trauma for diagnostic and therapeutic purposes. In this report we describe our single-institutional experience with VATS in the surgical treatment of patients with flail chest after high-energy trauma.

METHODS:

From January 2013 to July 2014, 15 patients with flail chest after high-energy trauma were treated in our hospital. The Injury Severity Score (ISS) ranged from 16 to 44. Rib fixation was performed with precontoured plates or intramedullary splints. In all, patients we additionally used VATS to explore the thoracic cavity and evacuate any hemothorax.

RESULTS:

In 10 patients a prominent hemothorax was present, which needed evacuation. The median operative time was 120 minutes (range, 60 to 180 minutes), with a median blood loss of 150 mL (range, <100 to 400 mL). The mean stay in the intensive care unit was 5.27 days (SD 6.79). Ten patients were extubated directly after operation in the operating room. The other 5 patients were extubated after 1 to 13 days. The mean duration of mechanical ventilation was 2 days (SD 4.17). No patient required a tracheostomy. Three patients had minor postoperative adverse events. All patients were discharged after 6 to 44 days (mean, 11.9 hospitalization days) (SD 9.57).

CONCLUSIONS:

We believe VATS is effective and safe and can be of additional value by providing the possibility to adjust the planned incision for rib fixation and decrease the area of muscle destruction. Additional pulmonary or mediastinal pathologic conditions can be identified and complete evacuation of hemothorax can be achieved simultaneously.

Impactfactor: 3.700

Anastomotic Leakage and Chronic Presacral Sinus Formation After Low Anterior Resection: Results From a Large Cross-sectional Study

Borstlap WA, Westerduin E, Aukema TS, Bemelman WA, Tanis PJ; Dutch Snapshot Research Group: **Nieuwenhuijzen GA, Rutten HJ**

Ann Surg. 2017 Nov;266(5):870-877.

OBJECTIVES:

Little is known about late detected anastomotic leakage after low anterior resection for rectal cancer, and the proportion of leakages that develops into a chronic presacral sinus.

METHODS:

In this collaborative snapshot research project, data from registered rectal cancer resections in the Dutch Surgical Colorectal Audit in 2011 were extended with additional treatment and long-term outcome data. Independent predictors for anastomotic leakage were determined using a binary logistic model.

RESULTS:

A total of 71 out of the potential 94 hospitals participated. From the 2095 registered patients, 998 underwent a low anterior resection, of whom 88.8% received any form of neoadjuvant therapy. Median follow-up was 43 months (interquartile range 35-47). Anastomotic leakage was diagnosed in 13.4% within 30 days, which increased to 20.0% (200/998) beyond 30 days. Nonhealing of the leakage at 12 months was 48%, resulting in an overall proportion of chronic presacral sinus of 9.5%. Independent predictors for anastomotic leakage at any time during follow-up were neoadjuvant therapy (odds ratio 2.85; 95% confidence interval 1.00-8.11) and a distal (=3?cm from the anorectal junction on magnetic resonance imaging) tumor location (odds ratio 1.88; 95% confidence interval 1.02-3.46).

CONCLUSIONS:

This cross-sectional study of low anterior resection for rectal cancer in the Netherlands in 2011, with almost routine use of neoadjuvant radiotherapy, shows that one third of anastomotic leakages is diagnosed beyond 30 days, and almost half of the leakages eventually do not heal. Chronic presacral sinus is a significant clinical problem that deserves more attention

Impactfactor: 8.980

Aortic Curvature Is a Predictor of Late Type Ia Endoleak and Migration After Endovascular Aneurysm Repair

Schuurmann RC, van Noort K, Overeem SP, Ouriel K, Jordan WD Jr, Muhs BE, **'t Mannetje Y**, Reijnen M, Fioole B, Ünlü Ç, Brummel P, de Vries JPM

J Endovasc Ther. 2017 Jun 24(3):411-417. Epub 2017 Mar 28

PURPOSE:

To evalute the association between aortic curvature and other preoperative anatomical characteristics and late (>1 year) type Ia endoleak and endograft migration in endovascular aneurysm repair (EVAR) patients.

METHODS:

Eight high-volume EVAR centers contributed 116 EVAR patients (mean age 81±7 years; 103 men) to the study: 36 patients (mean age 82±7 years; 31 men) with endograft migration and/or type Ia endoleak diagnosed >1 year after the initial EVAR and 80 controls without early or late complications. Aortic curvature was calculated from the preoperative computed tomography scan as the maximum and average curvature over 5 predefined aortic segments: the entire infrarenal aortic neck, aneurysm sac, and the suprarenal, juxtarenal, and infrarenal aorta. Other morphological characteristics included neck length, neck diameter, mural neck calcification and thrombus, suprarenal and infrarenal angulation, and largest aneurysm sac diameter. Independent risk factors were identified using backward stepwise logistic regression. Relevant cutoff values for each of the variables in the final regression model were determined with the receiver operator characteristic curve.

RESULTS:

Logistic regression identified maximum curvature over the length of the aneurysm sac (>47 m-1; p=0.023), largest aneurysm sac diameter (>56 mm; p=0.028), and mural neck thrombus (>11° circumference; p<0.001) as independent predictors of late migration and type Ia endoleak.

CONCLUSION:

Aortic curvature is a predictor for late type Ia endoleak and endograft migration after EVAR. These findings suggest that aortic curvature is a better parameter than angulation to predict post-EVAR failure and should be included as a hostile neck parameter.

Impactfactor: 2.838

Balancing demand and supply in the operating room: A study for the cardiothoracic department in a large teaching hospital

Stepaniak PS*, **Pouwels S**

J Clin Anesth. 2017 Nov;42:7-8

Geen abstract beschikbaar

Impactfactor: 1.677

Benchmarking recent national practice in rectal cancer treatment with landmark randomized controlled trials

Dutch Snapshot Research Group: **Rutten HJ**

Colorectal Dis. 2017 Jun;19(6):O219-O231

AIM:

A Snapshot study design eliminates changes in treatment and outcome over time. This population based Snapshot study aimed to determine current practice and outcome of rectal cancer treatment with published landmark randomized controlled trials as a benchmark.

METHOD:

In this collaborative research project, the dataset of the Dutch Surgical Colorectal Audit was extended with additional treatment and long-term outcome data. All registered patients who underwent resection for rectal cancer in 2011 were eligible. Baseline characteristics and outcome were evaluated against the results of the Dutch TME trial and the COLOR II trial from which the original datasets were obtained.

RESULTS:

A total of 71 hospitals participated, and data were completed for 2102 out of the potential 2633 patients (79.8%). Median follow-up was 41 (interquartile range 25-47) months. Overall circumferential resection margin (CRM) involvement was 9.3% in the Snapshot cohort and 18.5% in the Dutch TME trial. CRM positivity after laparoscopic resection was 7.8% in the Snapshot and 9.5% in the COLOR II trial. Three-year overall local recurrence rate in the Snapshot was 5.9%, with a disease-free survival of 67.1% and overall survival of 79.5%. Benchmarking with the randomized controlled trials revealed an overall favourable long-term outcome of the Snapshot cohort.

CONCLUSION:

This study showed that current rectal cancer care in a large unselected Dutch population is of high quality, with less positive CRM since the TME trial and oncologically safe implementation of minimally invasive surgery after the COLOR II trial.

Impactfactor: 2.689

Biological Mesh Closure of the Pelvic Floor After Extralevator Abdominoperineal Resection for Rectal Cancer: A Multicenter Randomized Controlled Trial (the BIOPEX-study)

Musters GD, Klaver CEL, Bosker RJI, Burger JWA, van Duijvendijk P, van Etten B, van Geloven AAW, de Graaf EJR, Hoff C, Leijtens JWA, **Rutten HJT**, Singh B, Vuylsteke RJCLM, de Wilt JHW, Dijkgraaf MGW, Bemelman WA, Tanis PJ

Ann Surg. 2017 Jun; 265(6):1074-1081

OBJECTIVE: To determine the effect of biological mesh closure on perineal wound healing after extralevator abdominoperineal resection (eAPR).

BACKGROUND: Perineal wound complications frequently occur after eAPR with preoperative radiotherapy for rectal cancer. Cohort studies have suggested that biological mesh closure of the pelvic floor improves perineal wound healing.

METHODS: Patients were randomly assigned to primary closure (standard arm) or biological mesh closure (intervention arm). A non-cross-linked porcine acellular dermal mesh was sutured to the pelvic floor remnants in the intervention arm, followed by a layered closure of the ischioanal and subcutaneous fat and skin similar to the control intervention. The outcome of the randomization was concealed from the patient and perineal wound assessor. The primary endpoint was the rate of uncomplicated perineal wound healing defined as a Southampton wound score of less than 2 at 30 days postoperatively. Patients were followed for 1 year.

RESULTS: In total, 104 patients were randomly assigned to primary closure (n =54; 1 dropouts) and biological mesh closure (n = 50; 2 dropouts). Uncomplicated perineal wound healing rate at 30 days was 66% (33/50; 3 not evaluable) after primary closure, which did not significantly differ from 63% (30/48) after biological mesh closure [relative risk 1.056; 95% confidence interval (CI) 0.7854-1.4197; P = 0.7177). Freedom from perineal hernia at 1 year was 73% (95% CI 60.93-85.07) versus 87% (95% CI 77.49-96.51), respectively (P = 0.0316).

CONCLUSIONS: Perineal wound healing after eAPR with preoperative radiotherapy for rectal cancer was not improved when using a biological mesh. A significantly lower 1-year perineal hernia rate after biological mesh closure is a promising secondary finding that needs longer follow-up to determine its clinical relevance.

Impactfactor: 8.980

Breast magnetic resonance imaging use in patients undergoing neoadjuvant chemotherapy is associated with less mastectomies in large ductal cancers but not in lobular cancers

Vriens IJH, Keymeulen K, Lobbes MB, van Bommel AC, **Nieuwenhuijzen GA**, Smidt ML, Boersma LJ, van Dalen T, Smorenburg CH, Struikmans H, Siesling S, Voogd AC, Tjan-Heijnen VC; National Breast Cancer Organization of the Netherlands – Breast Cancer Audit Scientific Committee (NBCA)

Eur J Cancer. 2017 Aug;81:74-80

BACKGROUND:

To assess the impact of breast magnetic resonance imaging (MRI) use on surgical outcome per histological breast cancer subtype in patients treated with neoadjuvant chemotherapy.

PATIENTS AND METHODS:

All patients aged 18-70 years who underwent neoadjuvant chemotherapy for stage I-III invasive breast cancer in the Netherlands in the years 2011-2013 were identified from the Netherlands Cancer Registry. Patients with cT4 tumours were excluded from the analysis. Use of breast MRI and impact on surgical treatment, resection margins and detection of contralateral breast cancer were analysed by multivariable analyses.

RESULTS:

Breast MRI was performed in 2879 (83.9%) out of 3433 patients treated with neoadjuvant chemotherapy. Younger age (odds ratio [OR] 1.42; 95% confidence interval [CI] 1.17-1.71 for 18-50 years compared with 50-70 years), larger tumour stage (OR 1.46 [95% CI 1.15-1.86] for cT3, compared to cT1-2 tumours) and multifocality (OR 1.30; 95% CI 1.04-1.61, versus unifocality) were associated with increased breast MRI use. In ductal breast cancer, after stratification for cT-status, breast MRI use is

associated with a significant lower OR for mastectomy as final surgery in cT3 tumours (OR 0.45, 95% CI 0.21-0.99). Resection margin involvement and detection of contralateral breast cancer were not associated with breast MRI use.

CONCLUSION:

In patients treated with neoadjuvant chemotherapy, the use of breast MRI was associated with a reduced mastectomy rate, particularly in patients with large invasive ductal breast tumours but not in patients with lobular breast cancer.

Impactfactor: 6.029

Breast MRI increases the number of mastectomies for ductal cancers, but decreases them for lobular cancers

Lobbes MB, Vriens IJ, van Bommel AC, **Nieuwenhuijzen GA**, Smidt ML, Boersma LJ, van Dalen T, Smorenburg C, Struikmans H, Siesling S, Voogd AC, Tjan-Heijnen VC

Breast Cancer Res Treat. 2017 Apr;162(2):353-364

PURPOSE: In this retrospective population-based cohort study, we analyzed breast MRI use and its impact on type of surgery, surgical margin involvement, and the diagnosis of contralateral breast cancer.

METHODS: All Dutch patients with cT1-4N0-3M0 breast cancer diagnosed in 2011-2013 and treated with primary surgery were eligible for inclusion. Using multivariable analyses, we analyzed in different categories whether MRI use was related to surgery type, margin involvement, and diagnosis of contralateral breast cancer (CBC).

RESULTS: MRI was performed in 10,740 out of 36,050 patients (29.8%). Patients with invasive ductal cancer undergoing MRI were more likely to undergo primary mastectomy than those without MRI (OR 1.30, 95% confidence interval (CI) 1.22-1.39, p < 0.0001). Patients with invasive lobular cancer undergoing MRI were less likely to undergo primary mastectomy than those without MRI (OR 0.86, 95% CI 0.76-0.99, p = 0.0303). A significantly lower risk of positive surgical margins after breast-conserving surgery was only seen in patients with lobular cancer who had undergone MRI as compared to those without MRI (OR 0.59, 95% CI 0.44-0.79, p = 0.0003) and, consequently, a lower risk of secondary mastectomy (OR 0.61, 95% CI 0.42-0.88, p = 0.0088). Patients who underwent MRI were almost four times more likely to be diagnosed with CBC (OR 3.55, 95% CI 3.01-4.17, p < 0.0001).

CONCLUSIONS: Breast MRI use was associated with a reduced number of mastectomies and less positive surgical margins in invasive lobular cancer, but with an increased number of mastectomies in ductal cancers. Breast MRI use was associated with a fourfold higher incidence of CBC.

Impactfactor: 3.626

Comparison of midterm results for the Talent and Endurant stent graft

't Mannetje YW, Cuypers PW, Saleem BR, Bode AS, Teijink JA, van Sambeek MR

J Vasc Surg. 2017 Sep 66(3):735-742. Epub 2017 Mar 31

OBJECTIVE:

Stent graft evolution is often addressed as a cause for improved outcomes of endovascular aneurysm repair for patients with an abdominal aortic aneurysm. In this study, we directly compared the midterm result of Endurant stent graft with its predecessor, the Talent stent graft (both Medtronic, Santa Rosa, Calif).

METHODS:

Patient treated from January 2005 to December 2010 in a single tertiary center in The Netherlands with a Talent or Endurant stent graft were eligible for inclusion. Ruptured abdominal aortic aneurysms or patients with previous aortic surgery were excluded. The primary end point was the Kaplan-Meier estimated freedom from secondary interventions. Secondary end points were perioperative outcomes and indications for secondary interventions.

RESULTS:

In total, 221 patients were included (131 Endurant and 90 Talent). At baseline, the median aortic bifurcation was narrower for the Endurant (30 mm vs 39 mm; P < .001). Median follow-up was 64.1 ± 37.9 months and 59.2 ± 25.3 months for Talent and Endurant, respectively. The estimated freedom from secondary interventions at 30 days, 1 year, 5 years, and 7 years was 94.3%, 89.4%, 72.2%, and 64.1% for Talent and 96.8%, 89.3%, 75.2%, and 69.2% for Endurant (P = .528). The indication for secondary interventions does differ; more patients required an intervention for a proximal neck-related complication (type Ia endoleak or migration) in the Talent group (18.2% vs 4.8%; P = .001), whereas more interventions for iliac limb stenosis were seen in the Endurant group (0.0% vs 4.8%; P = .044). In a

binomial regression analysis, suprarenal angulation, infrarenal neck length, and type of stent graft were independent predictors of neck-related complications.
CONCLUSIONS:
Evolution from the Talent stent graft into the Endurant has resulted in significant reduction of infrarenal neck-related complications; on the other hand, iliac interventions increased. The overall midterm secondary intervention rate was comparable.

Impactfactor: 3.536

Conversion to Gastric Bypass After Either Failed Gastric Band or Failed Sleeve Gastrectomy
van Wezenbeek MR, van Oudheusden TR, de Zoete JP, Smulders JF, Nienhuijs SW
Obes Surg. 2017 Jan;27(1):83-89

BACKGROUND:
Roux-en-Y gastric bypass (RYGB) is still considered the gold standard in bariatric surgery. Before, adjustable gastric banding (AGB) was regarded as an alternative; nowadays, sleeve gastrectomy (SG) is a more favorable alternative. In case of unsatisfactory results, RYGB is often performed as a secondary procedure. Conversion of an AGB is associated with a high risk of complications; the hypothesis was that this would be less after conversion of an SG.
METHODS:
All patients undergoing conversion to RYGB after AGB or SG between 2005 and 2012 were included for retrospective analysis. Patient characteristics, operative details, postoperative complications, the relief of complaints, weight loss, reasons for failure, and evolution of known comorbidities up to 2 years were analyzed.
RESULTS:
A total of 178 patients were included (79.8 % female): AGB 110 (61.8 %) versus SG 68 (38.2 %). Main reasons for conversion were weight regain/insufficient weight loss (48.4 %) or dysphagia/reflux complaints (39.9 %). Surgical complications were found in 19 patients (AGB 13 vs SG 6; p = 0.530). Infectious complications occurred in 13 patients (AGB 11 vs SG 2; p = 0.135). Total body weight loss was equal between groups after 2 years (AGB 31.6 ± 11.0 % vs SG 31.6 ± 12.0 %; p = 0.998). Similar results were found in a subgroup analysis on patients undergoing conversion for additional weight loss (AGB 31.7 ± 11.7 % vs SG 27.0 ± 13.1 %; p = 0.173).
CONCLUSIONS:
Conversion to RYGB after failed AGB or SG showed comparable short-term results in terms of postoperative complications and weight loss.

Impactfactor: 3.947

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal metastases of colorectal origin
Kok NF, **de Hingh IH**
Br J Surg. 2017 Mar;104(4):313-315
Geen abstract beschikbaar
Impactfactor: 5.899

Defining Benchmarks for Transthoracic Esophagectomy: A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients
Schmidt HM, Gisbertz SS, Moons J, Rouvelas I, Kauppi J, Brown A, Asti E, **Luyer M**, Lagarde SM, Berlth F, Philippron A, Bruns C, Hölscher A, Schneider PM, Raptis DA, van Berge Henegouwen MI, Nafteux P, Nilsson M, Räsanen J, Palazzo F, Rosato E, Mercer S, Bonavina L, **Nieuwenhuijzen G**, Wijnhoven BPL, Schröder W, Pattyn P, Grimminger PP, Gutschow CA
Ann Surg. 2017 Nov;266(5):814-821

OBJECTIVE:
To define "best possible" outcomes in total minimally invasive transthoracic esophagectomy (ttMIE).
BACKGROUND:
TtMIE, performed by experts in patients with low comorbidity, may serve as a benchmark procedure for esophagectomy.
PATIENTS AND METHODS:
From a cohort of 1057 ttMIE, performed over a 5-year period in 13 high-volume centers for esophageal surgery, we selected a study group of 334 patients (31.6%) that fulfilled criteria of low comorbidity

(American Society of Anesthesiologists score =2, WHO/ECOG score =1, age =65 years, body mass index 19-29?kg/m). Endpoints included postoperative morbidity measured by the Clavien-Dindo classification and the comprehensive complication index. Benchmark values were defined as the 75th percentile of the median outcome parameters of the participating centers to represent best achievable results.
RESULTS:
Benchmark patients were predominantly male (82.9%) with a median age of 58 years (53-62). High intrathoracic (Ivor Lewis) and cervical esophagogastrostomy (McKeown) were performed in 188 (56.3%) and 146 (43.7%) patients, respectively. Median (IQR) ICU and hospital stay was 0 (0-2) and 12 (9-18) days, respectively. 56.0% of patients developed at least 1 complication, and 26.9% experienced major morbidity (=grade III), mostly related to pulmonary complications (25.7%), anastomotic leakage (15.9%), and cardiac events (13.5%). Benchmark values at 30 days after hospital discharge were =55.7% and =30.8% for overall and major complications, =18.0% for readmission, =3.1% for positive resection margins, and =23 for lymph node yield. Benchmarks at 30 and 90 days were =1.0% and =4.6% for mortality, and =40.8 and =42.8 for the comprehensive complication index, respectively.
CONCLUSION:
This outcome analysis of patients with low comorbidity undergoing ttMIE may serve as a reference to evaluate surgical performance in major esophageal resection.

Impactfactor: 8.980

Different Supplementation Regimes to Treat Perioperative Vitamin B12 Deficiencies in Bariatric Surgery: a Systematic Review

Smelt HJ, **Pouwels S, Smulders JF**

Obes Surg. 2017 Jan;27(1):254-262

Vitamin B12 dosage in multivitamin supplementation in the current literature is quite variable. There is no consensus about the optimal treatment of vitamin B12 deficiency. A systematic literature search on different supplementation regimes to treat perioperative vitamin B12 deficiencies in bariatric surgery was performed. The methodological quality of ten included studies was rated using the Newcastle Ottawa scale and ranged from moderate to good. The agreement between the reviewers was assessed with a Cohen's kappa (0.69). The current literature suggests that 350 µg oral vitamin B12 is the appropriate dose to correct low vitamin B12 levels in many patients. Further research must focus on a better diagnosis of a vitamin B12 deficiency, the optimal dose vitamin B12 supplementation, and clinical relevance next to biochemical data.

Impactfactor: 3.947

Effect of Antibiotic Prophylaxis on Surgical Site Infections Following Removal of Orthopedic Implants Used for Treatment of Foot, Ankle, and Lower Leg Fractures: A Randomized Clinical Trial

Backes M, Dingemans SA, Dijkgraaf MG, van den Berg HR, van Dijkman B, Hoogendoorn JM, Joosse P, Ritchie ED, Roerdink WH, **Schots JP**, Sosef NL, Spijkerman IJB, Twigt BA, **van der Veen AH**, van Veen RN, Vermeulen J, Vos DI, Winkelhagen J, Goslings JC, Schepers T; WIFI Collaboration Group

JAMA. 2017 Dec 26;318(24):2438-2445

Importance: Following clean (class I, not contaminated) surgical procedures, the rate of surgical site infection (SSI) should be less than approximately 2%. However, an infection rate of 12.2% has been reported following removal of orthopedic implants used for treatment of fractures below the knee.
Objective:
To evaluate the effect of a single dose of preoperative antibiotic prophylaxis on the incidence of SSIs following removal of orthopedic implants used for treatment of fractures below the knee.
Design, Setting, and Participants:
Multicenter, double-blind, randomized clinical trial including 500 patients aged 18 to 75 years with previous surgical treatment for fractures below the knee who were undergoing removal of orthopedic implants from 19 hospitals (17 teaching and 2 academic) in the Netherlands (November 2014-September 2016), with a follow-up of 6 months (final follow-up, March 28, 2017). Exclusion criteria were an active infection or fistula, antibiotic treatment, reimplantation of osteosynthesis material in the same session, allergy for cephalosporins, known kidney disease, immunosuppressant use, or pregnancy.
Interventions:
A single preoperative intravenous dose of 1000 mg of cefazolin (cefazolin group, n?=?228) or sodium chloride (0.9%; saline group, n?=?242).
Main Outcomes and Measures:

Primary outcome was SSI within 30 days as measured by the criteria from the US Centers for Disease Control and Prevention. Secondary outcome measures were functional outcome, health-related quality of life, and patient satisfaction.

Results:

Among 477 randomized patients (mean age, 44 years [SD, 15]; women, 274 [57%]; median time from orthopedic implant placement, 11 months [interquartile range, 7-16]), 470 patients completed the study. Sixty-six patients developed an SSI (14.0%): 30 patients (13.2%) in the cefazolin group vs 36 in the saline group (14.9%) (absolute risk difference, -1.7 [95% CI, -8.0 to 4.6], P?=?.60).

Conclusions and Relevance:

Among patients undergoing surgery for removal of orthopedic implants used for treatment of fractures below the knee, a single preoperative dose of intravenous cefazolin compared with saline did not reduce the risk of surgical site infection within 30 days following implant removal.

Impactfactor: 44.405

Effect of diabetes mellitus on walking distance parameters after supervised exercise therapy for intermittent claudication: A systematic review

Hageman D, Gommans LN, Scheltinga MR**, Teijink JA**

Vasc Med. 2017 Feb;22(1):21-27

Some believe that certain patients with intermittent claudication may be unsuitable for supervised exercise therapy (SET), based on the presence of comorbidities and the possibly increased risks. We conducted a systematic review (MEDLINE, EMBASE and CENTRAL) to summarize evidence on the potential influence of diabetes mellitus (DM) on the response to SET. Randomized and nonrandomized studies that investigated the effect of DM on walking distance after SET in patients with IC were included. Considered outcome measures were maximal, pain-free and functional walking distance (MWD, PFWD and FWD). Three articles met the inclusion criteria (n = 845). In one study, MWD was 111 meters (128%) longer in the non-DM group compared to the DM group after 3 months of follow-up (p = 0.056). In a second study, the non-DM group demonstrated a significant increase in PFWD (114 meters, p ? 0.05) after 3 months of follow-up, whereas there was no statistically significant increase for the DM group (54 meters). On the contrary, the largest study of this review did not demonstrate any adverse effect of DM on MWD and FWD after SET. In conclusion, the data evaluating the effects of DM on SET were inadequate to determine if DM impairs the exercise response. While trends in the data do not suggest an impairment, they are not conclusive. Practitioners should consider this limitation when making clinical decisions.

Impactfactor: 1.866

Endovascular Treatment of Common Iliac Artery Aneurysms With an Iliac Branch Device: Multicenter Experience of 140 Patients

Jongsma H, Bekken JA, Bekkers WJ, Zeebregts CJ, van Herwaarden J, Hoksbergen A, **Cuypers P**, de Vries JP, Verhagen HJ, Fioole B

J Endovasc Ther. 2017 Apr;24(2):239-245

PURPOSE:

To evaluate the efficacy, feasibility, and long-term outcomes of the Zenith ZBIS iliac branch device (IBD) to preserve internal iliac artery (IIA) perfusion in a large Dutch multicenter cohort.

METHODS:

Between September 2004 and August 2015, 140 patients (mean age 70.9±7.4 years; 130 men) with 162 IBD implantations were identified in 7 vascular centers. The indication for IBD implantation was an abdominal aortic aneurysm >55 mm with a concomitant common iliac artery (CIA) aneurysm >20 mm (n=40), a CIA aneurysm with a diameter >30 mm (n=89), or revision of a type Ib endoleak after endovascular aneurysm repair (n=11).

RESULTS:

Technical success (aneurysm exclusion, no type I or III endoleak, and a patent IIA) was obtained in 157 (96.9%) of 162 IBD implantations. Six (4.3%) patients developed major complications; 2 (1.4%) died. Mean follow-up was 26.6±24.1 months, during which 17 (12.1%) IBD-associated secondary interventions were performed. Including technical failures and intentional IIA embolizations, 15 (9.3%) IIA branch occlusions were identified; buttock claudication developed in 6 of these patients. The freedom from secondary intervention estimate was 75.9% (95% confidence interval 59.7 to 86.3) at 5 years.

CONCLUSION:

CIA aneurysms can be treated safely and effectively by IBDs with preservation of antegrade flow to the IIA. Secondary interventions are indicated in >10% of patients during follow-up but can be performed endovascularly in most.

Impactfactor: 2.838

Extended adjuvant aromatase inhibition after sequential endocrine therapy (DATA): a randomised, phase 3 trial

Tjan-Heijnen VC, van Hellemond IE, Peer PG, Swinkels AC, Smorenburg CH, van der Sangen MJ, Kroep JR, De Graaf H, Honkoop AH, Erdkamp FL, van den Berkmortel FW, de Boer M, de Roos WK, Linn SC, Imholz AL, Seynaeve CM; Dutch Breast Cancer Research Group (BOOG) for the DATA Investigators.: **Nieuwenhuijzen GA**

Lancet Oncol. 2017 Nov;18(11):1502-1511

BACKGROUND: The effect of extended adjuvant aromatase inhibition in hormone receptor-positive breast cancer after sequential endocrine therapy of tamoxifen followed by an aromatase inhibitor for a 5-year treatment period still needs clarification. To address this issue, we began the DATA study to assess different durations of anastrozole therapy after tamoxifen.

METHODS: DATA was a prospective, randomised, open-label, multicentre, phase 3 study done in 79 hospitals in the Netherlands. We randomly assigned postmenopausal women with hormone receptor-positive early breast cancer with no signs of disease recurrence after 2-3 years of adjuvant tamoxifen to either 3 or 6 years of anastrozole treatment (1 mg orally once a day) in a 1:1 ratio. We used TENALEA (Trans European Network for Clinical Trials Services) for the randomisation procedure. Stratification factors were nodal status, hormone receptor status, HER2 status, and tamoxifen treatment duration. The primary study endpoint of this analysis was disease-free survival starting beyond 3 years after randomisation (adapted disease-free survival). Here we report the final analysis from the DATA trial, which is registered with ClinicalTrials.gov, number NCT00301457.

FINDINGS:

Between June 28, 2006, and Aug 10, 2009, we screened 1912 patients of whom 955 were assigned to the 3-year group and 957 to the 6-year anastrozole treatment group. 1860 patients were eligible (931 in the 6-year group and 929 in the 3-year group) and 1660 were disease free 3 years after randomisation. The 5-year adapted disease-free survival was 83·1% (95% CI 80·0-86·3) in the 6-year group and 79·4% (76·1-82·8) in the 3-year group (hazard ratio [HR] 0·79 [95% CI 0·62-1·02]; p=0·066). Patients in the 6-year treatment group had more adverse events than those in the 3-year treatment group, including all-grade arthralgia or myalgia (478 [58%] of 827 in the 6-year treatment group vs 438 [53%] of 833 in the 3-year treatment group) and osteopenia or osteoporosis (173 [21%] vs 137 [16%]).

INTERPRETATION: We cannot recommend the use of extended adjuvant aromatase inhibition after 5 years of sequential endocrine therapy in all postmenopausal women with hormone receptor-positive breast cancer.

Erratum in: Correction to Lancet Oncol 2017; 18: 1502-11. [Lancet Oncol. 2017]

Impactfactor: 33.900

Failure-to-rescue in patients undergoing surgery for esophageal or gastric cancer

Busweiler LA, Henneman D, Dikken JL, Fiocco M, van Berge Henegouwen MI5, Wijnhoven BP, van Hillegersberg R, Rosman C, Wouters MW, van Sandick JW; Dutch Upper GI Cancer Audit group.: **Nieuwenhuijzen GA**

Eur J Surg Oncol. 2017 Oct;43(10):1962-1969

BACKGROUND:

Complex surgical procedures such as esophagectomy and gastrectomy for cancer are associated with substantial morbidity and mortality. The purpose of this study was to evaluate trends in postoperative morbidity, mortality, and associated failure-to-rescue (FTR), in patients who underwent a potentially curative resection for esophageal or gastric cancer in the Netherlands, and to investigate differences between the two groups.

METHODS:

All patients with esophageal or gastric cancer who underwent a potentially curative resection, registered in the Dutch Upper GI Cancer Audit (DUCA) between 2011 and 2014, were included. Primary outcomes were (major) postoperative complications, postoperative mortality and FTR. To investigate groups' effect on the outcomes of interest a mixed model was used.

RESULTS:

Overall, 2644 patients with esophageal cancer and 1584 patients with gastric cancer were included in

this study. In patients with gastric cancer, postoperative mortality (7.7% in 2011 vs. 3.8% in 2014) and FTR (38% in 2011 and 19% in 2014) decreased significantly over the years. The adjusted risk of developing a major postoperative complication was lower (OR 0.54; 95% CI 0.42-0.70), but the risk of FTR was higher (OR 1.85; 95% CI 1.05-3.27) in patients with gastric cancer compared to patients with esophageal cancer.

CONCLUSION:

Once a postoperative complication occurred, patients with gastric cancer were more likely to die compared to patients with esophageal cancer. Underlying mechanisms like patient selection, and differences in structure and organization of care should be investigated. Next to morbidity and mortality, failure-to-rescue should be considered as an important outcome measure after esophagogastric cancer resections.

Impactfactor: 3.522

Identification of technical errors and hazard zones in sleeve gastrectomy using OCHRA : "OCHRA for sleeve gastrectomy"

van Rutte P, Nienhuijs SW, Jakimowicz JJ, van Montfort G

Surg Endosc. 2017 Feb;31(2):561-566. Epub 2016 Jun 10

BACKGROUND:

The sleeve gastrectomy is an example of minimally invasive surgery. It is important to determine the critical steps of the procedure in order to reduce complications and increase safety and efficiency.

OBJECTIVE:

The aim of this study was to detect the key elements of the sleeve gastrectomy and find the potential hazard zones of the procedure.

SETTING:

Bariatric department of a large teaching hospital in the Netherlands.

METHODS:

A prospective clinical observation study was performed including 60 sleeve gastrectomy procedures. An expert panel determined the key steps, and two experts assessed the procedures systematically for technical errors according to the principles of Observational Clinical Human Reliability Assessment (OCHRA).

RESULTS:

A total of 213 technical errors have been made, and the majority were made during mobilization of the greater curvature and during stapling of the stomach. In 44.6 %, errors had consequences and 96 additional actions were performed. There was a significant correlation between errors during opening of the lesser sac and postoperative complications, and between repositioning of the stapler and postoperative complications.

CONCLUSIONS:

In this study, the 13 key steps of the SG were defined, and OCHRA was considered a valuable assessment tool for surgical performance and potential hazard zones. Most consequential errors are made during dissection of the greater curvature and during stapling of the stomach. Errors during the start of mobilization of the greater curvature and repositioning of the stapler lead to longer duration of the procedure and are associated with a higher risk of postoperative complications.

Impactfactor: 3.747

Impact of hernia volume on pulmonary complications following complex hernia repair.

Mommers EH, Wegdam JA, van der Wolk S, **Nienhuijs SW**, de Vries Reilingh TS

J Surg Res. 2017 May 1;211:8-13. Epub 2016 Dec 7

BACKGROUND:

Despite a multitude of evidence-based prediction models and risk factors for postoperative complications after ventral hernia repair, estimating a patient's risk of postoperative complications after ventral hernia repair remains challenging. In an attempt to improve the preoperative assessment of complex hernia patients, some studies have examined pulmonary changes after hernia repair hypothesizing that large hernias lead to pulmonary changes and increased pulmonary complication rates. Some studies have described a correlation between hernia volume and pulmonary changes, although none provided compelling evidence to identify hernia volume as a risk factor for pulmonary complications. This study evaluates the relationship between hernia volume and postoperative pulmonary complications using computed tomography (CT)-based volume measurements.

MATERIALS AND METHODS:
Analysis of a prospectively maintained database of consecutive complex hernia patients from 2011 to 2014 undergoing endoscopic (ECST) or open component separation technique (CST) for a hernia defect with a minimum width of 6 cm and visual protrusion of the hernia sac ventral of the rectus abdominis muscles in supine position was performed. Hernia volume was calculated using multiple plane reconstruction of a standard abdominal CT-scan. Noted endpoints were pulmonary complications.
RESULTS:
Thirty-five patients underwent ECST (n = 20) or CST (n = 15) with a median defect volume of 474 cm3 (range, 114-2086 cm3). Observed complications were pneumonia (n = 4), pulmonary infiltrate (n = 3), aspiration pneumonia (n = 2), and acute respiratory distress syndrome (n = 1). Univariate and multivariate analyses showed that pulmonary complications were associated with "hernia volume" (P = 0.045; 95% CI: 1.008-1.910).
CONCLUSIONS:
Hernia volume is a promising risk factor for postoperative pulmonary complications and can be calculated using a standard abdominal CT-scan.

Impactfactor: 2.187

Improved Adherence to a Stepped-care Model Reduces Costs of Intermittent Claudication Treatment in The Netherlands

Hageman D, Fokkenrood HJ, Essers PP, Koelemay MJ, Breek JC, Vahl AC, Scheltinga MR, **Teijink JA**.

Eur J Vasc Endovasc Surg. 2017 Jul; 54(1):51-57. Epub 2017 May 20

OBJECTIVE/BACKGROUND:
A previous budget impact analysis regarding a supervised exercise therapy (SET) first treatment strategy (stepped care model [SCM]) for Dutch patients with intermittent claudication (IC) showed a low referral rate in 2009, despite solid evidence of the effectiveness of SET programs. Recently, several campaigns have stimulated stakeholders in the field to adopt a SET first strategy in patients with IC. The aim of the present study was to reassess SCM adherence after a 2 year period.
METHODS:
IC related invoices of patients in 2011 were obtained from a large Dutch health insurance company (3.5 million persons). Patients were divided into two groups based on their initial treatment. A SET group had started SET between 12 months before (initiated by general practitioner) and 3 months after (initiated by vascular surgeon) presentation at a vascular surgery outpatient clinic. An intervention (INT) group was treated by revascularisation within 3 months of outpatient presentation. Costs of IC treatment in this 2011 cohort were compared with the earlier 2009 cohort.
RESULTS:
IC related invoices of 4135 patients were available. In 2011, the initial treatment was SET in 56% (2009: 34%; +22% [p < .001]) and INT in 44% (2009: 66%; -22% [p < .001]) of the IC population. Additional revascularisation was performed in 19% of patients in the SET group (2009: 6%; +13% [p < .001]) and also in 19% of patients in the INT group (2009: 35%; -16% [p < .001]). Later on, 29% of patients in the INT group were referred for SET (2009: 10%; +19% [p < .001]). Average costs of IC treatment per patient in 2011 were 6% lower than in 2009 (€6885 vs. €7300; p = .020).
CONCLUSION:
A 22% increase in adherence to SET as a first treatment strategy in Dutch patients with IC was attained between 2009 and 2011. This shift suggests successful SCM implementation resulting in lower costs for the national healthcare system.

Impactfactor: 4.061

Improved and more effective algorithms to screen for nutrient deficiencies after bariatric surgery

Bazuin I, **Pouwels S**, Houterman S, **Nienhuijs SW**, **Smulders JF**, Boer AK

Eur J Clin Nutr. 2017 Feb 71(2):198-202

BACKGROUND/OBJECTIVES:
Most bariatric guidelines recommend frequent lab monitoring of patients to detect nutrient and vitamin deficiencies as early as possible. The aim of this study was to optimize the cost effectiveness of the nutrient panel, by developing an algorithm, which detects nutrient deficiencies at lower costs.
SUBJECTS/METHODS:
In this retrospective study, 2055 patients who had undergone Laparoscopic Roux-Y Gastric Bypass (LRYGB) and Laparoscopic Sleeve Gastrectomy (LSG) surgery at Catharina Hospital Eindhoven between

January 2009 and December 2013 were included. Perioperative biochemical measurements (7 days before and 127 days after surgery) and measurements >549 days before surgery were excluded. For analysis, the most recent preoperative and postoperative measurements were selected for each biochemical parameter separately. First, the amount of moderate and severe deficiencies were calculated. Second, we investigated whether each variable (vitamins A, B1, B6, B12, D, folate, ferritin, zinc and magnesium) could predict the presence of deficiency.

RESULTS:

In total, 561 (LRYGB) and 831 (LSG) patients had at least preoperative and postoperative values of vitamin A, B1, B6, B12, D, folate, ferritin, zinc or magnesium. The algorithm reduces vitamin D, B12, B6, B1 and ferritin examinations by 15, 11, 28, 28 and 38%, respectively, without missing clinically relevant deficiencies. The corresponding potential cost savings was 14%.

CONCLUSIONS:

This study identified substantial cost savings in laboratory test for both LRYGB and LSG procedures. The potential cost reduction of 14% might even be increased to 42% when less frequent moderate deficiencies are not screened anymore, whereas >99.0 of moderate deficiencies will be detected.

Impactfactor: 3.057

Improved Functional Results After Minimally Invasive Esophagectomy: Intrathoracic Versus Cervical Anastomosis

van Workum F, van der Maas J, van den Wildenberg FJ, Polat F, Kouwenhoven EA, van Det MJ, **Nieuwenhuijzen GA, Luyer MD,** Rosman C

Ann Thorac Surg. 2017 Jan; 103(1):267-273

BACKGROUND:

Both cervical esophagogastric anastomosis (CEA) and intrathoracic esophagogastric anastomosis (IEA) are used to restore gastrointestinal integrity following minimally invasive esophagectomy (MIE). No prospective randomized data on functional outcome, postoperative morbidity, and mortality between these techniques are currently available.

METHODS:

A comparison was conducted including all consecutive patients with esophageal carcinoma of the distal esophagus or gastroesophageal junction undergoing MIE with CEA or MIE with IEA from October 2009 to July 2014 in 3 high-volume esophageal cancer centers. Functional outcome, postoperative morbidity, and mortality were analyzed.

RESULTS: MIE with CEA was performed in 146 patients and MIE with IEA in 210 patients. The incidence of recurrent laryngeal nerve palsy was 14.4% after CEA and 0% after IEA ($p < 0.001$). Dysphagia, dumping, and regurgitation were reported less frequently after IEA compared with CEA ($p < 0.05$). Dilatation of benign strictures occurred in 43.8% after CEA and this was 6.2% after IEA ($p < 0.001$). If a benign stricture was identified, it was dilated a median of 4 times in the CEA group and only once in the IEA group ($p < 0.001$). Anastomotic leakage for which reoperation was required occurred in 8.2% after CEA and in 11.4% after IEA (not significant). Median ICU stay, hospital stay, in-hospital mortality, 30-day mortality, and 90-day mortality were similar between the groups (not significant).

CONCLUSIONS: MIE with IEA was associated with better functional results than MIE with CEA with less dysphagia, less benign anastomotic strictures requiring fewer dilatations, and a lower incidence of recurrent laryngeal nerve palsy. Other postoperative morbidity and mortality did not differ between the groups.

Impactfactor: 3.700

Influence of the Extent and Dose of Radiation on Complications After Neoadjuvant Chemoradiation and Subsequent Esophagectomy With Gastric Tube Reconstruction With a Cervical Anastomosis

Koëter M, Kathiravetpillai N, Gooszen JA, van Berge Henegouwen MI, Gisbertz SS, van der Sangen MJ, **Luyer MD, Nieuwenhuijzen GA,** Hulshof MC

Int J Radiat Oncol Biol Phys. 2017 Mar 15;97(4):813-821

PURPOSE: To detrmine, in a large series, the influence of the extent and dose of radiation to the fundus of the stomach and mediastinum on the development and severity of anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation followed by esophagectomy with cervical anastomosis.

METHODS AND MATERIALS: Between 2005 and 2012, 364 consecutive patients with esophageal cancer treated with neoadjuvant chemoradiation (41.4 Gy combined with chemotherapy) followed by

esophagectomy were included. The future anastomotic region in the fundus was determined, and the mean dose, V20-V40, and upper planning target volume border in relation to mediastinal length, expressed as the mediastinal ratio, were calculated.

RESULTS: Anastomotic leakage occurred in 22% and anastomotic stenosis in 41%. Logistic regression analysis revealed no influence of age, comorbidity, mean fundus dose, V20-V40, or the mediastinal ratio on the incidence of anastomotic leakage or anastomotic stenosis. In 28% of the patients severe complications (Clavien-Dindo score of =IIIB) occurred. The presence of multiple comorbidities (hazard ratio 2.4 [95% confidence interval 1.3-4.5], P=.006) and a mediastinal ratio of 0.5 to 1.0 (hazard ratio 1.9 [95% confidence interval 1.0-3.5], P=.036) were both independent predictors of severe complications.

CONCLUSION: With a mean radiation dose of 24.2 Gy to the future anastomotic region of the gastric fundus, the radiation dose was not associated with the incidence of anastomotic leakage or anastomotic stenosis. The incidence of severe complications was associated with a high superior mediastinal planning target volume border.

Impactfactor: 5.133

Initial non-operative management of uncomplicated appendicitis in children: a protocol for a multicentre randomised controlled trial (APAC trial)

Knaapen M, van der Lee JH, Bakx R, The SL, van Heurn EW, Heij HA, Gorter RR; APAC collaborative study group: **Luyer MD, Vugts G**

BMJ Open. 2017 Nov 15;7(11):e018145

INTRODUCTION: Based on epidemiological, immunological and pathology data, the idea that appendicitis is not necessarily a progressive disease is gaining ground. Two types are distinguished: simple and complicated appendicitis. Non-operative treatment (NOT) of children with simple appendicitis has been investigated in several small studies. So far, it is deemed safe. However, its effectiveness and effect on quality of life (QoL) have yet to be established in an adequately powered randomised trial. In this article, we provide the study protocol for the APAC (Antibiotics versus Primary Appendectomy in Children) trial.

METHODS AND ANALYSIS: This multicentre, non-inferiority, randomised controlled trial randomises children aged 7-17 years with imaging-confirmed simple appendicitis between appendectomy and NOT. Patients are recruited in 15 hospitals. The intended sample size, based on the primary outcome, rate of complications and a non-inferiority margin of 5%, is 334 patients.NOT consists of intravenous antibiotics for 48-72 hours, daily blood tests and ultrasound follow-up. If the patient meets the predefined discharge criteria, antibiotic treatment is continued orally at home. Primary outcome is the rate of complications at 1-year follow-up. An independent adjudication committee will assess all complications and their relation to the allocated treatment. Secondary outcomes include, but are not limited to, delayed appendectomies, QoL, pain and (in)direct costs.The primary outcome will be analysed both according to the intention-to-treat principle and the per-protocol principle, and is presented with a one-sided 97.5% CI. We will use multiple logistic and linear regression for binary and continuous outcomes, respectively, to adjust for stratification factors.

ETHICS AND DISSEMINATION: The protocol has been approved by the Medical Ethics Review Committee of the Academic Medical Center, Amsterdam. Data monitoring is performed by an independent institute and a Data Safety Monitoring Board has been assigned. Results will be presented in peer-reviewed academic journals and at (international) conferences.

Impactfactor: 2.369

Is There Any Reason to Still Consider Lateral Lymph Node Dissection in Rectal Cancer? Rationale and Technique

Kusters M, Uehara K, Velde CJ, Moriya Y

Clin Colon Rectal Surg. 2017 Nov;30(5):346-356

Nodal dissemination in locally advanced rectal cancer occurs mainly in two directions: upward and lateral. Lateral node involvement has been demonstrated; however, lateral lymph node dissection (LLND) is not routinely performed in Western countries and the focus is more on neoadjuvant treatment regimens. The main reasons for this are the high morbidity associated with the operation and the uncertain oncological benefit. There is, however, recent evidence that in selected cases, neoadjuvant treatment combined with total mesorectal excision only might not be sufficient. In this article, the historical developments in the East and the West, the current evidence regarding lateral nodal disease, and the surgical steps in the LLND are discussed.

Impactfactor: 0.839

Long-term Recurrence-free Survival After Standard Endoscopic Resection Versus Surgical Resection of Submucosal Invasive Colorectal Cancer: A Population-based Study

Belderbos TD, van Erning FN, **de Hingh IH**, van Oijen MG, Lemmens VE, Siersema PD

Clin Gastroenterol Hepatol. 2017 Mar; 15(3):403-411.e1

BACKGROUND & AIMS: There is controversy over the optimal management for T1 colorectal cancer (T1 CRC). This study compared initial endoscopic resection with or without additional surgery, or initial surgery for T1 CRC, and assessed risk factors for lymph node metastases (LNMs) and long-term recurrence. METHODS: We performed a registration study that included all patients diagnosed with T1 CRC from 1995 through 2011 in the southeast area of The Netherlands (n = 1315). High-risk histology (with regard to LNM) was defined as the presence of

poor differentiation, lymphangio-invasion, and/or deep submucosal invasion. The primary outcome measure was the combined rate of local and distant CRC recurrence during a mean follow-up period of 6.6 years. Logistic regression and Cox proportional hazards regression analyses were performed to evaluate independent risk factors for LNM and CRC recurrence, respectively. RESULTS: Endoscopic resection was performed in 590 patients (44.9%); of these, 220 (16.7%) underwent additional surgery. Initial surgery was performed in 725 patients (55.1%). The risk of LNM was higher in T1 CRC with histologic risk factors (15.5% vs 7.1% without histologic risk factors; odds ratio, 2.21; 95% confidence interval, 1.33-3.70). Thirty-day mortality did not differ between patients who received additional surgery (0.9%) and those who underwent only endoscopic resection (1.4%; P = .631). Rates of CRC recurrence were 6.2% (9.8/1000 patient-years) after only endoscopic resection vs 6.4% (9.4/1000

patient-years) after additional surgery (P = .912), and 3.4% (5.2/1000 patient-years) after initial surgery (P = .031). In multivariate analysis, this difference was not significant. The only independent risk factor for long-term recurrence was a positive resection margin (hazard ratio, 6.88; 95% confidence interval, 2.27-20.87).

CONCLUSIONS: Based on a population analysis of patients diagnosed with T1 CRC, additional surgery after endoscopic resection should be considered only for patients with high-risk histology or a positive resection margin.

Impactfactor: 7.398

Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms

van Schaik TG, Yeung KK, Verhagen HJ, de Bruin JL, **van Sambeek MR**, Balm R, Zeebregts CJ, van Herwaarden JA, Blankensteijn JD; DREAM trial participants: **Teijink JA, Cuypers PhW**

J Vasc Surg. 2017 Nov;66(5):1379-1389

OBJECTIVE: andomized trials have shown an initial survival benefit of endovascular over conventional open abdominal aortic aneurysm repair but no long-term difference up to 6 years after repair. Longer follow-up may be required to demonstrate the cumulative negative impact on survival of higher reintervention rates associated with endovascular repair.

METHODS: We updated the results of the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, a multicenter, randomized controlled trial comparing open with endovascular aneurysm repair, up to 15 years of follow-up. Survival and reinterventions were analyzed on an intention-to-treat basis. Causes of death and secondary interventions were compared by use of an events per person-year analysis.

RESULTS: There were 178 patients randomized to open and 173 to endovascular repair. Twelve years after randomization, the cumulative overall survival rates were 42.2% for open and 38.5% for endovascular repair, for a difference of 3.7 percentage points (95% confidence interval, -6.7 to 14.1; P = .48). The cumulative rates of freedom from reintervention were 78.9% for open repair and 62.2% for endovascular repair, for a difference of 16.7 percentage points (95% confidence interval, 5.8-27.6; P = .01). No differences were observed in causes of death. Cardiovascular and malignant disease account for the majority of deaths after prolonged follow-up.

CONCLUSIONS: During 12 years of follow-up, there was no survival difference between patients who underwent open or endovascular abdominal aortic aneurysm repair, despite a continuously increasing number of reinterventions in the endovascular repair group. Endograft durability and the need for continued endograft surveillance remain key issues.

Impactfactor: 3.536

Management of Severe Pancreatic Fistula After Pancreatoduodenectomy

Smits FJ, van Santvoort HC, Besselink MG, Batenburg MC, Slooff RA, Boerma D, Busch OR, Coene PP, van Dam RM, van Dijk DP, van Eijck CH, Festen S, van der Harst E, **de Hingh IH**, de Jong KP, Tol JA, Borel Rinkes IH, Molenaar IQ, Dutch Pancreatic Cancer Group

JAMA Surg. 2017 Jun 1 152(6):540-548

Importance:

Postoperative pancreatic fistula is a potentially life-threatening complication after pancreatoduodenectomy. Evidence for best management is lacking.

Objective:

To evaluate the clinical outcome of patients undergoing catheter drainage compared with relaparotomy as primary treatment for pancreatic fistula after pancreatoduodenectomy.

Design, Setting, and Participants:

A multicenter, retrospective, propensity-matched cohort study was conducted in 9 centers of the Dutch Pancreatic Cancer Group from January 1, 2005, to September 30, 2013. From a cohort of 2196 consecutive patients who underwent pancreatoduodenectomy, 309 patients with severe pancreatic fistula were included. Propensity score matching (based on sex, age, comorbidity, disease severity, and previous reinterventions) was used to minimize selection bias. Data analysis was performed from January to July 2016.

Exposures:

First intervention for pancreatic fistula: catheter drainage or relaparotomy.

Main Outcomes and Measures:

Primary end point was in-hospital mortality; secondary end points included new-onset organ failure.

Results:

Of the 309 patients included in the analysis, 209 (67.6%) were men, and mean (SD) age was 64.6 (10.1) years. Overall in-hospital mortality was 17.8% (55 patients): 227 patients (73.5%) underwent primary catheter drainage and 82 patients (26.5%) underwent primary relaparotomy. Primary catheter drainage was successful (ie, survival without relaparotomy) in 175 patients (77.1%). With propensity score matching, 64 patients undergoing primary relaparotomy were matched to 64 patients undergoing primary catheter drainage. Mortality was lower after catheter drainage (14.1% vs 35.9%; P?=?.007; risk ratio, 0.39; 95% CI, 0.20-0.76). The rate of new-onset single-organ failure (4.7% vs 20.3%; P?=?.007; risk ratio, 0.15; 95% CI, 0.03-0.60) and new-onset multiple-organ failure (15.6% vs 39.1%; P?=?.008; risk ratio, 0.40; 95% CI, 0.20-0.77) were also lower after primary catheter drainage.

Conclusions and Relevance:

In this propensity-matched cohort, catheter drainage as first intervention for severe pancreatic fistula after pancreatoduodenectomy was associated with a better clinical outcome, including lower mortality, compared with primary relaparotomy.

Impactfactor: 7.956

McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis

van Workum F, **Berkelmans GH**, Klarenbeek BR, **Nieuwenhuijzen GA, Luyer MD**, Rosman C

J Thorac Dis. 2017 Jul;9(Suppl 8):S826-S833

BACKGROUND: Minimally invasive esophagectomy (MIE) has consistently been associated with improved perioperative outcome and similar oncological safety compared to open esophagectomy. However, it is currently unclear what type of MIE is preferred for patients with resectable esophageal cancer.

METHODS: Literature was searched in Medline, Embase and the Cochrane library combining relevant search terms. Articles that included patients undergoing totally minimally invasive esophagectomy (TMIE) or hybrid minimally invasive esophagectomy (HMIE) and compared McKeown with Ivor Lewis procedures were included. Studies were excluded if they included >10% of patients undergoing a procedure other than MIE McKeown or MIE Ivor Lewis (i.e., transhiatal resections). The primary outcome parameter was anastomotic leakage. Secondary outcome parameters were: other complications, reinterventions, reoperations, hospital length of stay, ICU length of stay, postoperative mortality, operative time, blood loss, R0 resection rate, lymph nodes examined, quality of life and costs.

RESULTS: Five studies with a total of 1,681 patients undergoing TMIE were included. There were no studies comparing HMIE McKeown versus HMIE Ivor Lewis. There were no randomized controlled trials and all included studies were cohort studies with a moderate risk of bias. No meta-analysis could be

performed for R0 resection rate, survival, quality of life and costs because there was insufficient data available for these parameters. The incidence of anastomotic leakage did not differ between the groups [relative risk (RR) =1.39, 95% confidence interval (CI) =0.90-10.38, P=0.14]. TMIE Ivor Lewis was associated with a lower incidence of recurrent laryngeal nerve (RLN) trauma (RR =6.70, 95% CI =3.09-14.55, P<0.001), a shorter hospital length of stay [standardized mean difference (SMD) =0.17, 95% CI =0.06-0.28, P=0.002] and less blood loss (SMD =0.69, 95% CI =0.25-1.12, P=0.002).

CONCLUSIONS:

TMIE Ivor Lewis is associated with improved outcome regarding RLN trauma, hospital length of stay and blood loss as compared to TMIE-McKeown, but the incidence of anastomotic leakage is not different. The evidence is limited, of low quality and at risk for bias. A randomized controlled trial is currently being performed in order to demonstrate whether a McKeown or Ivor Lewis procedure should be preferred in patients undergoing MIE.

Impactfactor: 2.365

Meta-Analysis of Genome-Wide Association Studies for Abdominal Aortic Aneurysm Identifies Four New Disease-Specific Risk Loci

Jones GT, Tromp G, Kuivaniemi H, Gretarsdottir S, Baas AF, Giusti B, Strauss E, Van't Hof FN, Webb TR, Erdman R, Ritchie MD, Elmore JR, Verma A, Pendergrass S, Kullo IJ, Ye Z, Peissig PL, Gottesman O, Verma SS, Malinowski J, Rasmussen-Torvik LJ, Borthwick KM, Smelser DT, Crosslin DR, de Andrade M, Ryer EJ, McCarty CA, Böttinger EP, Pacheco JA, Crawford DC, Carrell DS, Gerhard GS, Franklin DP, Carey DJ, Phillips VL, Williams MJ, Wei W, Blair R, Hill AA, Vasudevan TM, Lewis DR, Thomson IA, Krysa J, Hill GB, Roake J, Merriman TR, Oszkinis G, Galora S, Saracini C, Abbate R, Pulli R, Pratesi C, Saratzis A, Verissimo AR, Bumpstead S, Badger SA, Clough RE, Cockerill G, Hafez H, Scott DJ, Futers TS, Romaine SP, Bridge K, Griffin KJ, Bailey MA, Smith A, Thompson MM, van Bockxmeer FM, Matthiasson SE, Thorleifsson G, Thorsteinsdottir U, Blankensteijn JD, **Teijink JA**, Wijmenga C, de Graaf J, Kiemeney LA, Lindholt JS, Hughes A, Bradley DT, Stirrups K, Golledge J, Norman PE, Powell JT, Humphries SE, Hamby SE, Goodall AH, Nelson CP, Sakalihasan N, Courtois A, Ferrell RE, Eriksson P, Folkersen L, Franco-Cereceda A, Eicher JD, Johnson AD, Betsholtz C, Ruusalepp A, Franzén O, Schadt EE, Björkegren JL, Lipovich L, Drolet AM, Verhoeven EL, Zeebregts CJ, Geelkerken RH, **van Sambeek MR**, van Sterkenburg SM, de Vries JP, Stefansson K, Thompson JR, de Bakker PI, Deloukas P, Sayers RD, Harrison SC, van Rij AM, Samani NJ, Bown MJ.

Circ Res. 2017 Jan 20;120(2):341-353. Epub 2016 Nov

RATIONALE:

Abdominal aortic aneurysm (AAA) is a complex disease with both genetic and environmental risk factors. Together, 6 previously identified risk loci only explain a small proportion of the heritability of AAA.

OBJECTIVE:

To identify additional AAA risk loci using data from all available genome-wide association studies.

METHODS AND RESULTS:

Through a meta-analysis of 6 genome-wide association study data sets and a validation study totaling 10?204 cases and 107?766 controls, we identified 4 new AAA risk loci: 1q32.3 (SMYD2), 13q12.11 (LINC00540), 20q13.12 (near PCIF1/MMP9/ZNF335), and 21q22.2 (ERG). In various database searches, we observed no new associations between the lead AAA single nucleotide polymorphisms and coronary artery disease, blood pressure, lipids, or diabetes mellitus. Network analyses identified ERG, IL6R, and LDLR as modifiers of MMP9, with a direct interaction between ERG and MMP9.

CONCLUSIONS:

The 4 new risk loci for AAA seem to be specific for AAA compared with other cardiovascular diseases and related traits suggesting that traditional cardiovascular risk factor management may only have limited value in preventing the progression of aneurysmal disease.

Impactfactor: 13.965

Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years

Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, Greenhalgh RM; EVAR-1, DREAM, OVER and ACE Trialists: **Teijink JA, Cuypers PhW, Sambeek MR**

Br J Surg. 2017 Feb;104(3):166-178

BACKGROUND:

The erosion of the early mortality advantage of elective endovascular aneurysm repair (EVAR) compared with open repair of abdominal aortic aneurysm remains without a satisfactory explanation.

METHODS:

An individual-patient data meta-analysis of four multicentre randomized trials of EVAR versus open repair was conducted to a prespecified analysis plan, reporting on mortality, aneurysm-related mortality and reintervention.

RESULTS:

The analysis included 2783 patients, with 14?245 person-years of follow-up (median 5·5?years). Early (0-6 months after randomization) mortality was lower in the EVAR groups (46 of 1393 versus 73 of 1390 deaths; pooled hazard ratio 0·61, 95 per cent c.i. 0·42 to 0·89; P = 0·010), primarily because 30-day operative mortality was lower in the EVAR groups (16 deaths versus 40 for open repair; pooled odds ratio 0·40, 95 per cent c.i. 0·22 to 0·74). Later (within 3 years) the survival curves converged, remaining converged to 8 years. Beyond 3 years, aneurysm-related mortality was significantly higher in the EVAR groups (19 deaths versus 3 for open repair; pooled hazard ratio 5·16, 1·49 to 17·89; P = 0·010). Patients with moderate renal dysfunction or previous coronary artery disease had no early survival advantage under EVAR. Those with peripheral artery disease had lower mortality under open repair (39 deaths versus 62 for EVAR; P?=?0·022) in the period from 6 months to 4 years after randomization.

CONCLUSION:

The early survival advantage in the EVAR group, and its subsequent erosion, were confirmed. Over 5?years, patients of marginal fitness had no early survival advantage from EVAR compared with open repair. Aneurysm-related mortality and patients with low ankle?:?brachial pressure index contributed to the erosion of the early survival advantage for the EVAR group. Trial registration numbers: EVAR-1, ISRCTN55703451; DREAM?(Dutch Randomized Endovascular Aneurysm Management), NCT00421330; ACE (Anévrysme de l'aorte abdominale, Chirurgie versus Endoprothèse), NCT00224718; OVER (Open Versus Endovascular Repair Trial for Abdominal Aortic Aneurysms).

Impactfactor: 5.899

Minimally invasive versus open distal pancreatectomy (LEOPARD): study protocol for a randomized controlled trial

de Rooij T, van Hilst J, Vogel JA, van Santvoort HC, de Boer MT, Boerma D, van den Boezem PB, Bonsing BA, Bosscha K, Coene PP, Daams F, van Dam RM, Dijkgraaf MG, van Eijck CH, Festen S, Gerhards MF,
Groot Koerkamp B, Hagendoorn J, van der Harst E, **de Hingh IH**, Dejong CH, Kazemier G, Klaase J, de Kleine RH, van Laarhoven CJ, Lips DJ, **Luyer MD**, Molenaar IQ, Nieuwenhuijs VB, Patijn GA, Roos D, Scheepers JJ,
van der Schelling GP, Steenvoorde P, Swijnenburg RJ, Wijsman JH, Abu Hilal M, Busch OR, Besselink MG; Dutch Pancreatic Cancer Group

Trials. 2017 Apr 8 18(1):166

BACKGROUND:

Observational cohort studies have suggested that minimally invasive distal pancreatectomy (MIDP) is associated with better short-term outcomes compared with open distal pancreatectomy (ODP), such as less intraoperative blood loss, lower morbidity, shorter length of hospital stay, and reduced total costs. Confounding by indication has probably influenced these findings, given that case-matched studies failed to confirm the superiority of MIDP. This accentuates the need for multicenter randomized controlled trials, which are currently lacking. We hypothesize that time to functional recovery is shorter after MIDP compared with ODP even in an enhanced recovery setting.

METHODS:

LEOPARD is a randomized controlled, parallel-group, patient-blinded, multicenter, superiority trial in all 17 centers of the Dutch Pancreatic Cancer Group. A total of 102 patients with symptomatic benign, premalignant or malignant disease will be randomly allocated to undergo MIDP or ODP in an enhanced recovery setting. The primary outcome is time (days) to functional recovery, defined as all of the following: independently mobile at the preoperative level, sufficient pain control with oral medication alone, ability to maintain sufficient (i.e. >50%) daily required caloric intake, no intravenous fluid administration and no signs of infection. Secondary outcomes are operative and postoperative outcomes, including clinically relevant complications, mortality, quality of life and costs.

DISCUSSION:

The LEOPARD trial is designed to investigate whether MIDP reduces the time to functional recovery compared with ODP in an enhanced recovery setting.

Impactfactor: 1.969

Nasogastric decompression following esophagectomy: a systematic literature review and meta-analysis

Weijs TJ, Kumagai K, **Berkelmans GH**, **Nieuwenhuijzen GA**, Nilsson M, **Luyer MD**

Dis Esophagus. 2017 Feb 1; 30(3):1-8

Routine use of nasogastric tubes for gastric decompression has been abolished in nearly all types of gastro-intestinal surgery after introduction of enhanced recovery after surgery programs. However, in esophagectomy the routine use of nasogastric decompression is still a matter of debate. To determine the effectsof routine nasogastric decompression following esophagectomy compared with early or peroperative removal of the nasogastric tube on pulmonary complications, anastomotic leakage, mortality, and postoperative recovery.

A systematic literature review and meta-analysis of studies comparing early or peroperative versus late removal of nasogastric tubes. A total of seven comparative studies were included (n?=?608). In two randomized trials, and one retrospective cohort study, peroperative removal of the nasogastric tube was compared with routine nasogastric decompression. In one randomized trial early removal of the nasogastric tube (on postoperative day 2) was compared with removal of the nasogastric tube on the 6th-10th postoperative day. In the remaining three trials a fast-track protocol without a nasogastric tube was compared with conventional care with a nasogastric tube during the first postoperative days. Peroperative or early removal of the nasogastric tube did not result in a significantly different rate of anastomotic leakage, pulmonary complications or mortality in individual studies, nor in the meta-analysis. In the meta-analysis, hospital stay was significantly shorter with peroperative or early removal of the nasogastric tube when all studies were included, but not when the meta-analysis was limited to randomized trials. This systematic review did not find a difference in adverse outcomes between nasogastric decompression or no nasogastric decompression following esophagectomy.

Impactfactor: 2.571

Nationwide outcomes in patients undergoing surgical exploration without resection for pancreatic cancer

van der Geest LG, Lemmens VE, **de Hingh IH**, van Laarhoven CJ, Bollen TL, Nio CY, van Eijck CH, Busch OR, Besselink MG; Dutch Pancreatic Cancer Group

Br J Surg. 2017 Oct;104(11):1568-1577

BACKGROUND: Despite improvements in diagnostic imaging and staging, unresectable pancreatic cancer is still encountered during surgical exploration with curative intent. This nationwide study investigated outcomes in patients with unresectable pancreatic cancer found during surgical exploration.

METHODS: All patients diagnosed with primary pancreatic (adeno)carcinoma (2009-2013) in the Netherlands Cancer Registry were included. Predictors of unresectability, 30-day mortality and poor survival were evaluated using logistic and Cox proportional hazards regression analysis.

RESULTS: There were 10 595 patients with pancreatic cancer during the study interval. The proportion of patients undergoing surgical exploration increased from 19·9 to 27·0 per cent (P <?0·001). Among 2356 patients who underwent surgical exploration, the proportion of patients with tumour resection increased from 61·6 per cent in 2009 to 71·3 per cent in 2013 (P <?0·001), whereas the contribution of M1 disease (18·5 per cent overall) remained stable. Patients who had exploration only had an increased 30-day mortality rate compared with those who underwent tumour resection (7·8 versus 3·8 per cent; P <?0·001). In the non-resected group, among those with M0 (383 patients) and M1 (435) disease at surgical exploration, the 30-day mortality rate was 4·7 and 10·6 per cent (P = 0·002), median survival was 7·2 and 4·4?months (P <?0·001), and 1-year survival rates were 28·0 and 12·9 per cent, respectively. Among other factors, low hospital volume (0-20 resections per year) was an independent predictor for not undergoing tumour resection, but also for 30-day mortality and poor survival among patients without tumour resection.

CONCLUSION: Exploration and resection rates increased, but one-third of patients who had surgical exploration for pancreatic cancer did not undergo resection. Non-resectional surgery doubled the 30-day mortality rate compared with that in patients undergoing tumour resection.

Impactfactor: 5.899

Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit

van Rijssen LB, Koerkamp BG, Zwart MJ, Bonsing BA, Bosscha K, van Dam RM, van Eijck CH, Gerhards MF, van der Harst E, **de Hingh IH**, de Jong KP, Kazemier G, Klaase J, van Laarhoven CJ, Molenaar IQ, Patijn GA, Rupert CG, van Santvoort HC, Scheepers JJ, van der Schelling GP, Busch OR, Besselink MG; Dutch Pancreatic Cancer Group

HPB (Oxford). 2017 Oct;19(10):919-926

BACKGROUND:
Auditing is an important tool to identify practice variation and 'best practices'. The Dutch Pancreatic Cancer Audit is mandatory in all 18 Dutch centers for pancreatic surgery.
METHODS:
Performance indicators and case-mix factors were identified by a PubMed search for randomized controlled trials (RCT's) and large series in pancreatic surgery. In addition, data dictionaries of two national audits, three institutional databases, and the Dutch national cancer registry were evaluated. Morbidity, mortality, and length of stay were analyzed of all pancreatic resections registered during the first two audit years. Case ascertainment was cross-checked with the Dutch healthcare inspectorate and key-variables validated in all centers.
RESULTS:
Sixteen RCT's and three large series were found. Sixteen indicators and 20 case-mix factors were included in the audit. During 2014-2015, 1785 pancreatic resections were registered including 1345 pancreatoduodenectomies. Overall in-hospital mortality was 3.6%. Following pancreatoduodenectomy, mortality was 4.1%, Clavien-Dindo grade = III morbidity was 29.9%, median (IQR) length of stay 12 (9-18) days, and readmission rate 16.0%. In total 97.2% of >40,000 variables validated were consistent with the medical charts.
CONCLUSIONS:
The Dutch Pancreatic Cancer Audit, with high quality data, reports good outcomes of pancreatic surgery on a national level.

Impactfactor: 3.290

[Neurogenic thoracic outlet syndrome] - Neurogeen thoracic-outletsyndroom

Teijink JA, Pesser N, van Grinsven R, van Suijlekom H, **van Sambeek MR**, van Nuenen BF

Ned Tijdschr Geneeskd. 2017;161(0):D1385

Neurogenic thoracic outlet syndrome (nTOS) is a type of thoracic outlet syndrome (TOS) where compression of the brachial plexus is responsible for development of upper-extremity, head and neck symptoms. We present a 16-year-old and a 34-year-old patient with nTOS. Diagnosis in both cases was done by following the recently published reporting standards for (n)TOS. After this multidisciplinary diagnostic work-up we performed a transaxillary thoracic outlet decompression (TOD). Due to lack of literature, difficult nomenclature and complexity of diagnosis and treatment, diagnosis of nTOS is often delayed. Recent experience shows that treatment of nTOS is safe and effective, both in the short term and the long term.

Impactfactor: --

New insights into the surgical anatomy of the esophagus

Weijs TJ, Ruurda JP, **Luyer MD**, Cuesta MA, van Hillegersberg R, Bleys RL

J Thorac Dis. 2017 Jul;9(Suppl 8):S675-S680

Implementation of (robot assisted) minimally invasive esophagectomy and increased knowledge of the relation between the autonomic nervous system and the immune response have led to new insights regarding the surgical anatomy of the esophagus. First, two layers of connective tissue were identified; the aorto-esophageal and aorto-pleural ligaments that separate the peri-esophageal compartment, containing vagus nerves, carinal lymph nodes and trachea, from the para-aortic compartment; containing thoracic duct and azygos vein. Second the surgical anatomy of the pulmonary vagus nerve branches has been described in detail. Based on the hypothesis that sparing the vagal nerve branches may be important a method to spare the pulmonary branches of the vagus nerve during thoracoscopic esophagectomy was validated in a cadaver study. Further studies will now investigate the impact of these new insights in the surgical anatomy of the esophagus in clinical practice.

Impactfactor: 2.365

Patient selection for cytoreductive surgery and HIPEC for the treatment of peritoneal metastases from colorectal cancer

Simkens GA, Rovers KP, Nienhuijs SW, de Hingh IH

Cancer Manag Res. 2017 Jun 30;9:259-266

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a viable option for selected patients with peritoneal metastases (PM) from colorectal origin, resulting in long-term survival and even cure in some cases. However, adequate patient selection for this treatment is

currently one of the major challenges. The aim of this review is to provide a comprehensive overview of clinically relevant factors associated with overall survival. This may help to guide clinicians through the complex interplay of patient, tumor, and treatment characteristics to adequately select patients who benefit the most from this extensive surgical treatment. First, basic principles of colorectal PM and the CRS and HIPEC treatment will be discussed. According to available literature, especially extent of peritoneal disease, completeness of cytoreduction, and signet ring cell histology have great influence on the outcome after CRS and HIPEC. Other factors that seem to have a negative prognostic value are the presence of liver metastases and the absence of treatment with neo-adjuvant systemic therapy. Prognostic models combining the above-mentioned factors, such as the Colorectal Peritoneal Metastases Prognostic Surgical Score nomogram, may provide clinically relevant tools to use in everyday practice.

Impactfactor: --

Patient-reported outcomes (PROs) after total extraperitoneal hernia repair (TEP)

Mommers EHH, Hünen DRM, van Hout JCHM, Guit M, Wegdam JA, **Nienhuijs SW**, de Vries Reilingh TS

Hernia. 2017 Feb;21(1):45-50. Epub 2016 Dec 5

BACKGROUND:

Patient-reported outcomes (PROs) such as quality of life (QoL), patient satisfaction, and work impairment, are arguably the most important outcomes of any medical treatment. In 2011, Staerkle and Villiger developed the Core Outcome Measurements Index (COMI) to standardise PROs and PRO measurement for inguinal hernia patients, in an attempt to increase inter-study comparability. The aim of this study is to prospectively evaluate the short- and long-term postoperative QoL, function, patient well-being, pain, and social/work disability, after total extraperitoneal (TEP) inguinal hernia repair and to provide the first clinical experience with the COMI-hernia questionnaire.

METHODS:

Between January 2013 and December 2014, all patients =18 years that were scheduled for elective uni- or bilateral TEP in a regional hospital were approached to participate in this study. Measurements were taken preoperatively, and 6 weeks and 1 year postoperatively.

RESULTS:

One hundred and twenty patients (113 men, 7 women), mean age 59 years (SD ±12), completed the follow-up of 1 year. Ninety-seven percent of the population reported that the operation improved their complaints. QoL, function, well-being, and pain all improved after 6 weeks and 1 year after surgery. Patients experienced more social and work-related limitations 6 weeks after surgery compared to baseline measurements, though this improved to normal 1 year postoperatively. The incidence of chronic pain was 14% (VAS = 2), which had a negative impact on the patients' sense of well-being.

CONCLUSION:

Patients recovered well after TEP repair with a good quality of life and fast restore of function. Patient well-being was lower than expected due to a 14% incidence of chronic pain. The COMI-hernia scale provided reasonable insight into the patients' experience, though it was difficult to interpret for both patient and physician.

Impactfactor: *1.932*

Perioperative antibiotic prophylaxis in the treatment of acute cholecystitis (PEANUTS II trial): study protocol for a randomized controlled trial

Loozen CS, van Santvoort HC, van Geloven AA, **Nieuwenhuijzen GA**, de Reuver PR, Besselink MHG, Vlaminckx B, Kelder JC, Knibbe CA, Boerma D

Trials. 2017 Aug 23;18(1):390

BACKGROUND: The additional value of perioperative antibiotic prophylaxis in preventing infectious complications after emergency cholecystectomy for acute cholecystitis is a much-debated subject in the surgical community. Evidence-based guidelines are lacking, and consequently the use of antibiotic prophylaxis varies greatly among surgeons and hospitals. Recently, high-level evidence became available demonstrating that postoperative antibiotic prophylaxis in patients with acute cholecystitis does not reduce the risk of infectious complications. Preoperative antibiotic prophylaxis in relation to the risk of infectious complications, however, has never been studied.

METHODS: The PEANUTS II trial is a randomized, controlled, multicenter, open-label noninferiority trial whose aim is to determine the utility of preoperative antibiotic prophylaxis in patients undergoing emergency cholecystectomy for acute calculous cholecystitis. Patients with mild or moderate acute

cholecystitis, as defined according the Tokyo Guidelines, will be randomly assigned to a single preoperative dose of antibiotic prophylaxis (2000 mg of first-generation cephalosporin delivered intravenously) or no antibiotic prophylaxis before emergency cholecystectomy. The primary endpoint is a composite endpoint consisting of all postoperative infectious complications occurring during the first 30 days after surgery. Secondary endpoints include all the individual components of the primary endpoint, all other complications, duration of hospital stay, and total costs. The hypothesis is that the absence of antibiotic prophylaxis is noninferior to the presence of antibiotic prophylaxis. A noninferiority margin of 10% is assumed. With a 1-sided risk of 2.5% and a power of 80%, a total of 454 subjects will have to be included. Analysis will be performed according to the intention-to-treat principle.

DISCUSSION: The PEANUTS II trial will provide evidence-based advice concerning the utility of antibiotic prophylaxis in patients undergoing emergency cholecystectomy for acute calculous cholecystitis.

Impactfactor: 1.969

Perioperative systemic therapy for resectable colorectal peritoneal metastases: Sufficient evidence for its widespread use? A critical systematic review

Rovers KP, Simkens GA, Punt CJ, van Dieren S, Tanis PJ, **de Hingh IH**

Crit Rev Oncol Hematol. 2017 Jun; 114:53-62.Epub 2017 Mar 24

BACKGROUND/PURPOSE:

Despite its widespread use, no randomised studies have investigated the value of perioperative systemic therapy as adjunct to cytoreduction and HIPEC for colorectal peritoneal metastases. This systematic review evaluated the available evidence, which consists of non-randomised studies only.

METHODS:

A systematic search identified studies that investigated the influence of neoadjuvant, adjuvant, or perioperative systemic therapy on overall survival (OS).

RESULTS:

The 11 included studies (n=1708) were clinically heterogeneous and subject to selection bias. Studies on neoadjuvant systemic therapy revealed OS benefit (n=3), no OS benefit (n=1), and superiority of chemotherapy with bevacizumab vs. chemotherapy (n=2). Studies on adjuvant systemic therapy showed no OS benefit (n=3). Studies on perioperative systemic therapy demonstrated OS benefit (n=1), and superiority of modern vs. conventional systemic therapy(n=1).

CONCLUSION:

Significant limitations of available evidence question the widespread use of perioperative systemic therapy in this setting, stress the need for randomised studies, and impede conclusions regarding optimal timing and regimens. Included studies may suggest a survival benefit of neoadjuvant systemic therapy.

Impactfactor: --

Peritoneal Metastases from Gastroenteropancreatic Neuroendocrine Tumors: Incidence, Risk Factors and Prognosis

Madani A, Thomassen I van Gestel YR, van der Bilt JD, Haak HR, **de Hingh IH**, Lemmens VE

Ann Surg Oncol. 2017 Aug;24(8):2199-2205

BACKGROUND:

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are rare neoplasms and data on peritoneal metastases (PM) from these tumors are scarce.

OBJECTIVE:

The aim of this study was to present population-based data on the incidence, risk factors, and survival of synchronous PM in GEP-NETs.

METHODS:

Data from all patients diagnosed with a GEP-NET during 2007-2013 were collected from the Netherlands Cancer Registry. Age-standardized incidence rates were calculated and risk factors for developing PM were determined using multivariable logistic regression analysis. Survival was investigated using Kaplan-Meier and Cox regression analyses.

RESULTS:

A total of 4114 patients were diagnosed with a GEP-NET. PM were diagnosed in 234 patients (19% of patients with metastasized disease, representing 6% of all GEP-NETs). The incidence of patients diagnosed with PM was 1.6:1,000,000 persons per year. Risk factors for developing PM were higher age (odds ratio [OR] 1.4, 95% CI 1.0-2.0) and primary tumor location in the small intestine (OR 3.5, 95% CI

2.1-5.7) or colon (OR 2.5, 95% CI 1.4-4.4). Small intestinal NETs with PM had the best survival, while appendiceal NETs with PM had the poorest survival (5-year survival rates of 67 and 7%, respectively). Multivariate analysis showed that survival in patients with PM was worse compared with patients without metastases; however, the presence of PM among all metastasized patients was not associated with worse survival.

CONCLUSIONS:

This nationwide population-based study provides relevant insight into the incidence and risk factors of PM in GEP-NETs, and reveals detailed site-specific data on the presence of PM and survival data that may contribute to develop individualized treatment strategies in patients with these heterogeneous neoplasms.

Impactfactor: 4.041

Physical ExeRcise Following Esophageal Cancer Treatment (PERFECT) study: design of a randomized controlled trial

van Vulpen JK, Siersema PD, van Hillegersberg R, **Nieuwenhuijzen GA**, Kouwenhoven EA, Groenendijk RP, van der Peet DL, Hazebroek EJ, Rosman C, Schippers CC, Steenhagen E, Peeters PH, May AM

BMC Cancer. 2017 Aug 18;17(1):552

BACKGROUND: Following esophagectomy, esophageal cancer patients experience a clinically relevant deterioration of health-related quality of life, both on the short- and long-term. With the currently growing number of esophageal cancer survivors, the burden of disease- and treatment-related complaints and symptoms becomes more relevant. This emphasizes the need for interventions aimed at improving quality of life. Beneficial effects of post-operative physical exercise have been reported in several cancer types, but so far comparable evidence in esophageal cancer patients is lacking. The aim of this study is to investigate effects of physical exercise on health-related quality of life in esophageal cancer patients following surgery.

METHODS: The Physical ExeRcise Following Esophageal Cancer Treatment (PERFECT) study is a multicenter randomized controlled trial including 150 esophageal cancer patients after surgery with curative intent. Patients are randomly allocated to an exercise group or usual care group. The exercise group participates in a 12-week combined aerobic and resistance exercise program, supervised by a physiotherapist near the patient's home-address. In addition, participants in the exercise group are requested to be physically active for at least 30 min per day, every day of the week. Participants allocated to the usual care group are asked to maintain their habitual physical activity pattern. The primary outcome is health-related quality of life (EORTC-QLQ-C30). Secondary outcomes include esophageal cancer specific quality of life, fatigue, anxiety and depression, sleep quality, work-related factors, cardiorespiratory fitness (VO2peak), muscle strength, physical activity, malnutrition risk, anthropometry, blood markers, recurrence of disease and survival. All questionnaire outcomes, diaries and accelerometers are assessed at baseline, post-intervention (12 weeks post-baseline) and 24 weeks post-baseline. Physical fitness, anthropometry and blood markers are assessed at baseline and post-intervention. In addition, adherence and safety are monitored throughout the exercise program.

DISCUSSION: This randomized controlled trial investigates effects of physical exercise versus usual care in esophageal cancer patients after surgery. As the design of the exercise program closely resembles daily practice, this study can contribute both to evidence on effects of exercise in esophageal cancer patients, and to potential implementation strategies.

Impactfactor: 3.288

Prolonged stance phase during walking in intermittent claudication

Gommans LN, Smid AT, Scheltinga MRM, Cancrinus E, Brooijmans FAM, Meijer K, **Teijink JA**

J Vasc Surg. 2017 Aug; 66(2):515-522. Epub 2017 May 11

BACKGROUND:

Patients with intermittent claudication (IC) tend to walk slower and consume approximately 40% more oxygen during walking compared with healthy individuals. An unfavorable locomotion pattern has been suggested to explain this metabolic inefficiency. However, detailed knowledge of gait parameters in IC is lacking.

METHODS:

In a cross-sectional study, the gait pattern of newly diagnosed IC patients was compared with that of healthy controls. Spatiotemporal gait parameters such as step length and duration of stance phase were obtained by a photoelectric technique (OptoGait; Microgate, Bolzano, Italy). This system was previously

found to have favorable concurrent validity and test-retest reliability characteristics. Parameters were determined during pain-free and painful treadmill walking at a comfortable self-determined walking pace. Each parameter was averaged on the basis of 80 steps.
RESULTS:
A total of 28 patients and 28 controls were examined. IC patients walked 1.2 km/h (-27%) slower than controls (P < .001), coinciding with a significantly shorter step length (-20%) and lower cadence (-11%). IC patients demonstrated a longer stance and double support phase, even before the onset of ischemic pain. Differences were also observed in segments of the stance phase, as a 14% shorter propulsion (P < .001) and 17% longer flat foot phase (P < .001) during painful walking were found. In considering the absolute duration of these stance phase segments, differences were found only for the flat foot time (?0.10 second; P < .001).
CONCLUSIONS:
Patients with IC demonstrate an altered gait pattern compared with healthy controls. The most prominent differences were a prolonged relative and absolute duration of the flat foot position during the stance phase. This adaptation may be intuitive as an augmented arterial blood flow into skeletal muscles is allowed during a prolonged relaxation phase. Therefore, not only the lack of propulsion but also a gain of relaxation may explain these gait alterations.

Impactfactor: 3.536

Psoas hitch ureteral reimplantation after surgery for locally advanced and locally recurrent colorectal cancer: Complications and oncological outcome

van den Heijkant F, **Vermeer TA**, Vrijhof EJ, **Nieuwenhuijzen GA**, Koldewijn EL, **Rutten HJ**

Eur J Surg Oncol. 2017 Oct;43(10):1869-1875

INTRODUCTION:
The most important prognostic factor for oncological outcome of rectal cancer is radical surgical resection. In patients with locally advanced T4 rectal cancer (LARC) or locally recurrent rectal cancer (LRRC) (partial) resection of the urinary tract is frequently required to achieve radical resection. The psoas bladder hitch (PBH) technique is the first choice for reconstruction of the ureter after partial resection and this bladder-preserving technique should not influence the oncological outcome.
METHODS:
Demographic and clinical data were collected prospectively for all patients operated on for LARC or LRRC between 1996 and 2014 who also underwent a psoas hitch ureter reconstruction. Urological complications and oncological outcome were assessed.
RESULTS:
The sample comprised 70 patients, 30 with LARC and 40 with LRRC. The mean age was 62 years (range: 39-86). Postoperative complications occurred in 38.6% of patients, the most frequent were urinary leakage (22.9%), ureteral stricture with hydronephrosis (8.6%) and urosepsis (4.3%). Surgical re-intervention was required in 4 cases (5.7%), resulting in permanent loss of bladder function and construction of a ureter-ileo-cutaneostomy in 3 cases (4.3%). Oncological outcome was not influenced by postoperative complications.
CONCLUSION:
The rate of complications associated with the PBH procedure was higher in our sample than in previous samples with benign conditions, but most complications were temporary and did not require surgical intervention. We conclude that the bladder-sparing PBH technique of ureter reconstruction is feasible in locally advanced and recurrent rectal cancer with invasion of the urinary tract after pelvic radiotherapy.

Impactfactor: 3.522

Quality of life and bariatric surgery: a systematic review of short- and long-term results and comparison with community norms

Raaijmakers LC, Pouwels S, Thomassen SE, Nienhuijs SW

Eur J Clin Nutr. 2017 Apr;71(4):441-449

Currently the effects of bariatric surgery are generally expressed in excess weight loss or comorbidity reduction. Therefore the aim of this review was to provide insight in the available prospective evidence regarding the short and long-term effects of bariatric surgery on Quality of Life (QoL) and a comparison with community norms. A systematic multi-database search was conducted for 'QoL' and 'Bariatric surgery'. Only prospective studies with QoL before and after bariatric surgery were included. The 'Quality Assessment Tool for Before-After Studies with No Control Group' was used to assess the

methodological quality. Thirty-six studies met the inclusion criteria. Most studies were assessed to be of 'fair' to 'good' methodological quality. Ten different questionnaires were used to measure QoL. Follow-up ranged from 6 months to 10 years, sample sizes from 26 to 1276 and follow-up rates from 45 to 100%. A significant increase in QoL after bariatric surgery was found in all studies (P?0.05), however, mostly these outcomes stay below community norms. Only outcomes of the IWQoL, SF-36 and OWQoL show QoL outcomes that exceed community norms. The QoL is increased after bariatric surgery on both the short and long term. However, due to the heterogeneity of the studies and the generality of the questionnaires is it hard to make a distinction between different surgeries and difficult to see a relation with medical profit. Therefore, tailoring QoL measurements to the bariatric population is recommended as the focus of future studies.

Impactfactor: 3.057

Quality of life before and after different treatment modalities in peripheral facial palsy: A systematic review

Luijmes RE, **Pouwels S**, Beurskens CH, Kleiss IJ, Siemann I, Ingels KJ

Laryngoscope. 2017 May;127(5):1044-1051. doi: 10.1002/lary.26356. Epub 2016 Nov 12

OBJECTIVES:

A systematic review was conducted to investigate the effect of peripheral facial palsy (PFP) on the quality of life (QoL). Secondly, we investigated if different treatment modalities influence the QoL of patients with PFP.

METHODS:

A multidatabase systematic literature search was performed using the following databases: PubMed, Embase, MEDLINE, and The Cochrane Library from the earliest date of each database up to August 2015. The inclusion criteria were either prospective and/or retrospective cohort trials and/or case series measurement of QoL before and after treatment, patients with PFP (irrespective of etiology), and various treatment modalities (medication, physical therapy, botulinum toxin injections, and several types of surgical procedures). Two authors rated the methodological quality of the included studies independently using the Newcastle-Ottawa Quality Assessment Scale for nonrandomized studies.

RESULTS:

Two hundred fifty-eight studies were found, of which 14 studies met the inclusion criteria. Most studies were assessed to be of fair to good methodological quality. The Cohen's ? (between author r.e.l. and s.p.) was 0.68. Eight different questionnaires were used to measure QoL, of which the Facial Clinimetric Evaluation scale was used most frequent. After different modalities, all studies showed significant improvements in terms of QoL.

CONCLUSIONS:

This study found significant improvement when measuring QoL before and after different treatment modalities in patients with peripheral facial palsy. Future research should focus on patients with PFP due to the same etiology and use of valid QoL instruments for outcome measures.

Impactfactor: 2.471

Randomized clinical trial of extended versus single-dose perioperative antibiotic prophylaxis for acute calculous cholecystitis

Loozen CS, Kortram K, Kornmann VN, van Ramshorst B, Vlaminckx B, Knibbe CA, Kelder JC, Donkervoort SC, **Nieuwenhuijzen GA**, **Ponten JE**, van Geloven AA, van Duijvendijk P, Bos WJ, Besselink MG, Gouma DJ, van Santvoort HC, Boerma D

Br J Surg. 2017 Jan;104(2):e151-e157

BACKGROUND:

Many patients who have surgery for acute cholecystitis receive postoperative antibiotic prophylaxis, with the intent to reduce infectious complications. There is, however, no evidence that extending antibiotics beyond a single perioperative dose is advantageous. This study aimed to determine the effect of extended antibiotic prophylaxis on infectious complications in patients with mild acute cholecystitis undergoing cholecystectomy.

METHODS:

For this randomized controlled non-inferiority trial, adult patients with mild acute calculous cholecystitis undergoing cholecystectomy at six major teaching hospitals in the Netherlands, between April 2012 and September 2014, were assessed for eligibility. Patients were randomized to either a single preoperative dose of cefazolin (2000 mg), or antibiotic prophylaxis for 3 days after surgery (intravenous cefuroxime

750 mg plus metronidazole 500 mg, three times daily), in addition to the single dose. The primary endpoint was rate of infectious complications within 30 days after operation.
RESULTS:
In the intention-to-treat analysis, three of 77 patients (4 per cent) in the extended antibiotic group and three of 73 (4 per cent) in the standard prophylaxis group developed postoperative infectious complications (absolute difference 0·2 (95 per cent c.i. -8·2 to 8·9) per cent). Based on a margin of 5 per cent, non-inferiority of standard prophylaxis compared with extended prophylaxis was not proven. Median length of hospital stay was 3 days in the extended antibiotic group and 1 day in the standard prophylaxis group.
CONCLUSION:
Standard single-dose antibiotic prophylaxis did not lead to an increase in postoperative infectious complications in patients with mild acute cholecystitis undergoing cholecystectomy.

Impactfactor: 5.899

Registries on peritoneal surface malignancies throughout the world, their use and their options

Verwaal VJ, Rau B, Jamali F, Gilly FN, **de Hingh I**, Takala H, Syk I, Pelz J, Mulsow J, van der Speeten K, Shigeki K, Iversen LH, Mohamed F, Glehen O, Younan R, Yarema R, Gonzalez-Moreno S, O'Dwyer S, Yonemura Y, Sugarbaker P

Int J Hyperthermia. 2017 Aug;33(5):528-533

AIM:
The treatment of peritoneal surface malignancies ranges from palliative care to full cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy, HIPEC. Ongoing monitoring of patient recruitment and volume is usually carried out through dedicated registries. With multiple registries available worldwide, we sought to investigate the nature, extent and value of existing worldwide CRS and HIPEC registries.
METHODS:
A questionnaire was sent out to all known major treatment centres. The questionnaire covers: general purpose of the registry; inclusion criteria in the registry; the date the registry was first established; volume of patients in the registry and description of the data fields in the registries. Finally, the population size of the catchment area of the registry was collected.
RESULTS:
Twenty-seven questionnaires where returned. National databases are established in northwest European countries. There are five international general databases. Most database collect data on patients who have undergone an attempt to CRS and HIPEC. Two registries collect data on all patients with peritoneal carcinomatosis regardless the treatment. Most registries are primarily used for tracking outcomes and complications. When correlating the number of cases of CRS and HIPEC that are performed to the catchment area of the various registry, a large variation in the number of performed procedures related to the overall population was noted, ranging from 1.3 to 57 patients/million year with an average of 15 patients/1 million year.
CONCLUSIONS:
CRS and HIPEC is a well-established treatment for peritoneal surface malignancies worldwide. However, the coverage as well as the registration of treatment procedures differs widely. The most striking difference is the proportion of HIPEC procedures per capita which ranges from 1.3 to 57 patients per million. This suggests either a difference in patient selection, lack of access to HIPEC centres or lack of appropriate data collection.

Impactfactor: 3.262

Relation between postoperative ileus and anastomotic leakage after colorectal resection: a post hoc analysis of a prospective randomized controlled trial

Peters EG, **Dekkers M**, van Leeuwen-Hilbers FW, Daams F, Hulsewé KWE, de Jonge WJ, Buurman WA, **Luyer MD**

Colorectal Dis. 2017 Jul 19(7):667-674. doi: 10.1111/codi.13582

AIM:
Anastomotic leakage (AL) following abdominal surgery is a critical determinant of postoperative recovery, of which the aetiology is largely unknown. Interestingly, interventions aimed at reducing the inflammatory response and postoperative ileus (POI) have an unexpected effect on AL. The aim of this study was to investigate the relation of POI with inflammation and AL after colorectal resection.

METHOD:
A post hoc analysis of a prospective randomized controlled trial in which patients underwent a colorectal resection was performed. Patients undergoing a colorectal resection were stratified into having or not having POI. The incidence of AL and other clinical parameters was registered prospectively. Intestinal fatty acid binding protein (I-FABP, a marker for tissue damage) and the inflammatory response in plasma and colon tissue were determined.
RESULTS:
AL was present in nine of 43 patients in the POI group, and in one of 65 in the group without POI (P < 0.001). There was a significant association between POI and AL (OR 12.57, 95% CI: 2.73-120.65; P = 0.0005). Patients with POI had significantly higher plasma levels of soluble tumour necrosis factor receptor 1 (TNFRSF1A) at 4 h postoperatively (0.89 ng/l, interquartile range 0.56) than patients without POI (0.80 ng/l, interquartile range 0.37; P = 0.04) and higher plasma levels of C-reactive protein on the second day postoperatively (234 ± 77 vs 163 ± 86 mg/l; P = 0.001). Patients who developed AL had significantly higher plasma levels of I-FABP compared with patients without AL at 24 h after onset of surgery.
CONCLUSION:
POI is associated with a higher prevalence of AL and an increased inflammatory response.

Impactfactor: 2.689

Reply
Weijs TJ, Berkelmans GH, Luyer MD
Ann Thorac Surg. 2017 Nov;104(5):1756-1757

Comment on:
Immediate Postoperative Oral Nutrition Following Esophagectomy: A Multicenter Clinical Trial.
[Ann Thorac Surg. 2016]
Should Immediate Postoperative Oral Nutrition Following Esophagectomy Be Generalized Immediately?
[Ann Thorac Surg. 2017]

Impactfactor: 3.700

Response to: postoperative ileus, a diagnosis by exclusion?
Peters EG, Dekkers M, **Luyer MD**
Colorectal Dis. 2017 Aug 19(8):781-782

Comment on:
Postoperative ileus, a diagnosis by exclusion? Comment on relation between postoperative ileus and anastomotic leakage after colorectal resection: a post hoc analysis of a prospective randomized controlled trial.
[Colorectal Dis. 2017]
Relation between postoperative ileus and anastomotic leakage after colorectal resection: a post hoc analysis of a prospective randomized controlled trial.
[Colorectal Dis. 2017]

Impactfactor: 2.689

Results of a pooled analysis of IOERT containing multimodality treatment for locally recurrent rectal cancer: Results of 565 patients of two major treatment centres
Holman FA, **Bosman SJ**, Haddock MG, Gunderson LL, **Kusters M, Nieuwenhuijzen GA**, van den Berg H, Nelson H, **Rutten HJ**
Eur J Surg Oncol. 2017 Jan; 43(1):107-117. Epub 2016 Sep 9.

OBJECTIVE: Aim of this study is analysing the pooled results of Intra-Operative Electron beam Radiotherapy (IOERT) containing multimodality treatment of locally recurrent rectal cancer (LRRC) of two major treatment centres.
METHODS AND MATERIALS: Five hundred sixty five patients with LRRC who underwent multimodality-treatment up to 2010 were studied. The preferred treatment was preoperative chemo-radiotherapy, surgery and IOERT. In uni- and multivariate analyses risk factors for local re-recurrence, distant metastasis free survival, relapse free survival, cancer-specific survival and overall survival were studied.
RESULTS: Two hundred fifty one patients (44%) underwent a radical (R0) resection. In patients who had no preoperative treatment the R0 resection rate was 26%, and this was 43% and 50% for patients who

respectively received preoperative re-(chemo)-irradiation or full-course radiotherapy (p < 0.0001). After uni- and multivariate analysis it was found that all oncologic parameters were influenced by preoperative treatment and radicality of the resection. Patients who werere-irradiated had a similar outcome compared to patients, who were radiotherapy naive and could undergo full-course treatment, except the chance of local re-recurrence was higher for re-irradiated patients. Waiting-time between preoperative radiotherapy and IOERT was inversely correlated with the chance of local re-recurrence, and positively correlated with the chance of a R0 resection.

CONCLUSIONS: R0 resection is the most important factor influencing oncologic parameters in treatment of LRRC. Preoperative (chemo)-radiotherapy increases the chance of achieving radical resections and improves oncologic outcomes. Short waiting-times between preoperative treatment and IOERT improves the effectiveness of IOERT to reduce the chance of a local re-recurrence.

Impactfactor: 3.522

Role of Repeat Muscle Compartment Pressure Measurements in Chronic Exertional Compartment Syndrome of the Lower Leg

van Zantvoort AP, de Bruijn JA, Winkes MB, Hoogeveen AR, **Teijink JA**, Scheltinga MR

Orthop J Sports Med. 2017 Jun 9;5(6):2325967117711121

BACKGROUND: The diagnostic gold standard for diagnosing chronic exertional compartment syndrome (CECS) is a dynamic intracompartmental pressure (ICP) measurement of the muscle. The potential role of a repeat ICP (re-ICP) measurement in patients with persistent lower leg symptoms after surgical decompression or with ongoing symptoms after an earlier normal ICP is unknown.

PURPOSE:

To study whether re-ICP measurements in patients with persistent CECS-like symptoms of the lower leg may contribute to the diagnosis of CECS after both surgical decompression and a previously normal ICP measurement.

STUDY DESIGN: Case series; Level of evidence, 4.

METHODS: Charts of patients who underwent re-ICP measurement of lower leg compartments (anterior [ant], deep posterior [dp], and/or lateral [lat] compartments) between 2001 and 2013 were retrospectively studied. CECS was diagnosed on the basis of generally accepted cutoff pressures for newly onset CECS (Pedowitz criteria: ICP at rest =15 mmHg, =30 mmHg after 1 minute, or =20 mmHg 5 minutes after a provocative test). Factors predicting recurrent CECS after surgery or after a previously normal ICP measurement were analyzed.

RESULTS:

A total of 1714 ICP measurements were taken in 1513 patients with suspected CECS over a 13-year observation period. In all, 201 (12%) tests were re-ICP measurements for persistent lower leg symptoms. Based on the proposed ICP cutoff values, CECS recurrence was diagnosed in 16 of 62 previously operated compartments (recurrence rate, 26%; 53 patients [64% female]; median age, 24 years; age range, 15-78 years). Recurrence rates were not different among the 3 lower leg CECS compartments (ant-CECS, 17%; dp-CECS, 33%; lat-CECS, 30%; ?2 = 1.928, P = .381). Sex (?2 = 0.058, P = .810), age (U = 378, z = 1.840, P = .066), bilaterality (?2 = 0.019, P = .889), and prefasciotomy ICP did not predict recurrence. Re-ICP measurements evaluating 20 compartments with previously normal ICP measurements (15 patients [53% female]; mean age, 31 ± 10 years) detected CECS in 3 compartments (15%, all ant-CECS).

CONCLUSION:

Previous fasciotomy for lower leg CECS or previously normal muscle pressure (ICP) do not rule out CECS as a cause of persisting lower leg symptoms. Repeat ICP measurement may have a potential role in the evaluation of patients with persistent lower leg complaints. However, other reasons for lower leg exertional pain must always be considered prior to secondary surgery.

Impactfactor: 0.105

Routine jejunostomy tube feeding following esophagectomy

Weijs TJ, van Eden HW, Ruurda JP, **Luyer MD**, Steenhagen E, **Nieuwenhuijzen GA**, van Hillegersberg R

J Thorac Dis. 2017 Jul;9(Suppl 8):S851-S860

BACKGROUND: Malnutrition is an important problem following esophagectomy. A surgically placed jejunostomy secures an enteral feeding route, facilitating discharge with home-tube feeding and long-term nutritional support. However, specific complications occur, and data are lacking that support its use over other enteral feeding routes. Therefore routine jejunostomy tube feeding and discharge with home-tube feeding was evaluated, with emphasis on weight loss, length of stay and re-admissions.

METHODS: Consecutive patients undergoing esophagectomy for cancer, with gastric tube reconstruction and jejunostomy creation, were analyzed. Two different regimens were compared. Before January 07, 2011 patients were discharged when oral intake was sufficient, without tube feeding. After that discharge with home-tube feeding was routinely performed. Logistic regression analysis corrected for confounders.

RESULTS: Some 236 patients were included. The median duration of tube feeding was 35 days. Reoperation for a jejunostomy-related complication was needed in 2%. The median body mass index (BMI) remained stable during tube feeding. The BMI decreased significantly after stopping tube feeding: from 25.6 (1st-3rd quartile 23.0-28.6) kg/m2 to 24.4 (22.0-27.1) kg/m2 at 30 days later [median weight loss: 3.0 (1.0-5.3) kg; 3.9% (1.5-6.3%)]. Weight loss was not affected by the duration of tube feeding duration. Routine home-tube feeding did not affect weight loss, admission time or the readmission rate.

CONCLUSIONS: Weight loss following esophagectomy occurs once that tube feeding is stopped, independently from the time interval after esophagectomy. Moreover routine discharge with home-tube feeding does not reduce length of stay or readmissions. These findings question the value of routine jejunostomy placement and emphasize the need for further research.

Impactfactor: 2.365

Self-assessment in laparoscopic surgical skills training: Is it reliable?

Ganni S, Chmarra MK, Goossens RHM, **Jakimowicz JJ**

Surg Endosc. 2017 Jun; 31(6):2451-2456.

BACKGROUND: The concept of self-assessment has been widely acclaimed for its role in the professional development cycle and self-regulation. In the field of medical education, self-assessment has been most used to evaluate the cognitive knowledge of students. The complexity of training and evaluation in laparoscopic surgery has previously acted as a barrier in determining the benefits self-assessment has to offer in comparison with other fields of medical
education.

METHODS: Thirty-five surgical residents who attended the 2-day Laparoscopic Surgical Skills Grade 1 Level 1 curriculum were invited to participate from The
Netherlands, India and Romania. The competency assessment tool (CAT) for laparoscopic cholecystectomy was used for self- and expert-assessment and the
resulting distributions assessed.

RESULTS: A comparison between the expert- and self-assessed aggregates of scores from the CAT agreed with previous studies. Uniquely to this study, the aggregates
of individual sub-categories-'use of instruments'; 'tissue handling'; and errors 'within the component tasks' and the 'end product' from both self- and
expert-assessments-were investigated. There was strong positive correlation ($r_s > 0.5$; $p < 0.001$) between the expert- and self-assessment in all categories
with only the 'tissue handling' having a weaker correlation ($r_s = 0.3$; $p = 0.04$). The distribution of the mean of the differences between
self-assessment and expert-assessment suggested no significant difference between the scores of experts and the residents in all categories except the 'end
product' evaluation where the difference was significant ($W = 119$, $p = 0.03$).

CONCLUSION: Self-assessment using the CAT form gives results that are consistently not different from expert-assessment when assessing one's
proficiency in surgical skills. Areas where there was less agreement could be explained by variations in the level of training and understanding of the
assessment criteria.

Impactfactor:3.747

Short-Course Radiotherapy Followed by Neoadjuvant Bevacizumab, Capecitabine, and Oxaliplatin and Subsequent Radical Treatment in Primary Stage IV Rectal Cancer: Long-Term Results of a Phase II Study

Bisschop C, van Dijk TH, Beukema JC, Jansen RL, Gelderblom H, de Jong KP, **Rutten HJ,** van de Velde CJ, Wiggers T, Havenga K, Hospers GA

Ann Surg Oncol. 2017 Sep;24(9):2632-2638

BACKGROUND:

In a Dutch phase II trial conducted between 2006 and 2010, short-course radiotherapy followed by systemic therapy with capecitabine, oxaliplatin, and bevacizumab as neoadjuvant treatment and

subsequent radical surgical treatment of primary tumor and metastatic sites was evaluated. In this study, we report the long-term results after a minimum follow-up of 6 years.
METHODS:
Patients with histologically confirmed rectal adenocarcinoma with potentially resectable or ablatable metastases in liver or lungs were eligible. Follow-up data were collected for all patients enrolled in the trial. Overall and recurrence-free survival were calculated using the Kaplan-Meier method.
RESULTS:
Follow-up data were available for all 50 patients. After a median follow-up time of 8.1 years (range 6.0-9.8), 16 patients (32.0%) were still alive and 14 (28%) were disease-free. The median overall survival was 3.8 years (range 0.5-9.4). From the 36 patients who received radical treatment, two (5.6%) had a local recurrence and 29 (80.6%) had a distant recurrence.
CONCLUSIONS:
Long-term survival can be achieved in patients with primary metastatic rectal cancer after neoadjuvant radio- and chemotherapy. Despite a high number of recurrences, 32% of patients were alive after a median follow-up time of 8.1 years.

Impactfactor: 4.041

Short-Term Changes in Cardiovascular Hemodynamics in Response to Bariatric Surgery and Weight Loss Using the Nexfin® Non-invasive Continuous Monitoring Device: a Pilot Study

Pouwels S, Lascaris B**, Nienhuijs SW,** Bouwman AR, Buise MP

Obes Surg. 2017 Jul;27(7):1835-1841

BACKGROUND:
Compared to healthy individuals, obese have significantly higher systolic and diastolic blood pressure, mean arterial pressure, heart rate, and cardiac output. The aim of this study was to evaluate cardiovascular hemodynamic changes before and 3 months after bariatric surgery.
METHODS:
Patients scheduled for bariatric surgery between the 29th of September 2016 and 24th of March 2016 were included and compared with 24 healthy individuals. Hemodynamic measurements were performed preoperatively and 3 months after surgery, using the Nexfin® non-invasive continuous hemodynamic monitoring device (Edwards Lifesciences/BMEYE B.V., Amsterdam, the Netherlands).
RESULTS:
Eighty subjects were included in this study, respectively, 56 obese patients scheduled for bariatric surgery and 24 healthy individuals. Baseline hemodynamic measurements showed significant differences in cardiac output (6.5 ± 1.6 versus 5.7 ± 1.6 l/min, p = 0.046), mean arterial pressure (107 ± 19 versus 89 ± 11 mmHg, p = 0.001), systolic (134 ± 24 versus 116 ± 18 mmHg, p = 0.001) and diastolic blood pressure (89 ± 17 versus 74 ± 10 mmHg, p = 0.001), and heart rate (87 ± 12 versus 76 ± 14 bpm, p = 0.02) between obese and healthy subjects. Three months after surgery, significant changes occurred in mean arterial pressure (89 ± 17 mmHg, p = 0.001), systolic (117 ± 24 mmHg, p = 0.001) and diastolic blood pressure (71 ± 15 mmHg, p = 0.001), stroke volume (82.2 ± 22.4 ml, p = 0.03), and heart rate (79 ± 17 bpm, p = 0.02)
CONCLUSIONS: Three months after bariatric surgery, significant improvements occur in hemodynamic variables except cardiac output and cardiac index, in the patient group.

Impactfactor: 3.947

Socio-economic status influences the likelihood of undergoing surgical treatment for pancreatic cancer in the Netherlands

Bakens MJ, Lemmens VE, **de Hingh IH**

HPB (Oxford). 2017 May 19(5):443-448. Epub 2017 Feb 20

Surgical resection offers the only prospect of cure in pancreatic cancer patients. The probability of undergoing surgery is determined by several factors. The influence of socio-economic status (SES) on surgical treatment and survival was investigated in the Netherlands, a country with a widely accessiblehealthcare system.METHODS: Data on all patients with non-metastasised pancreatic cancer between 2005-2013 were analysed in the Eindhoven Cancer Registry (ECR).SES was categorized as low, intermediate or high. The influence of SES on the
likelihood for surgery was assessed by multivariable logistic regressionanalyses. The influence on overall survival was analysed by multivariable Coxregression analyses.
RESULTS: 698 M0-patients were included, of whom 276 underwent surgery. Patients
with low and intermediate SES were less likely to undergo surgery (32% vs 37%)

than high-SES patients (48%) (p = 0.002; low SES: OR0.63, 95%CI [0.40-0.98];
intermediate SES: OR0.62, 95%CI [0.42-0.92]). Survival did not differ between SES groups (low SES: HR1.05 95%CI [0.85-1.30]; intermediate SES: HR1.11, 95%CI [0.91-1.35]), p = 0.181. SES in pancreatic cancer patients determined the likelihood for surgery. However, SES had no influence on survival. It is important to provide more insights in the causes of these inequalities to minimalize the effects of SES in pancreatic cancer care.

Impactfactor: 3.290

Subjective outcome after laparoscopic hiatal hernia repair for intrathoracic stomach

Castelijns PS, Ponten JE, Van de Poll, **Nienhuijs SW, Smulders JF**

Langenbecks Arch Surg. 2017 May;402(3):521-530. Epub 2016 Nov 9

PURPOSE:

For decades, an intrathoracic stomach (ITS) has been a definite indication for surgery due to the perceived risk of an acute volvulus with perforation, gangrene, or hemorrhage. At the present time, elective laparoscopic repair is the first choice for treatment of ITS. There is a lack of evidence in the long-term quality of life after a hiatal hernia repair for an intrathoracic stomach.

METHODS:

A retrospective analysis was performed on all patients undergoing a hiatal hernia repair for an intrathoracic stomach between January 2004 and January 2015. Additionally, to a hiatal closure, the patients received an antireflux procedure. Outcome measures included patient characteristics, operative details, complications, and postoperative morbidity and mortality. All patients were sent a quality of life questionnaire to assess long-term quality of life and patient satisfaction. A higher quality of life score represents a better quality of life.

RESULTS:

Eighty-six patients underwent laparoscopic repair for ITS, from which, one patient died during surgery. Eighty-five patients were contacted and 81 completed the questionnaire, resulting in a response rate of 95.3 %. At a median follow-up of 2.7 years (range 0.1-9.6), the mean quality of life score was 13.5 (standard deviation 2.8). The mean overall satisfaction was 8.4. There were four recurrences: three in the first 12 days after surgery and one in 2.4 years.

CONCLUSIONS:

Very good results in patient satisfaction and symptom reduction were achieved after a median follow-up of 2.7 years in this laparoscopic repair of the intrathoracic stomach single center experience study. The symptomatic recurrence rate was very low.

Impactfactor: 2.203

Supervised exercise therapy: it does work, but how to set up a program?

Hageman D, van den Houten MM, Spruijt S, **Gommans LN**, Scheltinga MR, **Teijink JA**

J Cardiovasc Surg (Torino). 2017 Apr 58(2):305-312

Review. Intermittent claudication (IC) is a manifestation of peripheral arterial disease. IC has a high prevalence in the older population, is closely associated with other expressions of atherosclerotic disease and often co-exists in multimorbid patients. Treatment of IC should address reduction of cardiovascular risk and improvement of functional capacity and health-related quality of life (QoL). As recommended by contemporary international guidelines, the first-line treatment includes supervised exercise therapy (SET). In several randomized controlled trials and systematic reviews, SET is compared with usual care, placebo, walking advice and endovascular revascularization. The evidence supporting the efficacy of SET programs to alleviate claudication symptoms is robust. SET improves walking distance and health-related QoL and appears to be the most cost-effective treatment for IC. Nevertheless, only few of all newly diagnosed IC patients worldwide receive this safe, efficient and structured treatment. Worldwide implementation of structured SET programs is seriously impeded by outdated arguments favoring an invasive intervention, absence of a network of specialized physical therapists providing standardized SET and lack of awareness and/or knowledge of the importance of SET by referring physicians. Besides, misguiding financial incentives and lack of reimbursement hamper actual use of SET programs. In the Netherlands, a national integrated care network (ClaudicatioNet) was launched in 2011 to combat treatment shortcomings and stimulate cohesion and collaboration between stakeholders. This care intervention has resulted in optimized quality of care for all patients with IC.

Impactfactor: 2.179

Survival of patients with colorectal peritoneal metastases is affected by treatment disparities among hospitals of diagnosis: A nationwide population-based study

Rovers KP, Simkens GA, Vissers PA, Lemmens VE, Verwaal VJ, Bremers AJ, Wiezer MJ, Burger JW, Hemmer PH, Boot H, van Grevenstein WM, Meijerink WJ, Aalbers AG, Punt CJ, Tanis PJ, **de Hingh IH**, Dutch Peritoneal Oncology Group (DPOG)

Eur J Cancer. 2017 Apr 75:132-140. doi: 10.1016/j.ejca.2016.12.034. Epub 2017 Feb 20

BACKGROUND:

In the Netherlands, surgery for peritoneal metastases of colorectal cancer (PMCRC) is centralised, whereas PMCRC is diagnosed in all hospitals. This study assessed whether hospital of diagnosis affects treatment selection and overall survival (OS).

METHODS:

Between 2005 and 2015, all patients with synchronous PMCRC without systemic metastases were selected from the Netherlands Cancer Registry. Treatment was classified as cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC), systemic therapy or other/no treatment. Hospitals of diagnosis were classified as: (1) non-teaching or academic/teaching hospital and (2) HIPEC centre or referring hospital. Referring hospitals were further classified based on the frequency of CRS/HIPEC as high-, medium- or low-frequency hospital. Multivariable regression analyses were used to assess the independent influence of hospital categories on the likelihood of CRS/HIPEC and OS.

RESULTS:

A total of 2661 patients, diagnosed in 89 hospitals, were included. At individual hospital level, CRS/HIPEC and systemic therapy ranged from 0% to 50% and 6% to 67%, respectively. Hospital of diagnosis influenced the likelihood of CRS/HIPEC: 33% versus 13% for HIPEC centres versus referring hospitals (odds ratio (OR) 3.66 [2.40-5.58]) and 11% versus 17% for non-teaching hospitals versus academic/teaching hospitals (OR 0.60 [0.47-0.77]). Hospital of diagnosis affected median OS: 14.1 versus 9.6 months for HIPEC centres versus referring hospitals (hazard ratio (HR) 0.82 [0.67-0.99]) and 8.7 versus 11.5 months for non-teaching hospitals versus academic/teaching hospitals (HR 1.15 [1.06-1.26]). Compared with diagnosis in medium-frequency referring hospitals, median OS was increased in high-frequency referring hospitals (12.6 months, HR 0.82 [0.73-0.91]) and reduced in low-frequency referring hospitals (8.1 months, HR 1.12 [1.01-1.24]).

CONCLUSION:

Treatment disparities among hospitals of diagnosis and their impact on survival indicate suboptimal treatment selection for PMCRC.

Impactfactor: 6.029

Synchronous peritoneal metastases of small bowel adenocarcinoma: Insights into an underexposed clinical phenomenon

Legué LM, **Simkens GA**, Creemers GJ, Lemmens VE, **de Hingh IH**

Eur J Cancer. 2017 Nov 10;87:84-91

BACKGROUND:

The aim of this population-based study was to provide insight into the incidence, risk factors and treatment-related survival of patients with peritoneal metastases (PM) of small bowel adenocarcinoma (SBA).

METHODS:

Data from the Netherlands Cancer Registry were used. All patients diagnosed with SBA between 2005 and 2014 were included. The influence of patient and tumour characteristics on the odds of developing PM was analysed. Subsequently, for all further analyses, patients without synchronous PM of SBA were excluded. The log-rank test and Kaplan-Meier analyses were conducted to estimate survival, and the Cox proportional hazards model was used to evaluate the risk of death.

RESULTS:

Of the 1428 included patients diagnosed with SBA, 181 (13%) presented with synchronous PM. Synchronous PM was found in 9% of the duodenal tumours and in 17% of the more distal tumours. Median overall survival of all patients with PM was 5.9 months, whereas survival of both 11 months was observed in patients treated with primary tumour resection or palliative chemotherapy and 32 months after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Poor prognostic factors for survival were age =70 years (hazard ratio [HR] 1.6, 95% confidence interval [CI] 1.1-2.2), systemic metastases other than PM (HR 2.0, 95% CI 1.4-2.9) and an advanced (HR 1.9, 95% CI 1.3-3.0) or unknown T-stage (HR 2.1, 95% CI 1.2-3.5).

CONCLUSIONS:
Synchronous PM was frequently encountered in SBA. Without treatment, prognosis was extremely poor. Survival was higher after primary tumour resection, palliative chemotherapy and CRS+HIPEC, but selection bias probably played a significant role calling for further clinical research.

Impactfactor: 6.029

Techniques and short-term outcomes for total minimally invasive Ivor Lewis esophageal resection in distal esophageal and gastroesophageal junction cancers: pooled data from six European centers

Straatman J, van der Wielen N, **Nieuwenhuijzen GA**, Rosman C, Roig J, Scheepers JJ, Cuesta MA, **Luyer MD**, van Berge Henegouwen MI, van Workum F, Gisbertz SS, van der Peet DL

Surg Endosc. 2017 Jan;31(1):119-126

INTRODUCTION:
Esophagectomy for cancer can be performed in a two-stage procedure with an intrathoracic anastomosis: the Ivor Lewis esophagectomy. A growing incidence of distal and gastroesophageal junction adenocarcinomas and increasing use of minimally invasive techniques have prompted interest in this procedure. The aim of this study was to assess short-term results of minimally invasive Ivor Lewis esophagectomy (MIE-IL).
METHODS:
A retrospective cohort study was performed from June 2007 until September 2014, including patients that underwent MIE-IL for distal esophageal and gastroesophageal junction cancer in six different hospitals in the Netherlands and Spain. Data were collected with regard to operative techniques, pathology and postoperative complications.
RESULTS:
In total, 282 patients underwent MIE-IL, of which 90.2 % received neoadjuvant therapy. Anastomotic leakage was observed in 43 patients (15.2 %), of whom 13 patients (4.6 %) had empyema, necessitating thoracotomy for decortication. With an aggressive treatment of complications, the 30-day and in-hospital mortality rate was 2.1 %. An R0-resection was obtained in 92.5 % of the patients. After neoadjuvant therapy, 20.1 % of patients had a complete response.
CONCLUSIONS:
Minimally invasive Ivor Lewis esophagectomy for distal esophageal and gastroesophageal junction adenocarcinomas is an upcoming approach for reducing morbidity caused by laparotomy and thoracotomy. Anastomotic leakage rate is still high possibly due to technical diversity of anastomotic techniques, and a high percentage of patients treated by neoadjuvant chemoradiotherapy. An aggressive approach to complications leads to a low mortality of 2.1 %. Further improvement and standardization in the anastomotic technique are needed in order to perform a safe intrathoracic anastomosis.

Impactfactor: 3.747

Ten-year outcomes of a randomised trial of laparoscopic versus open surgery for colon cancer

Deijen CL, Vasmel JE, de Lange-de Klerk ES, Cuesta MA, Coene PL, Lange JF, Meijerink WJ, **Jakimowicz JJ**, Jeekel J, Kazemier G, Janssen IM, Påhlman L, Haglind E, Bonjer HJ; COLOR (COlon cancer Laparoscopic or Open Resection) study group**: Nieuwenhuijzen GA**

Surg Endosc. 2017 Jun;31(6):2607-2615

BACKGROUND:
Laparoscopic surgery for colon cancer is associated with improved recovery and similar cancer outcomes at 3 and 5 years in comparison with open surgery. However, long-term survival rates have rarely been reported. Here, we present survival and recurrence rates of the Dutch patients included in the COlon cancer Laparoscopic or Open Resection (COLOR) trial at 10-year follow-up.
METHODS:
Between March 1997 and March 2003, patients with non-metastatic colon cancer were recruited by 29 hospitals in eight countries and randomised to either laparoscopic or open surgery. Main inclusion criterion for the COLOR trial was solitary adenocarcinoma of the left or right colon. The primary outcome was disease-free survival at 3 years, and secondary outcomes included overall survival and recurrence. The 10-year follow-up data of all Dutch patients were collected. Analysis was by intention-to-treat. The trial was registered at ClinicalTrials.gov (NCT00387842).
RESULTS:

In total, 1248 patients were randomised, of which 329 were Dutch. Fifty-eight Dutch patients were excluded and 15 were lost to follow-up, leaving 256 patients for 10-year analysis. Median follow-up was 112 months. Disease-free survival rates were 45.2 % in the laparoscopic group and 43.2 % in the open group (difference 2.0 %; 95 % confidence interval (CI) -10.3 to 14.3; p = 0.96). Overall survival rates were 48.4 and 46.7 %, respectively (difference 1.7 %; 95 % CI -10.6 to 14.0; p = 0.83). Stage-specific analysis revealed similar survival rates for both groups. Sixty-two patients were diagnosed with recurrent disease, accounting for 29.4 % in the laparoscopic group and 28.2 % in the open group (difference 1.2 %; 95 % CI -11.1 to 13.5; p = 0.73). Seven patients had port- or wound-site recurrences (laparoscopic n = 3 vs. open n = 4).

CONCLUSIONS:

Laparoscopic surgery for non-metastatic colon cancer is associated with similar rates of disease-free survival, overall survival and recurrences as open surgery at 10-year follow-up.

Impactfactor: 3.747

Textbook outcome as a composite measure in oesophagogastric cancer surgery

Busweiler LA, Schouwenburg MG, van Berge Henegouwen MI, Kolfschoten NE, de Jong PC, Rozema T, Wijnhoven BP, van Hillegersberg R, Wouters MW, van Sandick JW; Dutch Upper Gastrointestinal Cancer Audit (DUCA) group: **Nieuwenhuijzen GA**

Br J Surg. 2017 May;104(6):742-750

BACKGROUND:

Quality assurance is acknowledged as a crucial factor in the assessment of oncological surgical care. The aim of this study was to develop a composite measure of multiple outcome parameters defined as 'textbook outcome', to assess quality of care for patients undergoing oesophagogastric cancer surgery.

METHODS:

Patients with oesophagogastric cancer, operated on with the intent of curative resection between 2011 and 2014, were identified from a national database (Dutch Upper Gastrointestinal Cancer Audit). Textbook outcome was defined as the percentage of patients who underwent a complete tumour resection with at least 15 lymph nodes in the resected specimen and an uneventful postoperative course, without hospital readmission. Hospital variation in textbook outcome was analysed after adjustment for case-mix factors.

RESULTS:

In total, 2748 patients with oesophageal cancer and 1772 with gastric cancer were included in this study. A textbook outcome was achieved in 29·7 per cent of patients with oesophageal cancer and 32·1 per cent of those with gastric cancer. Adjusted textbook outcome rates varied from 8·5 to 52·4 per cent between hospitals. The outcome parameter 'at least 15 lymph nodes examined' had the greatest negative impact on a textbook outcome both for patients with oesophageal cancer and for those with gastric cancer.

CONCLUSION:

Most patients did not achieve a textbook outcome and there was wide variation between hospitals.

Impactfactor: 5.899

The Complex Interplay of Physical Fitness, Protein Intake, and Vitamin D Supplementation After Bariatric Surgery

Pouwels S, Smelt HJ, Celik A, Gupta A, **Smulders JF**

Obes Surg. 2017 Nov;27(11):3008-3009

Geen abstract beschikbaar

Impactfactor: 3.947

The Correlation Between a Numerical Rating Scale of Patient Satisfaction With Current Management of an Upper Extremity Disorder and a General Measure of Satisfaction With the Medical Visit

van Berckel MM, Bosma NH, Hageman MG, Ring D, Vranceanu AM

Hand (N Y). 2017 Mar;12(2):202-206

Background: Patient satisfaction is used as an indicator of quality of care, but the measures currently available are lengthy and cumbersome and may not be feasible in orthopedic surgical practices. We set out to assess the relationship between the Medical Interview Satisfaction Scale (MISS-21) and a numerical rating scale (NRS) of patient satisfaction with current management of an orthopedic upper extremity condition. Methods: In this cross-sectional study, 86 patients from the practices of 2 hand

surgeons were included during an initial or follow-up visit. Questionnaires assessing demographics, upper extremity specific disability, pain during rest and activity, satisfaction with the medical visits (MISS-21), and satisfaction with current management of an orthopedic upper extremity condition (NRS satisfaction) were completed. Results: Eighty-six patients completed all questionnaires. A small correlation of .21 (P = .050) was found between the MISS-21 and the NRS satisfaction. In bivariate analysis, NRS pain at rest and during activity had small correlations with the MISS-21 (-.29, P = .05 and -.23, P = .034) and with NRS satisfaction (-.27, P = .011 and -0.27, P = 0.012). Quick Disability of Arm, Shoulder and Hand (QuickDASH) had a small correlation with NRS satisfaction (-0.023, P = 0.001), but did not correlate with MISS-21. Conclusions: Although there is small overlap about the 2 satisfaction measures, a complex patient satisfaction questionnaire consisting of multiple facets of patient satisfaction like MISS-21 is not replaceable by 1 simple NRS patient satisfaction question.

Impactfactor: --

The feeding route after esophagectomy: a review of literature

Berkelmans GH, van Workum F, Weijs TJ, **Nieuwenhuijzen GA**, Ruurda JP, Kouwenhoven EA, van Det MJ, Rosman C, van Hillegersberg R, **Luyer MD**

J Thorac Dis. 2017 Jul;9(Suppl 8):S785-S791

Enhanced recovery programs effectively optimize perioperative care and reduce postoperative morbidity. In esophagectomy, several components of the ERAS program are successfully introduced. However, timing and type of postoperative feeding remain a matter of debate. Adequate nutritional support is essential in patients undergoing an esophagectomy. These patients often present with weight loss and their eating pattern is strongly altered by the procedure and reconstruction. Total parenteral nutrition (TPN) is associated with severe septic complications and enteral nutrition (EN) does not increase major complications. Therefore, early EN after esophagectomy is favored over TPN. However, with enteral feeding tubes minor complications occur frequently (13-38%) and in some cases this can hamper recovery. Based on experience in other types of upper gastro-intestinal surgery, early start of oral feeding could improve time to functional recovery after surgery. The total length of stay was significantly shorter in four prospective studies (6-12 vs. 8-13 days). However, large randomized controlled trials are lacking and the potential benefit of early oral feeding after esophageal surgery remains elusive. EN is nowadays the optimal feeding route after esophagectomy. TPN should only be used in specific cases in which EN is contraindicated. Early initiation of oral intake is promising and could improve postoperative recovery. However, further research is needed to substantiate these results.

Impactfactor: *2.365*

The general surgeon's perspective of rectus diastasis. A systematic review of treatment options

Mommers EH, **Ponten JE**, Al Omar AK, de Vries Reilingh TS, Bouvy ND, **Nienhuijs SW**

Surg Endosc. 2017 Dec;31(12):4934-4949

BACKGROUND:

Diastasis of the rectus abdominis muscles (DRAM) is characterised by thinning and widening of the linea alba, combined with laxity of the ventral abdominal musculature. This causes the midline to "bulge" when intra-abdominal pressure is increased. Plastic surgery treatment for DRAM has been thoroughly evaluated, though general surgical treatments and the efficacy of physiotherapy remain elusive. The aim of this systematic literature review is to evaluate both general surgical and physiotherapeutic treatment options for restoring DRAM in terms of postoperative complications, patient satisfaction, and recurrence rates.

METHOD:

MEDLINE®, Embase, PubMed, PubMed Central®, The cochrane central registry of controlled trials (CENTRAL), Google Scholar, and the Physiotherapy Evidence Database (PEDro) were searched using the following terms: 'rectus diastasis', 'diastasis recti', 'midline', and 'abdominal wall'. All clinical studies concerning general surgical or physiotherapeutic treatment of DRAM were eligible for inclusion.

RESULT:

Twenty articles describing 1.691 patients (1.591 surgery/100 physiotherapy) were included. Surgical interventions were classified as plication techniques (313 patients; 254 open/59 laparoscopic), modified hernia repair techniques (68 patients, all open), and combined hernia & DRAM techniques (1.210 patients; 1.149 open/40 hybrid). The overall methodological quality was low. Plication techniques with interrupted sutures and mesh reinforcement were applied most frequently for DRAM repair. Open repairs were performed in 85% of patients. There was no difference in postoperative complications or

recurrence rate after laparoscopic or open procedures, or between plication and modified hernia repair techniques. Physiotherapy programmes were unable to reduce IRD in a relaxed state. Though reduction of IRD during muscle contraction was described.
CONCLUSION:
Both plication-based methods and hernia repair methods are used for DRAM repair. Based on the current literature, no clear distinction in recurrence rate, postoperative complications, or patient reported outcomes can be made. Complete resolution of DRAM, measured in a relaxed state, following a physiotherapy training programme is not described in current literature. Physiotherapy can achieve a limited reduction in IRD during muscle contraction, though the impact of this finding on patient satisfaction, cosmesis, or function outcome is unclear.

Impactfactor: 3.747

The influence of hospital volume on long-term oncological outcome after rectal cancer surgery

Jonker FH, Hagemans JA, Burger JW, Verhoef C, Borstlap WA, Tanis PJ; Dutch Snapshot Research Group: **Rutten HJ, Simkens GA**

Int J Colorectal Dis. 2017 Dec;32(12):1741-1747

PURPOSE:
The association between hospital volume and outcome in rectal cancer surgery is still subject of debate. The purpose of this study was to assess the impact of hospital volume on outcomes of rectal cancer surgery in the Netherlands in 2011.
METHODS:
In this collaborative research with a cross-sectional study design, patients who underwent rectal cancer resection in 71 Dutch hospitals in 2011 were included. Annual hospital volume was stratified as low (< 20), medium (20-50), and high (= 50).
RESULTS:
Of 2095 patients, 258 patients (12.3%) were treated in 23 low-volume hospitals, 1329 (63.4%) in 40 medium-volume hospitals, and 508 (24.2%) in 8 high-volume hospitals. Median length of follow-up was 41 months. Clinical tumor stage, neoadjuvant therapy, extended resections, circumferential resection margin (CRM) positivity, and 30-day or in-hospital mortality did not differ significantly between volume groups. Significantly, more laparoscopic procedures were performed in low-volume hospitals, and more diverting stomas in high-volume hospitals. Three-year disease-free survival for low-, medium-, and high-volume hospitals was 75.0, 74.8, and 76.8% (p = 0.682). Corresponding 3-year overall survival rates were 75.9, 79.1, and 80.3% (p = 0.344). In multivariate analysis, hospital volume was not associated with long-term risk of mortality.
CONCLUSIONS:
No significant impact of hospital volume on rectal cancer surgery outcome could be observed among 71 Dutch hospitals after implementation of a national audit, with the majority of patients being treated at medium-volume hospitals.

Impactfactor: 2.426

The Patients' Perspective Is the Missing Link in Current Bariatric Surgical Practice

Pouwels S, **Alebeek MK**, Smelt HJ, **Smulders JF**

Obes Surg. 2017 Sep;27(9):2467-2468

Geen abstract beschikbaar

Impactfactor: 3.947

The Underestimated Effect of Perioperative Exercise Interventions in Bariatric Surgery: Increasing Need for Large Impact Studies

Pouwels S, Smelt HJ, **Smulders JF**

Obes Surg. 2017 Oct;27(10):2690-2691

Geen abstract beschikbaar

Impactfactor: 3.947

The use of near-infrared fluorescence imaging in the surgical treatment of esophageal cancer

Schaap DP, Nieuwenhuijzen GA, Luyer MD

J Thorac Dis. 2017 Feb;9(2):240-243

Geen abstract beschikbaar

Impactfactor: 2.365

Ticagrelor versus Clopidogrel in Symptomatic Peripheral Artery Disease

Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, Katona BG, Mahaffey KW, Norgren L, Jones WS, Blomster J, Millegård M, Reist C, Patel MR; EUCLID Trial Steering Committee and Investigators: **van Sambeek MR**

N Engl J Med. 2017 Jan 5;376(1):32-40

BACKGROUND:

Peripheral artery disease is considered to be a manifestation of systemic atherosclerosis with associated adverse cardiovascular and limb events. Data from previous trials have suggested that patients receiving clopidogrel monotherapy had a lower risk of cardiovascular events than those receiving aspirin. We wanted to compare clopidogrel with ticagrelor, a potent antiplatelet agent, in patients with peripheral artery disease.

METHODS:

In this double-blind, event-driven trial, we randomly assigned 13,885 patients with symptomatic peripheral artery disease to receive monotherapy with ticagrelor (90 mg twice daily) or clopidogrel (75 mg once daily). Patients were eligible if they had an ankle-brachial index (ABI) of 0.80 or less or had undergone previous revascularization of the lower limbs. The primary efficacy end point was a composite of adjudicated cardiovascular death, myocardial infarction, or ischemic stroke. The primary safety end point was major bleeding. The median follow-up was 30 months.

RESULTS:

The median age of the patients was 66 years, and 72% were men; 43% were enrolled on the basis of the ABI and 57% on the basis of previous revascularization. The mean baseline ABI in all patients was 0.71, 76.6% of the patients had claudication, and 4.6% had critical limb ischemia. The primary efficacy end point occurred in 751 of 6930 patients (10.8%) receiving ticagrelor and in 740 of 6955 (10.6%) receiving clopidogrel (hazard ratio, 1.02; 95% confidence interval [CI], 0.92 to 1.13; P=0.65). In each group, acute limb ischemia occurred in 1.7% of the patients (hazard ratio, 1.03; 95% CI, 0.79 to 1.33; P=0.85) and major bleeding in 1.6% (hazard ratio, 1.10; 95% CI, 0.84 to 1.43; P=0.49).

CONCLUSIONS:

In patients with symptomatic peripheral artery disease, ticagrelor was not shown to be superior to clopidogrel for the reduction of cardiovascular events. Major bleeding occurred at similar rates among the patients in the two trial groups.

Impactfactor: 72.406

Time to Glycemic Control - an Observational Study of 3 Different Operations

Celik A, **Pouwels S**, Karaca FC, Çagiltay E, Ugale S, Etikan Ä°, Büyükbozkirli D, Kiliç YE

Obes Surg. 2017 Mar; 27(3):694-702

BACKGROUND: Medical treatment fails to provide adequate control for many obesepatients with type 2 diabetes mellitus (T2DM). A comparative observational study of bariatric procedures was performed to investigate the time at which patientsachieve glycemic control within the first 30 postoperative days following sleeve gastrectomy (SG), mini-gastric bypass (MGB), and diverted sleeve gastrectomy withileal transposition (DSIT).

METHODS: Included patients had a body mass index (BMI) =30 kg/m2; T2DM fo=3 years, HbA1C > 7 % for =3 months, and no significant weight change (>3 %)within the prior 3 months. Surgical procedures performed were SG (n = 49), MGB(n = 93), and DSIT (n = 109). The primary endpoint was the day within the firstpostoperative month on which mean fasting capillary glucose levels reached<126 mg/dL. Multivariate logistic regression analysis was used to identifypredictors of glycemic control.

RESULTS: The cohort included 251 patients with a mean BMI of 36.04 ± 5.76 kg/m2; age, 52.84 ± 8.52 years; T2DM duration, 13.09 ± 7.54 years; HbA1C, 8.82 ± 1.58 %. On the morning of surgery, mean fasting plasma glucose was 177.63 ± 51.3 mg/dL; on day 30, 131.35 ± 28.7 mg/dL (p < 0.05). Mean fasting plasma glucose of <126 mg/dL was reached in the DSIT group (124.36 ± 20.21 mg/dL) on day 29, and in the MGB group (123.61 ± 22.51 mg/dL), on day 30. The SG group did not achieve target mean capillary glucose level within postoperative 30 days.

CONCLUSION: During the first postoperative month, glycemic control (<126 mg/dL) was achieved following DSIT and MGB, but not SG. Preoperative BMI and postprandial C-peptide levels were independent predictors of early glycemic control following DSIT.

Impactfactor: 3.947

Toward the detection of intraplaque hemorrhage in carotid artery lesions using photoacoustic imaging

Arabul MU, Heres M, Rutten MC, **van Sambeek MR**, van de Vosse FN, Lopata RG

J Biomed Opt. 2017 Apr 1 22(4):41010

Photoacoustic imaging (PAI) may have the ability to reveal the composition and the anatomical structure of carotid plaques, which determines its mechanical properties and vulnerability. We used PAI and plane wave ultrasound (PUS) imaging to obtain three-dimensional (3-D) images of endarterectomy samples ex vivo and compared the results with histology to investigate the potential of PAI-based identification of intraplaque hemorrhage. Seven carotid plaque samples were obtained from patients undergoing carotid endarterectomy and imaged with a fully integrated hand-held photoacoustic (PA) probe, consisting of a pulsed diode laser (t pulse = 130 ?? ns , E pulse = 1 ?? mJ , ? = 808 ?? nm) and a linear array transducer (f c = 7.5 ?? MHz). The samples were rotated 360 deg with 10 deg steps, and data were spatially compounded to obtain complete 3-D images of the plaques. Areas of high absorption in the 3-D datasets were identified and compared to histological data of the plaques. Data in six out of seven endarterectomy samples revealed the presence of intraplaque hemorrhages that were not visible in the PUS images. Due to the noninvasive nature of PAI, this ex vivo study may elucidate preclinical studies toward the in vivo, noninvasive, vulnerability assessment of the atherosclerotic carotid plaque

Impactfactor: 2.530

Treatment of peritoneal metastases from small bowel adenocarcinoma

Rovers KP, de Bree E, Yonemura Y, **de Hingh IH**

Int J Hyperthermia. 2017 Aug;33(5):571-578

BACKGROUND/PURPOSE:

Peritoneal metastases (PM) affect approximately one third of patients with metastatic small bowel adenocarcinoma (SBA). Treatment options are (1) systemic therapy?±?palliative surgery and (2) cytoreductive surgery with intraperitoneal chemotherapy (CRS?+?IPC). Due to scarce evidence, PM from SBA represents a therapeutic challenge. This narrative review summarised and discussed the evidence that investigated available treatment options.

METHODS:

Studies were discussed if they investigated first line systemic therapy for advanced SBA or CRS?+?IPC for PM from SBA. Extracted outcomes were objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), disease-free survival (DFS), overall survival (OS), and grade III-V toxicity/morbidity.

RESULTS:

Eighteen studies (15 observational, 3 phase II) that investigated systemic therapy and six observational studies that investigated CRS?+?IPC were reviewed. In studies that investigated systemic therapy, ORR, DCR, median PFS, median OS, and grade III-V toxicity ranged from 6% to 50%, 50% to 90%, 3 to 11 months, 8 to 20 months, and 10% to 68%, respectively. Fluoropyrimidine-oxaliplatin revealed favourable survival outcomes compared to fluoropyrimidine-irinotecan, fluoropyrimidine-cisplatin, fluoropyrimidine monotherapy, and other regimens. In studies that investigated CRS?+?IPC, median DFS, median OS, and grade III-V morbidity ranged from 10 to 12 months, 16 to 47 months, and 12% to 35%, respectively.

CONCLUSION:

Based on available evidence, fluoropyrimidine-oxaliplatin should be regarded as optimal first line systemic treatment. In selected patients, CRS?+?IPC appears safe and may be more effective than systemic therapy as single treatment. Future studies should evaluate survival and morbidity of CRS?+?IPC in larger cohorts, as well as the value of chemotherapy with targeted agents in metastatic SBA with subgroup analysis for PM from SBA.

Impactfactor: 3.262

Validation of the Nexfin®non-invasive continuous blood pressure monitoring validated against Riva-Rocci/Korotkoff in a bariatric patient population

Pouwels S, Lascaris B, **Nienhuijs SW**, Arthur Bouwman R, Buise MP

J Clin Anesth. 2017 Jun; 39:89-95. Epub 2017 Mar 31

STUDY OBJECTIVE:

The present study aimed to validate the Nexfin® monitor and to assess the accuracy compared to classical sphygmomanometry (Riva-Rocci/Korotkoff (RRK)) blood pressure (BP) measurements in patients with obesity scheduled for bariatric surgery.

DESIGN: Validation study.

SETTING: Outpatient clinic for bariatric surgery.
PATIENTS: 33 patients scheduled for bariatric surgery.
MEASUREMENTS:
The validation process was done according to the protocols developed by the European Society of Hypertension from 2010. The Nexfin® monitor (Edwards Lifesciences/BMEYE B.V., Amsterdam, The Netherlands) calculates beat-to-beat blood pressure from finger pulse wave analysis. Measurements of systolic and diastolic BP were obtained using classical sphygmomanometry and the Nexfin® alternatingly.
MAIN RESULTS:
In total 99 pairs of BP measurements were used. The device failed pass phase 1 as 65 systolic readings fell within 5mmHg (73 required). And 61, 76 and 90 diastolic readings fell within 5, 10 and 15mmHg respectively. Finally, it failed to pass phase 2 as 23 patients for systolic and 25 for diastolic had at least 2/3 of their comparisons falling within 5mmHg (24 required) but 10 subjects for systolic and 8 for diastolic had all three comparisons more than 5mmHg different from the RRK readings (zero allowed). Mean differences were 7.8±6.9mmHg for SBP and 8.0±7.2mmHg for DBP.
CONCLUSION:
Using the revised protocol, the Nexfin® device was not able to pass validation. However using the original protocol, the Nexfin® device passed phase 1 and 2.1 of the validation process and failed to pass phase 2.2.

Impactfactor: 1.677

What To Do With Lateral Nodal Disease in Low Locally Advanced Rectal Cancer? A Call for Further Reflection and Research

Kusters M, Slater A, Muirhead R, Hompes R, Guy RJ, Jones OM, George BD, Lindsey I, Mortensen NJ, Cunningham C.

Dis Colon Rectum. 2017 Jun; 60(6):577-585

BACKGROUND:
There remains a lack of international consensus on the appropriate management of lateral nodal disease. Although the East manages this more aggressively with lateral lymph node dissections, the West aims to eradicate small-volume disease with neoadjuvant chemoradiotherapy and lateral nodal disease is not considered for routine surgical treatment. However, recent studies have shown that, despite neoadjuvant treatment, a significant number of patients with lateral nodal disease develop local recurrence in the lateral compartment after total mesorectal excision.
OBJECTIVE: The aim of this study is to assess the role of the pretreatment features of lateral nodes on MRI in regard to local recurrence.
DESIGN: All patients operated on for low locally advanced rectal cancer over a 5-year period were evaluated retrospectively.
SETTINGS: This study was conducted at a single expert center.
PATIENTS: The MRIs of a total of 313 patients were reviewed, and only those with rectal cancers up to 8?cm from the anorectal junction, measured on MRI, were selected. This left 185 patients; of these, 58 patients had clinical T1 or T2 tumors as assessed on MRI, identifying 127 patients who had cT3/T4 tumors that were included in this study.
MAIN OUTCOME MEASURES:
The primary outcomes measured were lateral local recurrence and multivariate analyses.
RESULTS:
The lateral local recurrence rate was significantly higher (33.3% 4-year rate) in patients with nodes larger than 10?mm than in patients with smaller nodes (10.1%, p = 0.03), despite patients being irradiated in the lateral compartment.
LIMITATIONS:
Because this is a relatively uncommon disease, patient numbers are low, and a multicenter study is needed to further address lateral nodal disease in low rectal cancer.
CONCLUSIONS:
Chemoradiotherapy with total mesorectal excision might not be sufficient in a selected group of patients. Further research is needed about which pretreatment features of the lateral nodes predict local recurrence and what is needed to prevent these from developing

Impactfactor: 3.519

Dermatologie

A man with Bowen disease of the nail

Hendriks JC, Hamers ET, **Martens H**

Ned Tijdschr Geneeskd. 2017 161(0):D933

We describe a 40-year-old male patient with a 2-year history of a sensitive fingernail of the right hand. The nail had partly a rough surface, longitudinal cleavage and was brittle and vulnerable at the tip. Biopsy of the nail showed a Bowen disease (squamous cell carcinoma in situ) of the nail.

Impactfactor: --

Aesthetic outcome and complications of simple interrupted versus running subcuticular sutures in facial surgery: A randomized controlled trial

Liu X, Nelemans PJ, Frenk LD, **Sengers H,** Tuinder SM, **Steijlen PM, Mosterd K, Kelleners-Smeets NW**

J Am Acad Dermatol. 2017 Nov;77(5):911-919

BACKGROUND

The suturing technique and its associated complications could affect cosmetic outcome after facial surgery. Literature on this topic is limited.

OBJECTIVE:

To compare the cosmetic results 12 months after treatment and complications associated with simple interrupted sutures (SIS) versus running subcuticular sutures (RSS) in facial surgery.

METHODS:

A randomized, controlled multicenter trial was performed. Adults receiving dermatologic surgery on the face were randomized to receive SIS or RSS for wound closure. The primary outcome was the overall opinion score on the Patient and Observer Scar Assessment Scale (POSAS) 12 months after surgery. Secondary outcomes were the complication rates and scores according to alternative methods for assessment of cosmetic outcome. The observer of cosmetic outcome was blinded to treatment assignment.

RESULTS:

142 patients were randomized to receive SIS (n = 73) or RSS (n = 69). Twelve months after surgery, the median score of the overall opinion on the POSAS was 2.0 (range 1-8) according to the patients and 3.0 (range 1-8) according to the observer in both groups. In the RSS group, hyper- or hypoesthesia was reported more often.

LIMITATIONS:

The cosmetic result was assessed by 1 observer.

CONCLUSION:

SIS and RSS in facial surgery resulted in comparable cosmetic outcomes. RSS was more often associated with hyper- or hypoesthesia.

Impactfactor: *7.002*

Cancer survivors' preference for follow-up care providers: a cross-sectional study from the population-based PROFILES-registry

Huibertse LJ, van Eenbergen M, de Rooij BH, Bastiaens MT, Fossion LM, de la Fuente RB, Kil PJ, Koldewijn EL, Meier AH, Mommers RJ, Niemer AQ, Oddens JR, Oomens EH, Prins M, de Roos KP, **Thissen MR**, Timmermans MW, Wijsman BP, van de Poll-Franse LV, Ezendam NP

Acta Oncol. 2017 Feb;56(2):278-287

BACKGROUND:

The best practice for the organization of follow-up care in oncology is under debate, due to growing numbers of cancer survivors. Understanding survivors' preferences for follow-up care is elementary for designing patient-centred care. Based on data from prostate cancer and melanoma survivors, this study aims to identify: 1) preferences for follow-up care providers, for instance the medical specialist, the oncology nurse or the general practitioner; 2) characteristics associated with these preferences and 3) the preferred care provider to discuss cancer-related problems.

MATERIAL AND METHODS:

Survivors diagnosed with prostate cancer (N?=?535) and melanoma (N?=?232) between 2007 and 2013 as registered in The Netherlands Cancer Registry returned a questionnaire (response rate was 71% and 69%, respectively). A latent class cluster model analysis was used to define preferences and a multinomial logistic regression analysis was used to identify survivor-related characteristics associated with these preferences.

RESULTS:

Of all survivors, 29% reported no preference, 40% reported a preference for the medical specialist, 20% reported a preference for both the medical specialist and the general practitioner and 11% reported a preference for both the medical specialist and the oncology nurse. Survivors who were older, lower/intermediate educated and women were more likely to have a preference for the medical specialist. Lower educated survivors were less likely to have a preference for both the medical specialist and the general practitioner. Overall, survivors prefer to discuss diet, physical fitness and fatigue with the general practitioner, and hereditary and recurrence with the medical specialist. Only a small minority favored to discuss cancer-related problems with the oncology nurse.
CONCLUSION:
Survivors reported different preferences for follow-up care providers based on age, education level, gender and satisfaction with the general practitioner, showing a need for tailored follow-up care in oncology. The results indicate an urgency to educate patients about transitions in follow-up care.

Impactfactor: 3.730

Mendelian Disorders of Cornification Caused by Defects in Intracellular Calcium Pumps: Mutation Update and Database for Variants in ATP2A2 and ATP2C1 Associated with Darier Disease and Hailey-Hailey Disease.,

Nellen RG, **Steijlen PM**, van Steensel MA, Vreeburg M European Professional Contributors., Frank J, van Geel M
Hum Mutat. 2017 Apr 38(4):343-356. Epub 2017 Feb 15

The two disorders of cornification associated with mutations in genes coding for intracellular calcium pumps are Darier disease (DD) and Hailey-Hailey disease (HHD). DD is caused by mutations in the ATP2A2 gene, whereas the ATP2C1 gene is associated with HHD. Both are inherited as autosomal-dominant traits. DD is mainly defined by warty papules in seborrheic and flexural areas, whereas the major symptoms of HHD are vesicles and erosions in flexural skin. Both phenotypes are highly variable. In 12%-40% of DD patients and 12%-55% of HHD patients, no mutations in ATP2A2 or ATP2C1 are found. We provide a comprehensive review of clinical variability in DD and HHD and a review of all reported mutations in ATP2A2 and ATP2C1. Having the entire spectrum of ATP2A2 and ATP2C1 variants allows us to address the question of a genotype-phenotype correlation, which has not been settled unequivocally in DD and HHD. We created a database for all mutations in ATP2A2 and ATP2C1 using the Leiden Open Variation Database (LOVD v3.0), for variants reported in the literature and future inclusions. This data may be of use as a reference tool in further research on treatment of DD and HHD.

mHealth App for Risk Assessment of Pigmented and Nonpigmented Skin Lesions-A Study on Sensitivity and Specificity in Detecting Malignancy

Thissen M, Udrea A, **Hacking M**, von Braunmuehl T, Ruzicka T
Telemed J E Health. 2017 Dec;23(12):948-954

BACKGROUND: With the advent of smartphone devices, an increasing number of mHealth applications that target melanoma identification have been developed, but none addresses the general context of melanoma and nonmelanoma skin cancer identification.
INTRODUCTION: In this study a smartphone application using fractal and classical image analysis for the risk assessment of skin lesions is systematically evaluated to determine its sensitivity and specificity in the diagnosis of melanoma and nonmelanoma skin cancer along with actinic keratosis and Bowen's disease.
MATERIALS AND METHODS: In the Department of Dermatology, Catharina Hospital Eindhoven, The Netherlands, 341 melanocytic and nonmelanocytic lesions were imaged using SkinVision app; 239 underwent histopathological examination, while the rest of 102 lesions were clinically diagnosed as clearly benign and not removed. The algorithm has been calibrated using the images of the first 233 lesions. The calibrated version of the algorithm was used in a subset of 108 lesions, and the obtained results were compared with the medical findings.
RESULTS: On the 108 cases used for evaluation the algorithm scored 80% sensitivity and 78% specificity in detecting (pre)malignant conditions.
DISCUSSION: Although less accurate than the dermatologist's clinical eye, the app may offer support to other professionals who are less familiar with differentiating between benign and malignant lesions.
CONCLUSION: An mHealth application for the risk assessment of skin lesions was evaluated. It adds value to diagnosis tools of its type by taking into consideration pigmented and nonpigmented lesions all together and detecting signs of malignancy with high sensitivity.

Impactfactor: 2.031

Multidrug-resistant Mycoplasma genitalium infections in Europe

Braam JF, van Dommelen L, **Henquet CJM**, van de Bovenkamp JHB, Kusters JG

Eur J Clin Microbiol Infect Dis. 2017 Sep 36(9):1565-1567. Epub 2017 Mar 30

In Japan and Australia, multidrug-resistant Mycoplasma genitalium infections are reported with increasing frequency. Although macrolide-resistant M. genitalium strains are common in Europe and North America, fluoroquinolone-resistant strains are still exceptional. However, an increase of multidrug-resistant M. genitalium in Europe and America is to be expected. The aim of this paper is to increase awareness on the rising number of multidrug-resistant M. genitalium strains. Here, one of the first cases of infection with a genetically proven multidrug-resistant M. genitalium strain in Europe is described. The patient was a native Dutch 47-year-old male patient with urethritis. Mycoplasma genitalium was detected, but treatment failed with azithromycin, doxycycline and moxifloxacin. A urogenital sample was used to determine the sequence of the 23S rRNA, gyrA, gyrB and parC genes. The sample contained an A2059G single nucleotide polymorphism (SNP) in the 23S rRNA gene and an SNP in the parC gene, resulting in an amino acid change of Ser83 ? Ile, explaining both azithromycin and moxifloxacin treatment failure. The SNPs associated with resistance were probably generated de novo, as a link with high-prevalence areas was not established. It is, thus, predictable that there is going to be an increase of multidrug-resistant M. genitalium strains in Europe. As treatment options for multidrug-resistant M. genitalium are limited, the treatment of M. genitalium infections needs to be carefully considered in order to limit the rapid increase of resistance to macrolides and fluoroquinolones.

Impactfactor: 2.727

Pareltjes van de S.V.P. (SOA-Vulva-Proctologie) poli

Henquet C

Nederlands tijdschrift voor dermatologie & venereologie 2017;27(10):543-9

Impactfactor: --

Postzygotic mosaicism in basal cell naevus syndrome.

Reinders MGHC, Boersma HJ, Leter EM, Vreeburg M, Paulussen ADC, **Arits AHMM**, Roemen GMJM, Speel EJM, **Steijlen PM,** van Geel M, **Mosterd K**

Br J Dermatol. 2017 Jul; 177(1):249-252. Epub 2017 Jun 6

Basal cell naevus syndrome (BCNS) is an autosomal dominant disorder most commonly caused by a germline mutation in the Drosophila homologue of patched-1 gene (PTCH1). Here we describe a patient with clinical signs of BCNS, caused by postzygotic mosaicism of a PTCH1 mutation. We performed restriction fragment length polymorphism analysis and Droplet Digital polymerase chain reaction to determine the degree of mosaicism in different tissues of this patient. Our case shows that a relatively low-grade mosaicism can lead to clinical signs reminiscent of those caused by a germline mutation. This finding has important implications for genetic counselling and therefore is pivotal to recognize for dermatologists, as well as for clinical geneticists and clinical laboratory geneticists.

Impactfactor: 4.706

Scleromyxoedema

van Leersum F, Abdul Hamid M, **Steijlen P**

Lancet. 2017 Apr 15;389(10078):1549. Epub 2016 Nov 26

Geen abstract beschikbaar

Impactfactor: 47.831

Topical Sinecatechins, 10%, Ointment for Superficial Basal Cell Carcinoma: A Randomized Clinical Trial

Kessels J, Voeten L, Nelemans P, Cleutjens J, Hillen LM, Mosterd K**,** Kelleners-Smeets NW

JAMA Dermatol. 2017 Oct 1;153(10):1061-1063

Geen abstract beschikbaar

Impactfactor: 5.817

Dietetiek

Different Supplementation Regimes to Treat Perioperative Vitamin B12 Deficiencies in Bariatric Surgery: a Systematic Review

Smelt HJ, Pouwels S, Smulders JF

Obes Surg. 2017 Jan;27(1):254-262

Vitamin B12 dosage in multivitamin supplementation in the current literature is quite variable. There is no consensus about the optimal treatment of vitamin B12 deficiency. A systematic literature search on different supplementation regimes to treat perioperative vitamin B12 deficiencies in bariatric surgery was performed. The methodological quality of ten included studies was rated using the Newcastle Ottawa scale and ranged from moderate to good. The agreement between the reviewers was assessed with a Cohen's kappa (0.69). The current literature suggests that 350 µg oral vitamin B12 is the appropriate dose to correct low vitamin B12 levels in many patients. Further research must focus on a better diagnosis of a vitamin B12 deficiency, the optimal dose vitamin B12 supplementation, and clinical relevance next to biochemical data

Impactfactor: 3.947

The Complex Interplay of Physical Fitness, Protein Intake, and Vitamin D Supplementation After Bariatric Surgery

Pouwels S, **Smelt HJ**, Celik A, Gupta A, Smulders JF

Obes Surg. 2017 Nov;27(11):3008-3009.

Geen abstract beschikbaar

Impactfactor: 3.947

The Patients' Perspective Is the Missing Link in Current Bariatric Surgical Practice

Pouwels S, Alebeek MK, **Smelt HJ**, Smulders JF

Obes Surg. 2017 Sep;27(9):2467-2468

Geen abstract beschikbaar

Impactfactor: 3.947

The Underestimated Effect of Perioperative Exercise Interventions in Bariatric Surgery: Increasing Need for Large Impact Studies

Pouwels S, **Smelt HJ**, Smulders JF

Obes Surg. 2017 Oct;27(10):2690-2691

Geen abstract beschikbaar

Impactfactor: 3.947

Geestelijke verzorging

Talking about end-of-life care in a timely manner

Smeenk FW, **Schrijver LA**, van Bavel HC, **van de Laar EF**

Breathe 2017; 3(4): e95-e102

Geen abstract beschikbaar

Impactfactor: --

Geriatrie

Haloperidol
Nijboer H, Nijboer P
Nurse Academy O&T, 2017;1

[Patient reported outcome measures in geriatric care: first experiences] / Eerste ervaringen met patiënt gerapporteerde uitkomstmaten in de geriatrie
Hems M, Harkes M, Moret-Hartman M, Melis RJ, Schoon Y
Tijdschr Gerontol Geriatr. 2017 Dec;48(6):287-296
BACKGROUND:
There are difficulties in expressing the value of geriatric care in outcome measures such as recovery or mortality rates. Rather, the goal of geriatric care is to maintain quality of life and functionality. As such, patient reported outcome measures (PROMs) may be more effective in measuring the value healthcare creates in geriatric patients. In 2015 the Dutch Geriatrics Society asked their Committee Quality of Care Measurement to select a suitable PROM for the purpose of measuring the outcomes of geriatric hospital care.
METHODS/RESULTS:
The goal of this PROM is to measure outcomes of an hospital admission in the perspective of the elderly patient who was admitted to a geriatric ward. A group of caregivers in geriatric care identified four possible PROMs in the literature and based on selection criteria the TOPICS-MDS was chosen as most suitable. To increase the feasibility of implementation in daily practice, an item reduction study was performed and this resulted in a short form: TOPICS-SF. Two pilot studies in three hospitals took place on a geriatric ward. A response of 62% was observed during the first pilot with TOPICS-MDS and a response of 37% was observed during the second pilot with TOPICS-SF. The Katz-15 improved during hospital stay and during one month at home after discharge.
CONCLUSION:
The TOPICS-SF has been selected as PROM for the older patient receiving geriatric care and is feasible in practice. More research in different settings and with different moments of measurements is needed to evaluate the responsiveness of TOPICS-SF and the conditions for feasible implementation in daily practice.

Gynaecologie

A multi-centre, non-inferiority, randomised controlled trial to compare a cervical pessary with a cervical cerclage in the prevention of preterm delivery in women with short cervical length and a history of preterm birth - PC study

Koullali B, van Kempen LE, van Zijl MD, Naaktgeboren CA, Schuit E, Bekedam DJ, Franssen MT, Nij Bijvank SW, Sueters M, van Baal M, de Boer MA, Hooker AB, Hermsen BB, Toolenaar TA, Zwart JJ, van der Ham DP, van der Made FW, Prefumo F, Martinez de Tejada B, Papatsonis DN, Huisjes AJ, Scheepers LH, van Hoorn ME, **Hasaart TH**, Schuitemaker NW, Vollebregt KC, Müller MA, Evers IM26, Post MS, de Boer K, Visser H, Mensing van Charante NA, Langenveld J, Steemers NY, Mol BW, Oudijk MA, Pajkrt E

BMC Pregnancy Childbirth. 2017 Jul 6;17(1):215

Geen abstract beschikbaar

Impactfactor: 2.263

Compliance with adjuvant treatment guidelines in endometrial cancer: room for improvement in high risk patients

Eggink FA, Mom CH, **Boll D**, Ezendam NP, Kruitwagen RF, Pijnenborg JM, van der Aa MA, Nijman HW

Gynecol Oncol. 2017 Aug;146(2):380-385

OBJECTIVES:

Compliance of physicians with guidelines has emerged as an important indicator for quality of care. We evaluated compliance of physicians with adjuvant therapy guidelines for endometrial cancer patients in the Netherlands in a population-based cohort over a period of 10years.

METHODS:

Data from all patients diagnosed with endometrial cancer between 2005 and 2014, without residual tumor after surgical treatment, were extracted from the Netherlands Cancer Registry (N=14,564). FIGO stage, grade, tumor type and age were used to stratify patients into risk groups. Possible changes in compliance over time and impact of compliance on survival were assessed.

RESULTS:

Patients were stratified into low/low-intermediate (52%), high-intermediate (21%) and high (20%) risk groups. Overall compliance with adjuvant therapy guidelines was 85%. Compliance was highest in patients with low/low-intermediate risk (98%, no adjuvant therapy indicated). The lowest compliance was determined in patients with high risk (61%, external beam radiotherapy with/without chemotherapy indicated). Within this group compliance decreased from 64% in 2005-2009 to 57% in 2010-2014. In high risk patients with FIGO stage III serous disease compliance was 55% (chemotherapy with/without radiotherapy indicated) and increased from 41% in 2005-2009 to 66% in 2010-2014.

CONCLUSION:

While compliance of physicians with adjuvant therapy guidelines is excellent in patients with low and low-intermediate risk, there is room for improvement in high risk endometrial cancer patients. Eagerly awaited results of ongoing randomized clinical trials may provide more definitive guidance regarding adjuvant therapy for high risk endometrial cancer patients.

Impactfactor: 4.959

Early enteral tube feeding in optimizing treatment of hyperemesis gravidarum: the Maternal and Offspring outcomes after Treatment of HyperEmesis by Refeeding (MOTHER) randomized controlled trial

Grooten IJ, Koot MH van der Post JA, Bais JM, Ris-Stalpers C, Naaktgeboren C, Bremer HA, van der Ham DP, Heidema WM, Huisjes A, Kleiverda G, **Kuppens S**, van Laar JO, Langenveld J, van der Made F, van Pampus MG, Papatsonis D, Pelinck MJ, Pernet PJ, van Rheenen L, Rijnders RJ, Scheepers HC, Vogelvang, Mol BW, Roseboom TJ, Painter RC

Am J Clin Nutr. 2017 Sep;106(3):812-820

Background: Hyperemesis gravidarum (HG) leads to dehydration, poor nutritional intake, and weight loss. HG has been associated with adverse pregnancy outcomes such as low birth weight. Information about the potential effectiveness of treatments for HG is limited.Objective: We hypothesized that in women with HG, early enteral tube feeding in addition to standard care improves birth weight.Design: We performed a multicenter, open-label randomized controlled trial [Maternal and Offspring outcomes after Treatment of HyperEmesis by Refeeding (MOTHER)] in 19 hospitals in the Netherlands. A total of 116 women hospitalized for HG between 5 and 20 wk of gestation were randomly allocated to enteral tube feeding for =7 d in addition to standard care with intravenous rehydration and antiemetic treatment or to standard care alone. Women were encouraged to continue tube feeding at home. On the basis of our power calculation, a sample size of 120 women was anticipated. Analyses were

performed according to the intention-to-treat principle.Results: Between October 2014 and March 2016 we randomly allocated 59 women to enteral tube feeding and 57 women to standard care. The mean ± SD birth weight was 3160 ± 770 g in the enteral tube feeding group compared with 3200 ± 680 g in the standard care group (mean difference: -40 g, 95% CI: -230, 310 g). Secondary outcomes, including maternal weight gain, duration of hospital stay, readmission rate, nausea and vomiting symptoms, decrease in quality of life, psychological distress, prematurity, and small-for-gestational-age, also were comparable. Of the women allocated to enteral tube feeding, 28 (47%) were treated according to protocol. Enteral tube feeding was discontinued within 7 d of placement in the remaining women, primarily because of its adverse effects (34%).Conclusions: In women with HG, early enteral tube feeding does not improve birth weight or secondary outcomes. Many women discontinued tube feeding because of discomfort, suggesting that it is poorly tolerated as an early routine treatment of HG

Impactfactor: 6.926

Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial

de Rooij BH, Ezendam NPM, Nicolaije KAH, Caroline Vos M, Pijnenborg JMA, **Boll D**, Boss EA, Hermans RHM, Engelhart KCM, Haartsen JE, Pijlman BM, van Loon-Baelemans IEAM, Mertens HJMM, Nolting WE, van Beek JJ, Roukema JA, Kruitwagen RFPM, van de Poll-Franse LV

Gynecol Oncol. 2017 May 145(2):319-328. Epub 2017 Mar 7

OBJECTIVE:

The aim of this study was to assess the long-term impact of an automatically generated Survivorship Care Plan (SCP) on patient reported outcomes in ovarian cancer in routine clinical practice. Outcome measures included satisfaction with information provision and care, illness perceptions and health care utilization.

METHODS:

In this pragmatic cluster randomized trial, twelve hospitals in the South of the Netherlands were randomized to 'SCP care' or 'usual care'. All newly diagnosed ovarian cancer patients in the 'SCP care' arm received an SCP that was automatically generated by the oncology provider, by clicking a button in the web-based Registrationsystem Oncological GYnecology (ROGY). Ovarian cancer patients (N=174, mean age 63.3, SD=11.4; all stages) completed questionnaires directly after initial treatment and after 6, 12 and 24months.

RESULTS:

First questionnaires were returned from 61 (67%) ovarian cancer patients in the 'SCP care' arm and 113 (72%) patients in the 'usual care' arm. In the 'SCP care' arm, 66% (N=41) of the patients reported receipt of an SCP. No overall differences were observed between the trial arms on satisfaction with information provision, satisfaction with care or health care utilization. Regarding illness perceptions, patients in the 'SCP care' arm had lower beliefs that the treatment would help to cure their disease (overall, 6.7 vs. 7.5, P<0.01).

CONCLUSIONS:

SCPs did not increase satisfaction with information provision or care in ovarian cancer patients. Our trial results suggest that ovarian cancer patients may not benefit from an SCP.

Impactfactor: 4.959

Endometrial scratching in women with implantation failure after a first IVF/ICSI cycle; does it lead to a higher live birth rate? The SCRaTCH study: a randomized controlled trial (NTR 5342)

Van Hoogenhuijze NE, Torrance HL, Mol F, Laven JSE, Scheenjes E, Traas MA, Janssen C, Cohlen B, Teklenburg G, de Bruin JP, van Oppenraaij R, Maas JWM, Moll E, Fleischer K, van Hooff MH, de Koning C, Cantineau A, Lambalk CB, Verberg M, Nijs M, Manger AP, **van Rumste M**, van der Voet LF, Preys-Bosman A, Visser J, Brinkhuis E, den Hartog JE, Sluijmer A, Jansen FW, Hermes W, Bandell ML, Pelinck MJ, van Disseldorp J, van Wely M, Smeenk J, Pieterse QD, Boxmeer JC, Groenewoud ER, Eijkemans MJ, Kasius JC, Broekmans FJM

BMC Womens Health. 2017 Jul 21;17(1):47

BACKGROUND:

Success rates of assisted reproductive techniques (ART) are approximately 30%, with the most important limiting factor being embryo implantation. Mechanical endometrial injury, also called 'scratching', has been proposed to positively affect the chance of implantation after embryo transfer, but the currently available evidence is not yet conclusive. The primary aim of this study is to determine the effect of

endometrial scratching prior to a second fresh in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycle on live birth rates in women with a failed first IVF/ICSI cycle.
METHOD:
Multicenter randomized controlled trial in Dutch academic and non-academic hospitals. A total of 900 women will be included of whom half will undergo an endometrial scratch in the luteal phase of the cycle prior to controlled ovarian hyperstimulation using an endometrial biopsy catheter. The primary endpoint is the live birth rate after the 2nd fresh IVF/ICSI cycle. Secondary endpoints are costs, cumulative live birth rate (after the full 2nd IVF/ICSI cycle and over 12 months of follow-up); clinical and ongoing pregnancy rate; multiple pregnancy rate; miscarriage rate and endometrial tissue parameters associated with implantation failure.
DISCUSSION:
Multiple studies have been performed to investigate the effect of endometrial scratching on live birth rates in women undergoing IVF/ICSI cycles. Due to heterogeneity in both the method and population being scratched, it remains unclear which group of women will benefit from the procedure. The SCRaTCH trial proposed here aims to investigate the effect of endometrial scratching prior to controlled ovarian hyperstimulation in a large group of women undergoing a second IVF/ICSI cycle.

Impactfactor: 1.572

Evaluation of p16/Ki-67 dual-stained cytology as triage test for high-risk human papillomavirus-positive women

Ebisch RM, van der Horst J, Hermsen M, Rijstenberg LL, Vedder JE, Bulten J, Bosgraaf RP, Verhoef VM, Heideman DA, Snijders PJ, Meijer CJ, van Kemenade FJ, Massuger LF, Melchers WJ, **Bekkers RL**, Siebers AG
Mod Pathol. 2017 Jul 30(7):1021-1031. Epub 2017 Mar 17

The aim of this study was to evaluate the clinical utility of p16/Ki-67 dual staining, for the identification of CIN in high-risk HPV-positive women from a non-responder screening cohort. P16/Ki-67 dual staining, Pap cytology, and HPV16/18 genotyping were performed on physician-taken liquid-based samples from 495 women who tested high-risk HPV positive on self-sampled material (PROHTECT-3B study). Different triage strategies involving p16/Ki-67 dual staining were evaluated for sensitivity, specificity, and predictive value for =CIN2 and =CIN3, and compared to Pap cytology with a threshold of atypical cells of undetermined significance. Centrally revised histology or an adjusted endpoint with combined high-risk HPV negative and cytology negative follow-up at 6 months was used as gold standard. Pap cytology (threshold atypical cells of undetermined significance) triage of high-risk HPV-positive samples showed a sensitivity of 93% (95% confidence interval: 85-98) with a specificity of 49% (95% confidence interval: 41-56) for =CIN3. Three triage strategies with p16/Ki-67 showed a significantly increased specificity with similar sensitivity. P16/Ki-67 triage of all high-risk HPV-positive samples had a sensitivity of 92% (95% confidence interval: 84-97) and a specificity of 61% (95% confidence interval: 54-69) for =CIN3. Applying p16/Ki-67 triage to only high-risk HPV-positive women with low-grade Pap cytology showed a similar sensitivity of 92% (95% confidence interval: 84-97), with a specificity for =CIN3 of 64% (95% confidence interval: 56-71). For high-risk HPV-positive women with low-grade and normal Pap cytology, triage with p16/Ki-67 showed a sensitivity of 96% (95% confidence interval: 89-99), and a specificity of 58% (95% confidence interval: 50-65). HPV16/18 genotyping combined with Pap cytology showed a sensitivity and specificity for =CIN3 similar to Pap cytology with an atypical cells of undetermined significance threshold. Because the quality of Pap cytology worldwide varies, and differences in sensitivity and specificity are limited between the three selected strategies, p16/Ki-67 triage of all high-risk HPV-positive samples would be the most reliable strategy in triage of high-risk HPV-positive women with an increased specificity and similar sensitivity compared with Pap cytology triage.

Impactfactor: 5.728

Experienced job autonomy among maternity care professionals in The Netherlands

Perdok H, Cronie D, van der Speld C, van Dillen J, de Jonge A, Rijnders M, de Graaf , Schellevis FG, Verhoeven CJ
Midwifery. 2017 Nov;54:67-72

OBJECTIVE: High levels of experienced job autonomy are found to be beneficial for healthcare professionals and for the relationship with their patients. The aim of this study was to assess how maternity care professionals in the Netherlands perceive their job autonomy in the Dutch maternity care system and whether they expect a new system of integrated maternity care to affect their experienced job autonomy.

DESIGN: A cross-sectional survey. The Leiden Quality of Work Life Questionnaire was used to assess experienced job autonomy among maternity care professionals.
SETTING: Data were collected in the Netherlands in 2015.
PARTICIPANTS: 799 professionals participated of whom 362 were primary care midwives, 240 obstetricians, 93 clinical midwives and 104 obstetric nurses.
FINDINGS: The mean score for experienced job autonomy was highest for primary care midwives, followed by obstetricians, clinical midwives and obstetric nurses. Primary care midwives scored highest in expecting to lose their job autonomy in an integrated care system.
KEY CONCLUSIONS: There are significant differences in experienced job autonomy between maternity care professionals.
IMPLICATIONS FOR PRACTICE: When changing the maternity care system it will be a challenge to maintain a high level of experienced job autonomy for professionals. A decrease in job autonomy could lead to a reduction in job related wellbeing and in satisfaction with care among pregnant women.

Impactfactor: 1.948

Factors influencing implementation of a survivorship care plan-a quantitative process evaluation of the ROGY Care trial

de Rooij BH, Ezendam NP, Nicolaije KA, Vos MC, Pijnenborg JM, **Boll D**, Kruitwagen RF, van de Poll-Franse LV
J Cancer Surviv. 2017 Feb;11(1):64-73. Epub 2016 Aug 1

PURPOSE:
The aim of this study is to investigate the factors that influence implementation of Survivorship Care Plans (SCPs) in the intervention arm of the ROGY Care trial by (1) assessing the level of SCP receipt in the ROGY Care trial and (2) identifying patient- and provider-level factors that influence SCP receipt.
METHODS:
Between 2011 and 2015, a pragmatic cluster randomized-controlled-trial was conducted on the effects of automatically generated SCPs. Endometrial (N = 117) and ovarian (N = 61) cancer patients were allocated to 'SCP care', as provided by their SCP care providers (N = 10). Associations between SCP receipt (self-reported SCP receipt and actually generated SCPs), patient-factors (socio-demographic-, clinical-, and personality factors), and care provider factors (profession and a-priori motivation regarding SCP provision) were tested in univariate analysis. The odds ratios of factors influencing self-reported SCP receipt were estimated with a multivariate regression model.
RESULTS:
Of all patients in the SCP care arm (N = 178), SCPs were generated by the care provider for 90 % of the patients and 70 % of the patients reported that they had received an SCP. Patients with older age, ovarian cancer, type D (distressed) personality, and patients that completed the questionnaire a longer period of time after the SCP consult were more likely to report no SCP receipt.
CONCLUSIONS:
SCP receipt was influenced by patient- but not care-provider factors.
IMPLICATIONS FOR CANCER SURVIVORS:
Certain patient groups were less likely to report SCP receipt. Whether all patients are in need of an SCP, requires further investigation. If they do, more efforts need to be made towards the implementation of SCPs.

Impactfactor: 3.051

Fetal heart rate abnormalities during and after external cephalic version: Which fetuses are at risk and how are they delivered?

Kuppens SM, Smailbegovic I, Houterman S, **de Leeuw I, Hasaart TH**
BMC Pregnancy Childbirth. 2017 Oct 17;17(1):363

BACKGROUND: Fetal heart rate abnormalitie (FHR) during and after external cephalic version (ECV) are relatively frequent. They may raise concern about fetal wellbeing. Only occasionally they may lead to an emergency cesarean section.
METHODS: Prospective cohort study in 980 women (>?34 weeks gestation) with a singleton fetus in breech presentation. During and after external cephalic version (ECV) FHR abnormalities were recorded. Obstetric variables and delivery outcome were evaluated. Primary outcome was to identify which fetuses are at risk for FHR abnormalities. Secondary outcome was to identify a possible relationship between FHR abnormalities during and after ECV and mode of delivery and fetal distress during subsequent labor.

RESULTS: The overall success rate of ECV was 60% and in 9% of the attempts there was an abnormal FHR pattern. In two cases FHR abnormalities after ECV led to an emergency CS. Estimated fetal weight per 100 g (OR 0.90, CI: 0.87-0.94) and longer duration of the ECV-procedure (OR 1.13, CI: 1.05-1.21) were factors significantly associated with the occurrence of FHR abnormalities. FHR abnormalities were not associated with the mode of delivery or the occurrence of fetal distress during subsequent labor.

CONCLUSIONS: FHR abnormalities during and after ECV are more frequent with lower estimated fetal weight and longer duration of the procedure. FHR abnormalities during and after ECV have no consequences for subsequent mode of delivery. They do not predict whether fetal distress will occur during labor.

Impactfactor: 2.263

From paradigm shift towards ovarian cancer prevention

Piek J

BJOG. 2017 Jan;124(2):321. doi: 10.1111/1471-0528.14278. Epub 2016 Aug 26.

Geen abstract beschikbaar

Impactfactor: 5.051

High-risk human papillomavirus detection in self-sampling compared to physician-taken smear in a responder population of the Dutch cervical screening: Results of the VERA study

Ketelaars PJW, Bosgraaf RP, Siebers AG, Massuger LFAG, van der Linden JC, Wauters CAP, Rahamat-Langendoen JC, van den Brule AJC, IntHout J, Melchers WJG, **Bekkers RLM***

Prev Med. 2017 Aug;101:96-101. Epub 2017 Jun 1.

In 2017 the cervical cancer screening program in The Netherlands will be revised. Cervical smears will primarily be tested for the presence of high-risk human papillomavirus (hrHPV) instead of cytology, and vaginal self-sampling will be offered to non-responders. This includes a potential risk that part of the women who would otherwise opt for a cervical smear will wait for self-sampling. However, self-sampling for hrHPV in a responder population has never been studied yet. The aim of this study was to investigate the applicability and accuracy of self-sampling in detecting hrHPV in a screening responder population. A total of 2049 women, aged 30-60years, participating in the screening program in The Netherlands were included from April 2013 to May 2015. After they had their cervical smear taken, women self-collected a cervicovaginal sample with a brush-based device, the Evalyn Brush. Both the cervical smear and self-sample specimen were tested with the COBAS 4800 HPV platform. The hrHPV prevalence was 8.0% (95% CI 6.9-9.2) among the physician-taken samples, and 10.0% (95% CI 8.7-11.3) among the self-samples. There was 96.8% (95% CI 96.0-97.5) concordance of hrHPV prevalence between self-samples and physician-taken samples. Women in our study evaluated self-sampling as convenient (97.1%), user-friendly (98.5%), and 62.8% preferred self-sampling over a physician-taken sampling for the next screening round. In conclusion, self-sampling showed high concordance with physician-taken sampling for hrHPV detection in a responder screening population and highly acceptable to women. Implementation of HPV-self-sampling for the responder population as a primary screening tool may be considered.

** Ten tijde van publicatie verbonden aan: Department of Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen*

Impactfactor: 3.434

Hysteroscopic Tissue Removal Systems: A Randomized In Vitro Comparison

Meulenbroeks D, Hamerlynck TW, **Saglam-Kara S**, Van Rijssel NK, **Van Vliet HA**, **Schoot BC**

J Minim Invasive Gynecol. 2017 Jan 1;24(1):159-164. doi: Epub 2016 Sep 3

STUDY OBJECTIVE:

To compare polyp resection time and myoma resection rate using 2 hysteroscopic tissue removal systems.

DESIGN:

Prospective randomized in vitro trial (Canadian Task Force classification I).

SETTING:

Clinical skills laboratory of a non-university teaching hospital.

SAMPLES:

Polyp surrogate and myoma tissue.

INTERVENTIONS:
Hysteroscopic tissue removal with the TRUCLEAR system, using the TRUCLEAR INCISOR 2.9 (TI), TRUCLEAR INCISOR Plus (TIP), or TRUCLEAR ULTRA Plus (TUP) device, and the MyoSure system, using the MyoSure Lite (ML), MyoSure Classic (MC), or MyoSure XL (MXL) device.
MEASUREMENTS AND MAIN RESULTS:
Forty-two fragments of umbilical cord weighing 5 g, as a surrogate for polyps, were randomly allocated to 4 types of devices (TI, TIP, ML, and MC). Three consecutive fragments were removed using a single device. In addition, 18 pieces of myoma tissue were divided into 2 equal parts and randomly allocated to 2 types of devices (TUP and MXL). A new device was used for each fragment. Each type of device was tested at 2 vacuum settings. When removing 1 polyp, the TIP (median time, 2:33 minutes [interquartile range (IQR), 1:32-3:27 minutes]), the MC (median time, 3:15 minutes [IQR, 2:42-3:42 minutes]), and the ML (median time, 3:00 minutes [IQR, 2:16-3:25 minutes]) performed significantly faster than the TI (median time, 14:09 minutes [IQR, 13:44-14:36 minutes]), by 84%, 78%, and 82% respectively ($p < .001$). The TIP performed 80% faster than the TI (median time, 2:27 minutes [IQR, 1:45-2:46 minutes] vs 10:37 minutes [IQR, 8:38-13:44 minutes]; $p < .001$) when removing a second polyp. For removal of a third polyp, the TIP performed significantly faster (median time, 2:22 minutes [IQR, 1:32-3:07 minutes]) than the TI (median time, 8:35 minutes [IQR, 7:37-9:03 minutes]) and the ML (median time, 10:02 minutes [IQR, 9:51-10:18 minutes]), by 74% and 78%, respectively ($p < .001$). The performance of the ML decreased ($p < .001$) during removal of 3 consecutive tissue samples. For myoma tissue, the estimated mean resection rate of the TUP (2.96 g/min [95% confidence interval (CI), 2.32-3.77 g/min]) was 24% (95% CI 0.2%-52.4%) higher than the mean resection rate of the MXL (2.39 g/min [95% CI 1.87-3.05 g/min]; $p = .048$). The resection rate of the MXL adjusted for vacuum setting declined by 3% per unit increase in myoma volume (95% CI, -0.6% to -5.7%; $p = .02$). For the TUP, no linear association was found (0.4%; 95% CI, -2.1% to 3.0%; $p = .72$).
CONCLUSION:
In vitro comparison of the removal of surrogate polyps showed that although the larger TIP, MC, and ML devices were significantly faster than the TI for removal of 1 polyp, only the TIP was consistently faster than the TI for consecutive removal of polyps. The performance of the ML decreased significantly during removal of 3 consecutive tissue samples, making it slower than the TIP with a similar window size in the third run. For removal of myoma tissue, the resection rate of the TUP was significantly higher than that of the MXL, and the resection rate of the MXL decreased with increasing myoma volume. In vitro testing can provide useful information on the time and rate of hysteroscopic tissue removal.
Impactfactor: 3.061

Illness perceptions and changes in lifestyle following a gynecological cancer diagnosis: A longitudinal analysis

van Broekhoven MECL, de Rooij BH, Pijnenborg JMA, Vos MC, **Boll D**, Kruitwagen RFPM, van de Poll-Franse LV, Ezendam NPM

Gynecol Oncol. 2017 May 145(2):310-318. Epub 2017 Mar 6

OBJECTIVE:
This study explores patterns of lifestyle change and whether more threatening illness perceptions are associated with lifestyle changes post-treatment for smoking, alcohol consumption and Body Mass Index (BMI) among gynecological cancer patients.
METHODS:
In total, 395 cancer patients (N=221 endometrial; N=174 ovarian) were included in this secondary analysis of longitudinal data. Lifestyle outcomes were assessed through self-reported questionnaires after initial treatment and 6, 12, and 18months of follow-up. Illness perceptions were assessed with the Brief Illness Perception Questionnaire (BIPQ). Latent class growth curve analyses were conducted to identify patterns of lifestyle change and linear mixed models using between-subject and within-subject effects to explore the association between BIPQ items and alcohol consumption (glasses/week) and BMI (kg/m2).
RESULTS:
After initial treatment, 15% (N=57) of the patients smoked, 53% (N=203) drank alcohol, and 60% (N=236) were overweight or obese. Overall, smokers made no considerable changes, but one subgroup of low level smokers reported positive decline. A slight decrease was observed for alcohol consumption among low and moderate level alcohol drinker subgroups, whereas BMI remained stable among endometrial cancer patients and increased for ovarian cancer patients. Moreover, patients with lower trust in their treatment to cure the disease drank more alcohol (ß=0.32 glasses/week [95% CI 0.09; 0.56]).

CONCLUSIONS:

Change in lifestyle after a gynecological cancer treatment is not self-evident. Moreover, more threatening illness perceptions were not related to a healthier lifestyle. This study underlines the need for lifestyle-promoting activities to facilitate lifestyle improvement among gynecological cancer patients.

Impactfactor: 4.959

Individualized versus standard FSH dosing in women starting IVF/ICSI: an RCT. Part 1: The predicted poor responder

van Tilborg TC, Torrance HL, Oudshoorn SC, Eijkemans MJ, Koks CA, Verhoeve HR, Nap AW, Scheffer GJ, Manger AP, **Schoot BC**, Sluijmer AV, Verhoeff , Groen H, Laven JS, Mol BW,, Broekmans FJ; OPTIMIST study group

Hum Reprod. 2017 Dec 1;32(12):2496-2505

STUDY QUESTION:

Does an increased FSH dose result in higher cumulative live birth rates in women with a predicted poor ovarian response, apparent from a low antral follicle count (AFC), scheduled for IVF or ICSI?

SUMMARY ANSWER:

In women with a predicted poor ovarian response (AFC < 11) undergoing IVF/ICSI, an increased FSH dose (225/450 IU/day) does not improve cumulative live birth rates as compared to a standard dose (150 IU/day).

WHAT IS KNOWN ALREADY:

In women scheduled for IVF/ICSI, an ovarian reserve test (ORT) can predict ovarian response to stimulation. The FSH starting dose is often adjusted based on the ORT from the belief that it will improve live birth rates. However, the existing RCTs on this topic, most of which show no benefit, are underpowered.

STUDY DESIGN, SIZE, DURATION:

Between May 2011 and May 2014, we performed an open-label multicentre RCT in women with an AFC < 11 (Dutch Trial Register NTR2657). The primary outcome was ongoing pregnancy achieved within 18 months after randomization and resulting in a live birth. We needed 300 women to assess whether an increased dose strategy would increase the cumulative live birth rate from 25 to 40% (two-sided alpha-error 0.05, power 80%).

PARTICIPANTS/MATERIALS, SETTING, METHODS:

Women with an AFC = 7 were randomized to an FSH dose of 450 IU/day or 150 IU/day, and women with an AFC 8-10 were randomized to 225 IU or 150 IU/day. In the standard group, dose adjustment was allowed in subsequent cycles based on pre-specified criteria. Both effectiveness and cost-effectiveness of the strategies were evaluated from an intention-to-treat perspective.

MAIN RESULTS AND THE ROLE OF CHANCE:

In total, 511 women were randomized, 234 with an AFC = 7 and 277 with an AFC 8-10. The cumulative live birth rate for increased versus standard dosing was 42.4% (106/250) versus 44.8% (117/261), respectively [relative risk (RR): 0.95 (95%CI, 0.78-1.15), P = 0.58]. As an increased dose strategy was more expensive [delta costs/woman: €1099 (95%CI, 562-1591)], standard FSH dosing was the dominant strategy in our economic analysis.

LIMITATIONS, REASONS FOR CAUTION:

Despite our training programme, the AFC might have suffered from inter-observer variation. As this open study permitted small dose adjustments between cycles, potential selective cancelling of cycles in women treated with 150 IU could have influenced the cumulative results. However, since first cycle live birth rates point in the same direction we consider it unlikely that the open design masked a potential benefit for the individualized strategy.

WIDER IMPLICATIONS OF THE FINDINGS:

Since an increased dose in women scheduled for IVF/ICSI with a predicted poor response (AFC < 11) does not improve live birth rates and is more expensive, we recommend using a standard dose of 150 IU/day in these women.

STUDY FUNDING/COMPETING INTEREST(S):

This study was funded by The Netherlands Organisation for Health Research and Development (ZonMW number 171102020). T.C.T., H.L.T. and S.C.O. received an unrestricted personal grant from Merck BV. H.R.V. receives monetary compensation as a member on an external advisory board for Ferring pharmaceutical BV. B.W.J.M. is supported by a NHMRC Practitioner Fellowship (GNT1082548) and reports consultancy for OvsEva, Merck and Guerbet. F.J.M.B. receives monetary compensation as a member of the external advisory board for Ferring pharmaceutics BV (the Netherlands) and Merck

Serono (the Netherlands) for consultancy work for Gedeon Richter (Belgium) and Roche Diagnostics on automated AMH assay development (Switzerland) and for a research cooperation with Ansh Labs (USA). All other authors have nothing to declare.

Impactfactor: 5.020

Less-favourable prognosis for low-risk endometrial cancer patients with a discordant pre- versus post-operative risk stratification

Eggink FA, Mom CH, Bouwman K, **Boll D**, Becker JH, Creutzberg CL, Niemeijer GC, van Driel WJ, Reyners AK, van der Zee AG, Bremer GL, Ezendam NP, Kruitwagen RF, Pijnenborg JM, Hollema H, Nijman HW, van der Aa MA

Eur J Cancer. 2017 Jun 78:82-90. Epub 2017 Apr 14. Corrigendum in: Eur J Cancer. 2017 Oct;84:370

BACKGROUND: Pre-operative risk stratification based on endometrial sampling determines the extent of surgery for endometrial cancer (EC). We investigated the concordance of pre- and post-operative risk stratifications and the impact of discordance on survival.

METHODS: Patients diagnosed with EC within the first 6 months of the years 2005-2014 were selected from the Netherlands Cancer Registry (N = 7875). Pre- and post-operative risk stratifications were determined based on grade and/or histological subtype for 3784 eligible patients.

RESULTS: A discordant risk stratification was found in 10% of patients: 4% (N = 155) had high pre- and low post-operative risk and 6% (N = 215) had low pre- and high post-operative risk. Overall survival of patients with high pre- and low post-operative risk was less favourable compared to those with a concordant low risk (80% versus 89%, p = 0.002). This difference remained significant when correcting for age, stage, surgical staging and adjuvant therapy (hazard ratio 1.80, 95% confidence interval 1.28-2.53, p = 0.001). Survival of patients with low pre- and high post-operative risk did not differ from those with a concordant high risk (64% versus 62%, p = 0.295).

CONCLUSION: Patients with high pre- and low post-operative risk have a less favourable prognosis compared to patients with a concordant low risk. Pre-operative risk stratifications contain independent prognostic information and should be incorporated into clinical decision-making.

Impactfactor: 6.029

Long-Lasting Increased Risk of Human Papillomavirus-Related Carcinomas and Premalignancies After Cervical Intraepithelial Neoplasia Grade 3: A Population-Based Cohort Study

Ebisch RM, Rutten DW, IntHout J, Melchers WJ, Massuger LF, Bulten J, **Bekkers RL**, Siebers AG

J Clin Oncol. 2017 Aug 1;35(22):2542-2550

Purpose The aim of this study was to determine the risk of human papillomavirus (HPV)-related carcinomas and premalignancies in women diagnosed with cervical intraepithelial neoplasia grade 3 (CIN3). Knowledge of this risk is important to preventing the development and progression of other HPV-related premalignancies and carcinomas, by considering prophylactic HPV vaccination and/or by paying increased attention to other HPV-related carcinomas and premalignancies when CIN3 is identified. Methods Women diagnosed with a CIN3 between 1990 and 2010 were identified from the Dutch nationwide registry of histopathology and cytopathology (PALGA) and matched with a control group of women without CIN3. Subsequently, all cases of high-risk (hr) HPV-associated high-grade lesions and carcinomas in the anogenital region and oropharynx between 1990 and 2015 were extracted. Incidence rate ratios were estimated for carcinomas and premalignancies of the vulva, vagina, anus, and oropharynx. Results A total of 178,036 women were identified: 89,018 with a previous diagnosis of CIN3 and 89,018 matched control subjects without a history of CIN3. Women with a history of CIN3 showed increased risk of HPV-related carcinomas and premalignancies, with incidence rate ratios of 3.85 (95% CI, 2.32 to 6.37) for anal cancer, 6.68 (95% CI, 3.64 to 12.25) for anal intraepithelial neoplasia grade 3, 4.97 (95% CI, 3.26 to 7.57) for vulvar cancer, 13.66 (93% CI, 9.69 to 19.25) for vulvar intraepithelial neoplasia grade 3, 86.08 (95% CI, 11.98 to 618.08) for vaginal cancer, 25.65 (95% CI, 10.50 to 62.69) for vaginal intraepithelial neoplasia grade 3, and 5.51 (95% CI, 1.22 to 24.84) for oropharyngeal cancer. This risk remained significantly increased, even after long-term follow-up of up to 20 years. Conclusion This population-based study shows a long-lasting increased risk for HPV-related carcinomas and premalignancies of the anogenital and oropharyngeal region after a CIN3 diagnosis. Studies that investigate methods to prevent this increased risk in this group of patients, such as intensified screening or vaccination, are warranted.

Impactfactor: 24.008

Measuring health-related quality of life in cervical cancer patients: a systematic review of the most used questionnaires and their validity

Tax C, Steenbergen ME, Zusterzeel PL, **Bekkers RL***, Rovers MM

BMC Med Res Methodol. 2017 Jan 26; 17(1):15

BACKGROUND:

Data on health-related quality of life (HRQoL) is paramount for shared and evidence based decision-making. Since an overview of cervical cancer HRQoL tools and their validity appears to be lacking, we performed a systematic review on usage of disease specific HRQoL instruments in cervical cancer patients and their psychometric properties to identify the most suitable cervical cancer specific HRQoL tool.

METHODS:

We searched Pubmed, EMBASE and PsycINFO from inception up to 18 October 2016 for studies on quality of life in cervical cancer patients. Data extraction and HRQoL identification was performed by two independent reviewers. Validation studies of the identified cervical cancer specific HRQoL tools were retrieved and assessed on psychometric properties using the COSMIN checklist. All used cervical cancer specific HRQoL instruments were scored and ranked according to their psychometric properties.

RESULTS:

We included 156 studies (20,690 patients) and identified 31 HRQoL tools. The EORTC QLQ-CX24 (35 studies; 5,556 patients) and FACT-Cx (22 studies; 4,224 patients) were the only cervical cancer specific tools. The EORTC QLQ-CX24 had 4 out of 9 positive rated psychometric properties; internal consistency, content and construct validity, and agreement. Criterion validity, reliability, and interpretability scored doubtful. Responsiveness and floor- and ceiling effects were not reported. The FACT-Cx had 2 out of 9 positive rated psychometric properties; internal consistency and agreement. Content validity, reliability, and interpretability scored doubtful while criterion and construct validity scored negative. Responsiveness and floor- and ceiling effects were not reported.

CONCLUSION:

The validity of the often used EORTC QLQ-CX24 questionnaire for cervical cancer patients remains uncertain as 5 out of 9 psychometric properties were doubtful or not reported in current literature. Cervical cancer specific HRQoL tools should therefore always be used in conjunction with validated generic cancer HRQoL tools until proper validity has been proven, or a more valid tool has been developed.

Ten tijde van publicatie verbonden aan: Department of Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen

Impactfactor: 3.295

Multimodal Hyperspectroscopic Imaging for Detection of High-Grade Cervical Intraepithelial Neoplasia

Ebisch RMF, Hermens M, van den Akker PAJ, Massuger LFAG, Melchers WJG, **Bekkers RLM**

J Low Genit Tract Dis. 2017 Jul 21(3):166-170

OBJECTIVE:

Numerous new alternative digital colposcopy techniques have been developed, of which multimodal hyperspectroscopy (MHS) showed a high sensitivity in previous studies. The objective of this prospective single-center cohort study was to evaluate the clinical value of MHS for detecting high-grade cervical intraepithelial neoplasia in a colposcopy referral population and colposcopy follow-up population, to assess whether MHS could be safely used to improve care for women at risk for high-grade cervical intraepithelial neoplasia.

MATERIALS AND METHODS:

A total of 125 women from a colposcopy referral population and colposcopy follow-up population were evaluated with MHS and tested for the presence of high-risk human papillomavirus (HPV) with HPV-16/18 genotyping. Spectroscopic measurements of the cervix were taken and compared with an end point based on histology, high-risk HPV, and cytology. Evaluable data for analysis were collected from 102 of the subjects. Sensitivity, specificity, and predictive values were calculated for MHS and colposcopic impression based on conventional colposcopic examination.

RESULTS:

From the total study population of the 102 patients, 47 were enrolled in the colposcopy referral group and 55 in the colposcopy follow-up group. The MHS yielded a sensitivity of 93.6% (95% CI = 78.6-99.2), with a corresponding specificity of 42.3% (95% CI = 30.6-54.6) in the group with a composite end point. No adverse effects occurred, and patient acceptability was high.

CONCLUSIONS:

Multimodal hyperspectroscopy is a digital colposcopy technique that offers an easy, rapid, well-tolerated point-of-care assessment with a high sensitivity for the presence of high-grade cervical intraepithelial lesions, however, with a low specificity, resulting in limited clinical value.

Impactfactor: 1.205

Practice variation of vaginal birth after cesarean and the influence of risk factors at patient level: a retrospective cohort study

Vankan E, Schoorel EN, van Kuijk SM, Mol BJ, Nijhuis JG, Aardenburg R, Alink M, de Boer K, Delemarre FM, Dirksen CD, van Dooren IM, Franssen MT, Kaplan M, Kleiverda G, **Kuppens SM**, Kwee A, Langenveld J, Lim FT, Melman S, Sikkema MJ, Smits LJ, Visser H, Woiski M, Scheepers HC, Hermens RP

Acta Obstet Gynecol Scand. 2017 Feb;96(2):158-165. doi: 10.1111/aogs.13059. Epub 2017 Jan 3

INTRODUCTION:

Large practice variation exists in mode of delivery after cesarean section, suggesting variation in implementation of contemporary guidelines. We aim to evaluate this practice variation and to what extent this can be explained by risk factors at patient level.

MATERIAL AND METHODS:

This retrospective cohort study was performed among 17 Dutch hospitals in 2010. Women with one prior cesarean section without a contraindication for a trial of labor were included. We used multivariate logistic regression analysis to develop models for risk factor adjustments. One model was derived to adjust the elective repeat cesarean section rates; a second model to adjust vaginal birth after cesarean rates. Standardized rates of elective repeat cesarean section and vaginal birth after cesarean per hospital were compared. Pseudo-R2 measures were calculated to estimate the percentage of practice variation explained by the models. Secondary outcomes were differences in practice variation between hospital types and the correlation between standardized elective repeat cesarean section and vaginal birth after cesarean rates.

RESULTS:

In all, 1068 women had a history of cesarean section, of whom 71% were eligible for inclusion. A total of 515 women (67%) had a trial of labor, of whom 72% delivered vaginally. The elective repeat cesarean section rate at hospital level ranged from 6 to 54% (mean 29.8, standard deviation 11.8%). Vaginal birth after cesarean rates ranged from 50 to 90% (mean 71.8%, standard deviation 11.1%). More than 85% of this practice variation could not be explained by risk factors at patient level.

CONCLUSION:

A large practice variation exists in elective repeat cesarean section and vaginal birth after cesarean rates that can only partially be explained by risk factors at patient level.

Impactfactor: 2.480

Prevalence and predictors of depression and well-being after hysterectomy: An observational study

Theunissen M, Peters ML, Schepers J, **Schoot DC**, Gramke HF, Marcus MA

Eur J Obstet Gynecol Reprod Biol. 2017 Oct;217:94-100

OBJECTIVES: To assess risk and predictive factors for depression and well-being, 3 and 12 months after elective hysterectomy. Secondary objectives were to assess the incidence of depression, level of well-being, and feelings of femininity.

STUDY DESIGN: A prospective multicenter cohort study was performed among 419 women, undergoing hysterectomy for benign indication. Data were collected in the week prior to surgery, and in the per- and postoperative period up to the fourth postoperative day and 3 and 12 months after surgery. Sociodemographic variables, baseline health status, psychosocial predictors, and surgery data were assessed. Outcome measures were Center for Epidemiological Studies-Depression scale (CES-D, range 0-60), the 12-item well-being questionnaire energy and positive well-being subscales (range 0-12), and feelings of femininity. Predictor analyses were performed using linear mixed model analyses.

RESULTS: Levels of depression, energy, and positive well-being after hysterectomy were predicted by their corresponding baseline levels (estimate 0.62 $p<0.001$, 0.39 $p<0.001$, 0.37 $p<0.001$, respectively) and baseline pain (0.31 $p=0.003$, -0.09 $p=0.026$, -0.10 $p=0.008$). Postoperative infection reported at 12 months affected CES-D and energy level. Several other gynaecological, psychosocial, or perioperative factors were also predictive for one of the outcomes. Prevalence of depression at baseline, 3 and 12 months was 24%, 19%, and 21%, respectively. In general, well-being scores were slightly higher 3 and 12

months after hysterectomy than at baseline. Feelings of femininity were not negatively affected in 92% of the patients.

CONCLUSIONS: Preoperative psychosocial status, perioperative pain, and postoperative infection were found as predictors of psychological outcome after hysterectomy. In the majority of patients we observed small but significant improvements with regard to postoperative depression and well-being, while feelings of femininity were unaffected.

Impactfactor: 1.666

Prevalence of intrauterine adhesions after the application of hyaluronic acid gel after dilatation and curettage in women with at least one previous curettage: short-term outcomes of a multicenter, prospective randomized controlled trial

Hooker AB, de Leeuw R, van de Ven PM, Bakkum EA, Thurkow AL, Vogel NEA, **van Vliet HAAM**, Bongers MY, Emanuel MH, Verdonkschot AEM, Brölmann HAM, Huirne JAF

Fertil Steril. 2017 May 107(5):1223-1231.e3. Epub 2017 Apr 6

OBJECTIVE:

To examine whether intrauterine application of auto-crosslinked hyaluronic acid (ACP) gel, after dilatation and curettage (D&C), reduces the incidence of intrauterine adhesions (IUAs).

DESIGN:

Multicenter; women and assessors blinded prospective randomized trial.

SETTING:

University and university-affiliated teaching hospitals.

PATIENT(S):

A total of 152 women with a miscarriage of <14 weeks with at least one previous D&C for miscarriage or termination of pregnancy.

INTERVENTION(S):

Women were randomly assigned to either D&C plus ACP gel (intervention group) or D&C alone (control group). A follow-up diagnostic hysteroscopy was scheduled 8-12 weeks after the D&C procedure.

MAIN OUTCOME MEASURE(S):

The primary outcome was the number of women with IUAs and the secondary outcome was the severity of IUAs.

RESULT(S):

Outcomes were available for 149 women: 77 in the intervention group and 72 in the control group. The IUAs were observed in 10 (13.0%) and 22 women (30.6%), respectively (relative risk, 0.43; 95% confidence interval 0.22-0.83). Mean adhesion score and the amount of moderate-to-severe IUAs were significantly lower in the intervention group according to the American Fertility Society (AFS) and European Society of Gynecological Endoscopy classifications systems of adhesions.

CONCLUSION(S):

Intrauterine application of ACP gel after D&C for miscarriage in women with at least one previous D&C seems to reduce the incidence and severity of IUAs but does not eliminate the process of adhesion formation completely. Future studies are needed to confirm our findings and to evaluate the effect of ACP gel on fertility and reproductive outcomes.

Impactfactor: 4.447

Reply II: Embryo culture media effects

Kleijkers SH, Mantikou E, **Slappendel E**, Consten D, van Echten-Arends J, Wetzels AM, van Wely M, Smits LJ, van Montfoort AP, Repping S, Dumoulin JC, Mastenbroek S

Hum Reprod. 2017 Mar 1 32(3):717-718

Geen abstract beschikbaar

Impactfactor: 5.020

Robotic and Advanced Laparoscopic Surgical Training in European Gynecological Oncology Trainees

Gan C, Bossart M, **Piek J**, Halaska M, Haidopoulos D, Zapardiel I, Grabowski JP, Kesic V, Kimmig R, Cibula D, Lambaudie E, Verheijen R, Manchanda R

Int J Gynecol Cancer. 2017 Feb;27(2):375-381

INTRODUCTION: Advanced minimal access surgical training is an important component of training in gynecological oncology (GO). Europe-wide data on this topic are lacking. We present data on availability

and trainee experience of advanced laparoscopic surgical (ALS) and robotic surgical (RS) training in GO across Europe.

METHOD: A prospective web-based anonymized survey of European GO trainees was sent to the European Network of Young Gynaecological Oncologists members/trainees. It included sociodemographic information and specific questions pertaining to training experience or satisfaction in laparoscopic and robotic surgery. ? test was used for evaluating categorical variables and Mann-Whitney/Kruskal-Wallis (nonparametric) tests for continuous variables between 2 and more independent groups.

RESULTS: A total of 113 GO trainees from 29 countries responded. The mean (standard deviation) age was 35.2 (6.1) years, 59.3% were men, 40.7% were women, and 46% were in accredited training posts. The ALS and RS training was offered in only 43% and 23% of institutes respectively, and 54% and 23% of trainees had undergone some form of formal or informal training in ALS and RS respectively. A total of 62.4% felt that RS should be a formal component of GO training programs. A total of 61% and 35% planned to go outside their institute for ALS or RS training respectively. Trainees rating (1-5 scale) of their open surgery and ALS or RS skills (3.3/2.6/1.9) and training experience (3.5/2.8/2.1), respectively, were higher for open surgery than ALS or RS ($P < 0.0005$). Accredited posts were more likely than nonaccredited posts to offer ALS training (60%/31%, $P = 0.002$), formal training schedules (27.9%/4.4%, $P = 0.003$), and use of logbooks (46%/23%, $P = 0.035$).

CONCLUSIONS: Training and experience in ALS and RS are poorly rated by GO trainees across Europe, and only few centers offer this. There is an urgent need to expand and harmonize training opportunities for ALS and RS. Most trainees want RS included as a formal component of their training.

Impactfactor: 2.369

The effect of video information on anxiety levels in women attending colposcopy: a randomized controlled trial

Ketelaars PJW, Buskes MHM, Bosgraaf RP, van Hamont D, Prins JB, Massuger LFAG, Melchers WJG, **Bekkers RLM***
Acta Oncol. 2017 Dec;56(12):1728-1733.Epub 2017 Aug 1

OBJECTIVE:

The aim was to investigate whether additional information, in video form, reduces anxiety, depression and pain levels in women referred for colposcopy.

MATERIAL AND METHODS:

Between September 2012 and March 2015, 136 patients referred for colposcopy were randomized into two study arms. Group A received video information in addition to the regular information leaflet, and group B (control group) received only the regular information leaflet. The patients were requested to complete standardized online questionnaires. The first online questionnaire (T1) was pre-randomization, and was completed at home, 5 days prior to the appointment. The second online questionnaire (T2) was completed directly before the colposcopy appointment, and the last online questionnaire (T3) was completed directly following colposcopy at the out-patient clinic. The questionnaires included the Spielberger State-Trait Anxiety Inventory (STAI), the Hospital Anxiety and Depression Scale (HADS), and the Numeric Rating Scale (NRS) to assess pain.

RESULTS:

The STAI state anxiety score was high (44.6), but there was no significant difference in STAI, HADS and NRS between the two groups at the three measuring points. A post hoc analysis showed that women with a generally higher baseline anxiety trait had significantly lower HADS anxiety levels following video information.

CONCLUSIONS:

Additional information (video) before colposcopy did not significantly reduce anxiety, depression, and expected or experienced pain, as measured by the STAI, HADS and NRS in patients attending their first colposcopy appointment. However, most patients positively appreciated the video information, which may reduce the anxiety of extremely anxious patients.

Ten tijde van publicatie verbonden aan: Department of Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen

Impactfactor: 3.156

The effectiveness of intrauterine insemination: A matched cohort study

Scholten I, **van Zijl M**, Custers IM, Brandes M, Gianotten J, van der Linden PJQ, Hompes PGA, van der Veen F, Mol BWJ

Eur J Obstet Gynecol Reprod Biol. 2017 May 212:91-95. Epub 2017 Mar 18

OBJECTIVE:

To study the effectiveness of an intrauterine insemination (IUI) program compared to no treatment in subfertile couples with unexplained subfertility and a poor prognosis on natural conception.

STUDY DESIGN:

A retrospective matched cohort study in which ongoing pregnancy rates in 72 couples who voluntarily dropped out of treatment with IUI were compared to ongoing pregnancy rates in 144 couples who continued treatment with IUI. Couples with unexplained subfertility, mild male subfertility or cervical factor subfertility who started treatment with IUI between January 2000 and December 2008 were included. Couples were matched on hospital, age, duration of subfertility, primary or secondary subfertility and diagnosis. Primary outcome was cumulative ongoing pregnancy rate after three years. Time to pregnancy was censored at the moment couples were lost to follow up or when their child wish ended and, for the no-treatment group, when couples re-started treatment.

RESULTS:

After three years, there were 18 pregnancies in the stopped treatment group (25%) versus 41 pregnancies in the IUI group (28%) (RR 1.1 (0.59-2.2)(p=0.4)). The cumulative pregnancy rate after three years was 40% in both groups, showing no difference in time to ongoing pregnancy (shared frailty model p=0.86).

CONCLUSIONS:

In couples with unexplained subfertility and a poor prognosis for natural conception, treatment with IUI does not to add to expectant management. There is need for a randomized clinical trial comparing IUI with expectant management in these couples.

Impactfactor: 1.666

The Paget Trial: A Multicenter, Observational Cohort Intervention Study for the Clinical Efficacy, Safety, and Immunological Response of Topical 5% Imiquimod Cream for Vulvar Paget Disease

van der Linden M, Meeuwis K, van Hees C, van Dorst E, Bulten J, Bosse T, IntHout J, **Boll D**, Slangen B, van Seters M, van Beurden M, van Poelgeest M, de Hullu J

JMIR Res Protoc. 2017 Sep 6;6(9):e178

BACKGROUND:

Vulvar Paget disease is a rare skin disorder, which is most common in postmenopausal Caucasian women. They usually present with an erythematous plaque that may show fine or typical "cake icing" scaling or ulceration that may cause itching, pain, irritation, or a burning sensation. Although most cases are noninvasive, vulvar Paget disease may be invasive or associated with an underlying vulvar or distant adenocarcinoma. The histological evidence of so-called "Paget cells" with abundant pale cytoplasm in the epithelium confirms the diagnosis. The origin of these Paget cells is still unclear. Treatment of choice is wide local excision with negative margins. Obtaining clear surgical margins is challenging and may lead to extensive and mutilating surgery. Even then, recurrence rates are high, ranging from 15% to 70%, which emphasizes the need for new treatment options. A number of case reports, retrospective case series, and one observational study have shown promising results using the topical immune response modifier imiquimod.

OBJECTIVE:

This study aims to investigate the efficacy, safety, and immunological response in patients with noninvasive vulvar Paget disease using a standardized treatment schedule with 5% imiquimod cream.

METHODS:

Topical 5% imiquimod cream might be an effective and safe treatment alternative for vulvar Paget disease. The Paget Trial is a multicenter observational cohort study including eight tertiary referral hospitals in the Netherlands. It is ethically approved by the Medical-Ethical Committee of Arnhem-Nijmegen and registered in the Central Committee on Research Involving Human Subjects (CCMO) Register by as NL51648.091.14. Twenty patients with (recurrent) noninvasive vulvar Paget disease will be treated with topical 5% imiquimod cream three times a week for 16 weeks. The primary efficacy outcome is the reduction in lesion size at 12 weeks after end of treatment. Secondary outcomes are safety, immunological response, and quality of life. Safety will be assessed by evaluation of adverse events and tolerability of treatment. To evaluate the immunological response, various immunological

markers will be tested on biopsy specimens taken before, during, and after treatment. Quality of life will be assessed with three questionnaires taken before, during, and after treatment.

Impactfactor: 5.175

The treatment of post-hysterectomy vaginal vault prolapse: a systematic review and meta-analysis

Coolen AW, Bui BN, **Dietz V**, Wang R, van Montfoort AP, Mol BW, Roovers JW, Bongers MY

Int Urogynecol J. 2017 Dec;28(12):1767-1783

INTRODUCTION AND HYPOTHESIS: The treatment of post-hysterectomy vaginal vault prolapse (VVP) has been investigated in several randomized clinical trials (RCTs), but a systematic review of the topic is still lacking. The aim of this study is to compare the effectiveness of treatments for VVP.

METHODS: We performed a systematic review and meta-analysis of the literature on the treatment of VVP found in PubMed and Embase. Reference lists of identified relevant articles were checked for additional articles. A network plot was constructed to illustrate the geometry of the network of the treatments included. Only RCTs reporting on the treatment of VVP were eligible, conditional on a minimum of 30 participants with VVP and a follow-up of at least 6 months.

RESULTS: Nine RCTs reporting 846 women (ranging from 95 to 168 women) met the inclusion criteria. All surgical techniques were associated with good subjective results, and without differences between the compared technique, with the exception of the comparison of vaginal mesh (VM) vs laparoscopic sacrocolpopexy (LSC). LSC is associated with a higher satisfaction rate. The anatomical results of the sacrocolpopexy (laparoscopic, robotic [RSC]. and abdominal [ASC]) are the best (62-91%), followed by the VM. However, the ranges of the anatomical outcome of VM were wide (43-97%). The poorest results are described for the sacrospinal fixation (SSF; 35-81%), which also correlates with the higher reoperation rate for pelvic organ prolapse (POP; 5-9%). The highest percentage of complications were reported after ASC (2-19%), VM (6-29%), and RSC (54%). Mesh exposure was seen most often after VM (8-21%). The rate of reoperations carried out because of complications, recurrence prolapse, and incontinence of VM was 13-22%. Overall, sacrocolpopexy reported the best results at follow-up, with an outlier of one trial reporting the highest reoperation rate for POP (11%). The results of the RSC are too small to make any conclusion, but LSC seems to be preferable to ASC.

CONCLUSIONS: A comparison of techniques was difficult because of heterogeneity; therefore, a network meta-analysis was not possible. All techniques have proved to be effective. The reported differences between the techniques were negligible. Therefore, a standard treatment for VVP could not be given according to this review.

Impactfactor: 1.937

Umbilical cord blood CD34(+) progenitor-derived NK cells efficiently kill ovarian cancer spheroids and intraperitoneal tumors in NOD/SCID/IL2Rg(null) mice

Hoogstad-van Evert JS, Cany J, van den Brand D, Oudenampsen M, Brock R, Torensma R, **Bekkers RL**, Jansen JH, Massuger LF, Dolstra H

Oncoimmunology. 2017 May 11;6(8):e1320630.eCollection 2017

Adoptive transfer of allogeneic natural killer (NK) cells is an attractive therapy approach against ovarian carcinoma. Here, we evaluated the potency of highly active NK cells derived from human CD34+ haematopoietic stem and progenitor cells (HSPC) to infiltrate and mediate killing of human ovarian cancer spheroids using an in vivo-like model system and mouse xenograft model. These CD56+Perforin+ HSPC-NK cells were generated under stroma-free conditions in the presence of StemRegenin-1, IL-15, and IL-12, and exerted efficient cytolytic activity and IFN? production toward ovarian cancer monolayer cultures. Live-imaging confocal microscopy demonstrated that these HSPC-NK cells actively migrate, infiltrate, and mediate tumor cell killing in a three-dimensional multicellular ovarian cancer spheroid. Infiltration of up to 30% of total HSPC-NK cells within 8 h resulted in robust tumor spheroid destruction. Furthermore, intraperitoneal HSPC-NK cell infusions in NOD/SCID-IL2R?null (NSG) mice bearing ovarian carcinoma significantly reduced tumor progression. These findings demonstrate that highly functional HSPC-NK cells efficiently destruct ovarian carcinoma spheroids in vitro and kill intraperitoneal ovarian tumors in vivo, providing great promise for effective immunotherapy through intraperitoneal HSPC-NK cell adoptive transfer in ovarian carcinoma patients.

Ten tijde van publicatie verbonden aan: Department of Obstetrics and Gynaecology, Radboud University Medical Center, Nijmegen

Impactfactor: 7.719

Uterine peristalsis and fertility: current knowledge and future perspectives: a review and meta-analysis
Kuijsters NPM, Methorst WG, Kortenhorst MSQ, Rabotti C, Mischi M, **Schoot BC**
Reprod Biomed Online. 2017 Jul 35(1):50-71. Epub 2017 Apr 12

Although uterine contractions in the non-pregnant uterus have been studied extensively, the knowledge gained has not been used in general fertility treatment work-up. In this review paper, we provide an overview of the current knowledge on uterine peristalsis (UP), based on the available literature. This literature shows that UP influences pregnancy chances in both natural and artificial cycles. Although the physiological background of these contractions is not completely clear, we know that several factors can be of influence, like uterine pathologies and hormones. Several options to alter pregnancy outcome by interfering with uterine contractions have been studied. Our meta-analysis on therapeutic options shows positive results of progesterone at time of embryo transfer in IVF cycles or prostaglandins at time of intrauterine insemination, although the quality of evidence is low. These therapies are probably most beneficial in selected groups of patients with abnormal contraction patterns. The introduction of an objective and user-friendly UP measuring tool suitable for use in daily practice would make it possible to identify and monitor these patients. We suggest that future research should focus on the physiology of initiation of UP and on the development of an effective standard measuring tool.

Impactfactor: 3.249

Volume-controlled versus short drainage after inguinofemoral lymphadenectomy in vulvar cancer patients: A Dutch nationwide prospective study
Pouwer AW, Hinten F, van der Velden J, Smolders RG, Slangen BF, Zijlmans HJ, IntHout J, van der Zee AG, **Boll D**, Gaarenstroom KN, Arts HJ, de Hullu JA
Gynecol Oncol. 2017 Sep;146(3):580-587

OBJECTIVE:
Inguinofemoral lymphadenectomy for patients with vulvar squamous cell carcinoma is associated with a high incidence of postoperative wound complications, which may be influenced by inguinal drain management. The aim of this nationwide prospective study (MAMBO: Morbidity And Measurement of the BOdy) was to assess the feasibility and the incidence of complications after volume-controlled versus short drainage.
METHODS:
The MAMBO study consisted of two observational studies in all eight oncology centers in the Netherlands, conducted between 2012 and 2016. In the first study, the drain was removed when the production was <30ml/24h, except in the first 48h, and after a maximum of 28days (MAMBO-IA). In the second study, the drain was removed five days postoperatively regardless of production (MAMBO-IB). We assessed the complications within eight weeks after surgery using logistic regression to compare the incidence of one or more complications between the two drainage protocols, adjusting for possible confounders.
RESULTS:
We included 77 patients (139 groins) for volume-controlled drainage and 64 patients (112 groins) for short drainage. Volume-controlled drainage was associated with significant less lymphocele formation. Moreover, we found no difference in wound infection or primary wound breakdown. The estimated incidence of one or more complications was 46% per groin after volume-controlled drainage versus 75% after short drainage, (RD 29% (95% CI 8, 49) p=0.006).
CONCLUSIONS:
This prospective study shows that volume-controlled drainage is associated with significantly less complications compared to short drainage. We therefore recommend volume-controlled drainage after inguinofemoral lymphadenectomy in patients with vulvar squamous cell carcinoma.

Impactfactor: 4.959

Which Factors Contribute to False-Positive, False-Negative, and Invalid Results in Fetal Fibronectin Testing in Women with Symptoms of Preterm Labor?
Bruijn MM, Hermans FJ, Vis JY, **Wilms FF**, Oudijk MA, Kwee A, Porath MM, Oei G, Scheepers HC, Spaanderman ME, Bloemenkamp KW, Haak MC, Bolte AC, Vandenbussche FP, Woiski MD, Bax CJ, Cornette JM, Duvekot JJ, Bijvank BW, van Eyck J, Franssen MT, Sollie KM, van der Post JA, Bossuyt PM, Kok M, Mol BW, van Baaren GJ
Am J Perinatol. 2017 Feb;34(3):234-239. Epub 2016 Jul 21

Objective We assessed the influence of external factors on false-positive, false-negative, and invalid fibronectin results in the prediction of spontaneous delivery within 7 days. Methods We studied

symptomatic women between 24 and 34 weeks' gestational age. We performed uni- and multivariable logistic regression to estimate the effect of external factors (vaginal soap, digital examination, transvaginal sonography, sexual intercourse, vaginal bleeding) on the risk of false-positive, false-negative, and invalid results, using spontaneous delivery within 7 days as the outcome. Results Out of 708 women, 237 (33%) had a false-positive result; none of the factors showed a significant association. Vaginal bleeding increased the proportion of positive fetal fibronectin (fFN) results, but was significantly associated with a lower risk of false-positive test results (odds ratio [OR], 0.22; 95% confidence intervals [CI], 0.12-0.39). Ten women (1%) had a false-negative result. None of the investigated factors was significantly associated with a significantly higher risk of false-negative results. Twenty-one tests (3%) were invalid; only vaginal bleeding showed a significant association (OR, 4.5; 95% CI, 1.7-12). Conclusion The effect of external factors on the performance of qualitative fFN testing is limited, with vaginal bleeding as the only factor that reduces its validity.

Impactfactor: 1.455

HACA

Talking about end-of-life care in a timely manner

Smeenk FW, Schrijver LA, **van Bavel HC**, van de Laar EF

Breathe 2017; 3(4): e95-e102

Geen abstract beschikbaar

Impactfactor: --

Intensive Care

Acenocoumarol as a risk factor for calciphylaxis: a feature clinicians should be aware of

Wenstedt EFE, Huysentruyt CJ, Konings CJAM

Neth J Med. 2017 May; 75(4):161-164

In contrast with uraemic calciphylaxis in end-stage renal disease, causes of and risk factors for non-uraemic calciphylaxis are relatively unknown to clinicians and have yet to become fully established. This report describes a case of non-uraemic calciphylaxis, in which the use of acenocoumarol might have been a risk factor. It is important to raise awareness about this association among clinicians, as vitamin K antagonists have to be stopped for an optimal treatment of this severe condition.

Impactfactor: 1.244

Current practice of closed-loop mechanical ventilation modes on intensive care units - a nationwide survey in the Netherlands

Wenstedt EFE, De Bie Dekker AJR, **Roos AN**, **Verberne JJM**, Korsten HHM, Schultz MJ, **Bindels AJGH**

Neth J Med. 2017 May; 75(4):145-150

BACKGROUND:
The most recent modes for mechanical ventilation are closed-loop modes, which are able to automatically adjust certain respiratory settings. Although closed-loop modes have been investigated in various clinical trials, it is unclear to what extent these modes are actually used in clinical practice. The aim of this study was to determine closed-loop ventilation practice on intensive care units (ICUs) in the Netherlands, and to explore reasons for not applying closed-loop ventilation. Our hypothesis was that closed-loop ventilation is increasingly used.
METHODS:
A short survey was conducted among all non-paediatric ICUs in the Netherlands. Use of closed-loop modes was classified as frequently, occasionally or never, if respondents stated they had used these modes in the last week, in the last month/year, or never, respectively.
RESULTS:
The response rate of the survey was 82% (72 of 88). Respondents had access to a closed-loop ventilation mode in 58% of the ICUs (42 of 72). Of these ICUs, 43% (18 of 42) frequently applied a closed-loop ventilation mode, while 57% (24 of 42) never or occasionally used it. Reasons for not using these modes were lack of knowledge (40%), insufficient evidence reporting a beneficial effect (35%) and lack of confidence (25%).
CONCLUSION:
This study does not support our hypothesis that closed-loop ventilation is increasingly used in the Dutch ICU setting. While industry continues to develop new closed-loop modes, implementation of these modes in clinical practice seems to encounter difficulties. Various barriers could play a role, and these all need attention in future investigation

Impactfactor: 1.244

Intelligent dynamic clinical checklists improved checklist compliance in the intensive care unit

De Bie AJ, **Nan S**, **Vermeulen LR**, Van Gorp PM, Bouwman RA, **Bindels AJ**, Korsten HH

Br J Anaesth. 2017 Aug 1;119(2):231-238

Background: Checklists can reduce medical errors. However, the effectiveness of checklists is hampered by lack of acceptance and compliance. Recently, a new type of checklist with dynamic properties has been created to provide more specific checklist items for each individual patient. Our purpose in this simulation-based study was to investigate a newly developed intelligent dynamic clinical checklist (DCC) for the intensive care unit (ICU) ward round.
Methods: Eligible clinicians were invited to participate as volunteers. Highest achievable scores were established for six typical ICU scenarios to determine which items must be checked. The participants 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 requiring a direct intervention.
Results: In total, 20 participants were included, who performed 116 scenarios. The median percentage of checked items was 100.0% with the DCC and 73.6% for the scenarios completed with local standard of care (P <0.001). Critical items remained unchecked in 23.1% of the scenarios performed with local standard of care and 0.0% of the scenarios where the DCC was available (P <0.001). The mean satisfaction score of the DCC was 4.13 out of 5.
Conclusions: This simulation study indicates that an intelligent DCC significantly increases compliance with best practice by reducing the percentage of unchecked items during ICU ward rounds, while the

user satisfaction rate remains high. Real-life clinical research is required to evaluate this new type of checklist further.

Impactfactor: 6.238

Notice of Retraction and Replacement: Oostdijk et al. Effects of Decontamination of the Oropharynx and Intestinal Tract on Antibiotic Resistance in ICUs: A Randomized Clinical Trial. JAMA. 2014;312(14):1429-1437

Oostdijk EA, Kesecioglu J, Schultz MJ, Visser CE, de Jonge E, van Essen EH, Bernards AT, Purmer I, Brimicombe R, Bergmans D, van Tiel F, Bosch FH, Mascini E, van Griethuysen A, **Bindels A**, Jansz A, van Steveninck FA, van der Zwet WC, Fijen JW, Thijsen S, de Jong R, Oudbier J, Raben A, van der Vorm E, Koeman M, Rothbarth P, Rijkeboer A, Gruteke P, Hart H, Peerbooms P, Winsser LJ, van Elsacker-Niele AW, Demmendaal K, Brandenburg A, de Smet AM, Bonten MJ

JAMA. 2017 Apr 18;317(15):1583-1584

Geen abstract beschikbaar

Impactfactor: 44.405

The Maastricht-Duke bridge: An era of mentoring in clinical research - A model for mentoring in clinical research - A tribute to Dr. Galen Wagner

Meijs L, Zusterzeel R, Wellens HJ, Gorgels AP

J Electrocardiol. 2017 Jan - Feb;50(1):16-20

OBJECTIVE:

With the passing of Dr. Galen Wagner, an exceptional collaboration between Maastricht University Medical Center, The Netherlands, and Duke Clinical Research Institute, USA, has come to an end. This article focuses on the background of what Galen coined the Maastricht-Duke bridge (MD-bridge), its merits, limitations and development throughout the years, and his special role.

METHODS:

Between 2004 and 2015, 23 Maastricht University medical students and post-graduate students were enrolled in the 4-month research elective, mentored by Galen and the Maastricht co-mentor. They were asked to complete a survey about their MD-bridge experience.

RESULTS:

Sixteen out of the 23 students responded. None but 1 participant had prior research experience. Following their MD bridge-program most participants published 1 or more manuscripts and/or presented their research in an international setting. They felt they had full responsibility as a leader of their project with all participants developing meaningful skills useful in their current job. Fourteen out of 16 would recommend the MD-bridge experience to others. Participants considered the program of great value for their personal growth and independence, giving a feeling of achievement. In addition, for some participants it led to careers in foreign countries including medical practice and research, or obtaining PhDs.

CONCLUSIONS:

With Galen's impressive career of mentoring students, including the 23 MD-bridge participants, he has left behind an amazing concept of self-development in research and personal life. The successes of the MD-bridge prove that it is possible for students to be young investigators during or just after medical school with the potential to contribute to developing meaningful skills and noteworthy careers. Collaborations between international universities, such as the MD-bridge, are feasible and should be embraced by other institutions.

Impactfactor: 1.514

Inwendige geneeskunde

Acenocoumarol as a risk factor for calciphylaxis: a feature clinicians should be aware of

Wenstedt EFE, Huysentruyt CJ, **Konings CJAM**

Neth J Med. 2017 May; 75(4):161-164

In contrast with uraemic calciphylaxis in end-stage renal disease, causes of and risk factors for non-uraemic calciphylaxis are relatively unknown to clinicians and have yet to become fully established. This report describes a case of non-uraemic calciphylaxis, in which the use of acenocoumarol might have been a risk factor. It is important to raise awareness about this association among clinicians, as vitamin K antagonists have to be stopped for an optimal treatment of this severe condition.

Impactfactor 1.244

Achieving high convection volumes in postdilution online hemodiafiltration: a prospective multicenter study

de Roij van Zuijdewijn CLM, Chapdelaine I, Nubé MJ, Blankestijn PJ, Bots ML, **Konings CJAM**, Kremer Hovinga TK, Molenaar FM, van der Weerd NC, Grooteman MPC

Clin Kidney J. 2017 Dec;10(6):804-812. Epub 2017 Feb 15

Background. Available evidence suggests a reduced mortality risk for patients treated with high-volume postdilution hemodiafiltration (HDF) when compared with hemodialysis (HD) patients. As the magnitude of the convection volume depends on treatment-related factors rather than patient-related characteristics, we prospectively investigated whether a high convection volume (defined as?=22?L/session) is feasible in the majority of patients (>75%). Methods. A multicenter study was performed in adult prevalent dialysis patients. Nonparticipating eligible patients formed the control group. Using a stepwise protocol, treatment time (up to 4?hours), blood flow rate (up to 400?mL/min) and filtration fraction (up to 33%) were optimized as much as possible. The convection volume was determined at the end of this optimization phase and at 4 and 8 weeks thereafter. Results. Baseline characteristics were comparable in participants (n?=?86) and controls (n?=?58). At the end of the optimization and 8 weeks thereafter, 71/86 (83%) and 66/83 (80%) of the patients achieved high-volume HDF (mean 25.5?±?3.6 and 26.0?±?3.4?L/session, respectively). While treatment time remained unaltered, mean blood flow rate increased by 27% and filtration fraction increased by 23%. Patients with?<22?L/session had a higher percentage of central venous catheters (CVCs), a shorter treatment time and lower blood flow rate when compared with patients with?=22?L/session. Conclusions. High-volume HDF is feasible in a clear majority of dialysis patients. Since none of the patients agreed to increase treatment time, these findings indicate that high-volume HDF is feasible just by increasing blood flow rate and filtration fraction.

Impactfactor --

Axillary staging in breast cancer patients treated with neoadjuvant chemotherapy in two Dutch phase III studies

Vriens BEPJ, Keymeulen KBMI, Kroep JR, Charehbili A, Peer PG, de Boer M, Aarts MJB, Heuts EM, Tjan-Heijnen VCG; Dutch Breast Cancer Research Group (BOOG)

Oncotarget. 2017 Jul 11;8(28):46557-46564

BACKGROUND:

Primary aim of our study was to assess the impact of timing of sentinel node procedure, pre- versus post-neoadjuvant chemotherapy, on final pathologic node-negative rate (pN0) in patients with clinically node-negative (cN0) breast cancer. Secondary endpoint was the usability of the sentinel node procedure in patients with clinically node-positive disease that converted to cN0 after neoadjuvant chemotherapy.

PATIENTS AND METHODS:

Patients were enrolled in two sequentially conducted Dutch phase III trials, studying the impact of two neoadjuvant chemotherapy schedules and use of zoledronic acid on complete pathologic response rate. For the present analyses, patients were excluded if they had not undergone surgical axillary staging.

RESULTS:

In total 439 patients were included, of whom 230 (52%) had pre-treatment cN0. In this group, pN0 status was seen in 58% (N = 23) of patients with a sentinel node biopsy post-neoadjuvant chemotherapy compared to 51% (N = 83) pre-neoadjuvant chemotherapy, including the axillary lymph node dissection whenever performed. In multivariable analysis, timing of sentinel node procedure (pre- versus post-neoadjuvant chemotherapy) was, however, not significantly associated with final pN0/pN0(i+) status, with an odds ratio of 1.18 (95% CI 0.64 - 2.18) after correction for age, clinical tumor status, histology,

grade, hormone- and HER2 receptor. Of patients with clinically node-positive disease only 15% had a final pN0 status, with a false-negative rate of the sentinel node of 30%.

CONCLUSION:

In breast cancer patients with cN0 disease, sentinel node procedure performed post-neoadjuvant chemotherapy led to nodal down staging, although not statistically significant after multivariate correction for patient and tumor characteristics.

Impactfactor 5.168

Cost-effectiveness of capecitabine and bevacizumab maintenance treatment after first-line induction treatment in metastatic colorectal cancer

Franken MD, van Rooijen EM, May AM, Koffijberg H, van Tinteren H, Mol L, Ten Tije AJ, **Creemers GJ**, van der Velden AMT, Tanis BC, Uyl-de Groot CA, Punt CJA, Koopman M, van Oijen MGH

Eur J Cancer. 2017 Apr 75:204-212. Epub 2017 Feb 24

AIM:

Capecitabine and bevacizumab (CAP-B) maintenance therapy has shown to be more effective compared with observation in metastatic colorectal cancer patients achieving stable disease or better after six cycles of first-line capecitabine, oxaliplatin, bevacizumab treatment in terms of progression-free survival. We evaluated the cost-effectiveness of CAP-B maintenance treatment.

METHODS:

Decision analysis with Markov modelling to evaluate the cost-effectiveness of CAP-B maintenance compared with observation was performed based on CAIRO3 study results (n = 558). An additional analysis was performed in patients with complete or partial response. The primary outcomes were the incremental cost-effectiveness ratio (ICER) defined as the additional cost per life year (LY) and quality-adjusted life years (QALY) gained, calculated from EQ-5D questionnaires and literature and LYs gained. Univariable sensitivity analysis was performed to assess the influence of input parameters on the ICER, and a probabilistic sensitivity analysis represents uncertainty in model parameters.

RESULTS:

CAP-B maintenance compared with observation resulted in 0.21 QALYs (0.18LYs) gained at a mean cost increase of €36,845, yielding an ICER of €175,452 per QALY (€204,694 per LY). Varying the difference in health-related quality of life between CAP-B maintenance and observation influenced the ICER most. For patients achieving complete or partial response on capecitabine, oxaliplatin, bevacizumab induction treatment, an ICER of €149,300 per QALY was calculated.

CONCLUSION:

CAP-B maintenance results in improved health outcomes measured in QALYs and LYs compared with observation, but also in a relevant increase in costs. Despite the fact that there is no consensus on cost-effectiveness thresholds in cancer treatment, CAP-B maintenance may not be considered cost-effective.

Impactfactor 6.029

Crisis checklists for in-hospital emergencies: expert consensus, simulation testing and recommendations for a template determined by a multi-institutional and multi-disciplinary learning collaborative

Subbe CP, Kellett J, Barach P, Chaloner C, Cleaver H, Cooksley T, Korsten E, Croke E, Davis E, **De Bie AJ**, Durham L, Hancock C, Hartin J, Savijn T, Welch J. Crisis Checklist Collaborative

BMC Health Serv Res. 2017 May 8; 17(1):334

BACKGROUND:

'Failure to rescue' of hospitalized patients with deteriorating physiology on general wards is caused by a complex array of organisational, technical and cultural failures including a lack of standardized team and individual expected responses and actions. The aim of this study using a learning collaborative method was to develop consensus recomendations on the utility and effectiveness of checklists as training and operational tools to assist in improving the skills of general ward staff on the effective rescue of patients with abnormal physiology.

METHODS:

A scoping study of the literature was followed by a multi-institutional and multi-disciplinary international learning collaborative. We sought to achieve a consensus on procedures and clinical simulation technology to determine the requirements, develop and test a safe using a checklist template that is rapidly accessible to assist in emergency management of common events for general ward use.

RESULTS:

Safety considerations about deteriorating patients were agreed upon and summarized. A consensus was

achieved among an international group of experts on currently available checklist formats performing poorly in simulation testing as first responders in general ward clinical crises. The Crisis Checklist Collaborative ratified a consensus template for a general ward checklist that provides a list of issues for first responders to address (i.e. 'Check In'), a list of prompts regarding common omissions (i.e. 'Stop & Think'), and, a list of items required for the safe "handover" of patients that remain on the general ward (i.e. 'Check Out'). Simulation usability assessment of the template demonstrated feasibility for clinical management of deteriorating patients.

CONCLUSIONS:

Emergency checklists custom-designed for general ward patients have the potential to guide the treatment speed and reliability of responses for emergency management of patients with abnormal physiology while minimizing the risk of adverse events. Interventional trials are needed.

Impactfactor 1.827

Current practice of closed-loop mechanical ventilation modes on intensive care units - a nationwide survey in the Netherlands

Wenstedt EFE, **De Bie Dekker AJR**, Roos AN, Verberne JJM, Korsten HHM, Schultz MJ, Bindels AJGH

Neth J Med. 2017 May; 75(4):145-150

BACKGROUND:

The most recent modes for mechanical ventilation are closed-loop modes, which are able to automatically adjust certain respiratory settings. Although closed-loop modes have been investigated in various clinical trials, it is unclear to what extent these modes are actually used in clinical practice. The aim of this study was to determine closed-loop ventilation practice on intensive care units (ICUs) in the Netherlands, and to explore reasons for not applying closed-loop ventilation. Our hypothesis was that closed-loop ventilation is increasingly used.

METHODS:

A short survey was conducted among all non-paediatric ICUs in the Netherlands. Use of closed-loop modes was classified as frequently, occasionally or never, if respondents stated they had used these modes in the last week, in the last month/year, or never, respectively.

RESULTS:

The response rate of the survey was 82% (72 of 88). Respondents had access to a closed-loop ventilation mode in 58% of the ICUs (42 of 72). Of these ICUs, 43% (18 of 42) frequently applied a closed-loop ventilation mode, while 57% (24 of 42) never or occasionally used it. Reasons for not using these modes were lack of knowledge (40%), insufficient evidence reporting a beneficial effect (35%) and lack of confidence (25%).

CONCLUSION:

This study does not support our hypothesis that closed-loop ventilation is increasingly used in the Dutch ICU setting. While industry continues to develop new closed-loop modes, implementation of these modes in clinical practice seems to encounter difficulties. Various barriers could play a role, and these all need attention in future investigate

Impactfactor 1.244

Double-Balloon Endoscopy in Overt and Occult Small Bowel Bleeding: Results, Complications, and Correlation with Prior Videocapsule Endoscopy in a Tertiary Referral Center

Hermans C, Stronkhorst A, Tjhie-Wensing A, Kamphuis J, Balkom BV, Dahlmans R, Gilissen L

Clin Endosc. 2017 Jan 50(1):69-75. Epub 2017 Jan 12

BACKGROUND/AIMS:

Videocapsule endoscopy (VCE) and double-balloon endoscopy (DBE) allow deep exploration in patients with suspected small bowel pathology. VCE is often performed as an initial small bowel examination to explore whether an intervention by DBE is indicated and to determine insertion route. The study aim was to evaluate the correlation between DBE and VCE in patients with obscure or overt bleeding or anemia, as well as intervention frequency, and complications.

METHODS:

Retrospective observational study.

RESULTS:

DBE procedures (n=205) showed small bowel lesions in 64% cases. Antegrade DBE showed positive results in 79% cases, mostly angiodysplasias (63%). Retrograde DBE showed positive results in 22% cases. An intervention was performed in 64% of DBE procedures. The major complication rate was 0.5%,

which was one case of perforation. Pancreatitis did not occur. The overall diagnostic agreement was 66% among the 134 DBEs with preceded VCE.

CONCLUSIONS:

In cases of overt or occult bleeding or anemia, DBE was positive in 64%, with only a few complications. Positive correlation was 66% among initially performed VCEs and DBEs. Owing to the time-consuming and invasive character of DBE, performing VCE before DBE might still be clinically relevant.

Impactfactor: --

Dynamics of Nutritional Competence in the Last Year Before Death in a Large Cohort of US Hemodialysis Patients

Ye X, Dekker MJ, Maddux FW, Kotanko P, **Konings CJ**, Raimann JG, van der Sande FM, Usvyat LA, Kooman JP, Thijssen S

J Ren Nutr. 2017 Nov;27(6):412-420

OBJECTIVES: Recently, a new Nutritional Competence Score (NCS) has been shown to associate with hospitalization and outcome in hemodialysis patients. The aim of this study was to investigate the dynamics, the individual components, and the impact of hospitalizations of this score's trajectory in the year before death. In addition, we investigated whether dynamics in the NCS add additional independent prognostic value over a single cross-sectional assessment.

DESIGN: We included all Fresenius Medical Care North America patients who initiated hemodialysis between January 1, 2006, and December 31, 2011 with data on all 5 NCS components (serum albumin, creatinine, phosphate, equilibrated normalized protein catabolic rate, and interdialytic weight gain) in at least 1 month. NCS was quantified monthly, and trajectories were compared between nonsurvivors and survivors across different dialysis vintage strata. Survivors and nonsurvivors were matched by dialysis vintage. The association of baseline NCS and NCS dynamics with mortality risk were assessed with Cox proportional hazards models.

RESULTS: In this cohort of 110,794 patients, we found that across all vintage groups, NCS was lower in patients who died than in survivors. NCS was found to significantly decline before death, whereas survivors showed no decline in NCS. The rate of NCS decline before death was not materially influenced by hospitalization in the months before death. Cox models showed that NCS dynamics over time carry significant predictive power above a cross-sectional NCS assessment.

CONCLUSIONS:

There are distinct differences in NCS values and their trajectories between patients who die and vintage-matched controls. These differences may be able to be exploited for implementation of a routine, prospective monitoring tool for early detection of patients at increased risk of death. Prospective studies are required to validate such an approach.

Impactfactor: *2.318*

Efficient organisation of intensive care units with a focus on quality: the non-physician provider

Kreeftenberg HG, Pouwels S, van der Voort PH

Crit Care. 2017 Jul 27;21(1):118

Geen abstract beschikbaar

Impactfactor: *5.358*

Familial longevity is characterized by high circadian rhythmicity of serum cholesterol in healthy elderly individuals

Rosa van den Berg, Raymond Noordam, Sander Kooijman, **Steffy W. M. Jansen**, Abimbola A. Akintola, P. Eline Slagboom, Hanno Pijl, Patrick C. N. Rensen, Nienke R. Biermasz, Diana van Heemst

Aging Cell. 2017 Apr;16(2):237-243. doi: Epub 2016 Nov 19

The biological clock, whose function deteriorates with increasing age, determines bodily circadian (i.e. 24h) rhythms, including that of cholesterol metabolism. Dampening of circadian rhythms has been associated with aging and disease. Therefore, we hypothesized that individuals with a familial predisposition for longevity have a higher amplitude circadian serum cholesterol concentration rhythm. The aim of this study was to investigate circadian rhythmicity of serum cholesterol concentrations in offspring of nonagenarian siblings and their partners. Offspring from nonagenarian siblings (n = 19), and their partners as controls (n = 18), were recruited from the Leiden Longevity Study. Participants (mean age 65 years) were studied in a controlled in-hospital setting over a 24-h period, receiving three isocaloric meals at 9:00 h, 12:00 h and 18:00 h. Lights were off between 23:00 h and 8:00 h. Serum total

cholesterol (TC), HDL cholesterol (HDL-C), non-HDL-C and triglycerides (TG) were determined every 30 min over a 24-h period. Serum TC concentrations were higher during day than during night in offspring (5.2 vs. 4.7 mm, P < 0.001) and in controls (5.3 vs. 5.0 mm, P < 0.001). The difference in TC concentrations between day and night tended to be greater in offspring than in controls (0.5 vs. 0.3 mm, P = 0.109), reaching statistical significance in females (P = 0.045). Notably, the day–night serum differences in non-HDL-C were twofold greater in offspring than in controls (0.43 vs. 0.21 mm, P = 0.044) and most explicit in females (0.53 vs. 0.22, P = 0.078). We conclude that familial longevity is characterized by a high circadian rhythmicity of non-HDL-C in healthy elderly offspring from nonagenarian siblings.

Ten tijde van publicatie verbonden aan: Section Gerontology and Geriatrics, Department of Internal Medicine, Leiden University Medical Center, Leiden
Impactfactor: 6.714

From intention to STI prevention: An online questionnaire on barriers and facilitators for discussing sexual risk behaviour among HIV nurses

de Munnik S, Vervoort SC, **Ammerlaan HS**, Kok G, den Daas C

J Adv Nurs. 2017 Dec;73(12):2953-2961

AIMS:
We aimed to elucidate facilitators and barriers that HIV nurses experience in discussing sexual risk behaviour with HIV-positive men who have sex with men, using variables from a previous qualitative study and the theory of planned behaviour.
BACKGROUND:
HIV-positive men who have sex with men are frequently diagnosed with sexually transmitted infections, which can be reduced if HIV nurses discuss sexual risk behaviour.
DESIGN:
An online questionnaire was disseminated in April 2015 among all HIV nurses in the Netherlands.
METHODS:
We assessed variables, such as attitudes, shame, ability, knowledge and time concerns. A regression analysis was conducted with "intention to discuss sexual risk behaviour" as an outcome variable.
RESULTS:
The questionnaire was completed by 60 of 79 HIV nurses. Overall, participants reported high intentions to discuss sexual risk behaviour, and 38% of the variance was explained by attitude, sexual preference, knowing ways to introduce the topic and experiencing enough time or viewing it as a priority. In addition, high intenders significantly differed from low intenders in "experienced shame," "relation with patients," "non-verbal communication," "subjective norm" and "knowledge."
CONCLUSION:
Improving sexual health in HIV care translates into improving opportunities and the facilitating factors in initiating the discussion of sexual risk behaviour rather than removing barriers HIV nurses experience. Interventions should mainly focus on improving the HIV nurses' perceived ability to initiate the topic of sexual risk behaviour and to utilize the jargon and terminology that is commonly used among men who have sex with men.

Impactfactor: 1.998

Impact of fluid status and inflammation and their interaction on survival: a study in an international hemodialysis patient cohort

Dekker MJ, Marcelli D, Canaud BJ, Carioni P, Wang Y, Grassmann A, **Konings CJ**, Kotanko P, Leunissen KM, Levin NW, van der Sande FM, Ye X, Maheshwari V, Usvyat LA, Kooman JP; MONDO Initiative

Kidney Int. 2017 May;91(5):1214-1223

In hemodialysis patients extracellular fluid overload is a predictor of all-cause and cardiovascular mortality, and a relation with inflammation has been reported in previous studies. The magnitude and nature of this interaction and the effects of moderate fluid overload and extracellular fluid depletion on survival are still unclear. We present the results of an international cohort study in 8883 hemodialysis patients from the European MONDO initiative database where, during a three-month baseline period, fluid status was assessed using bioimpedance and inflammation by C-reactive protein. All-cause mortality was recorded during 12 months of follow up. In a second analysis a three-month baseline period was added to the first baseline period, and changes in fluid and inflammation status were related to all-cause mortality during six-month follow up. Both pre-dialysis estimated fluid overload and fluid

depletion were associated with an increased mortality, already apparent at moderate levels of estimated pre-dialysis fluid overload (1.1-2.5L); hazard ratio 1.64 (95% confidence interval 1.35-1.98). In contrast, post-dialysis estimated fluid depletion was associated with a survival benefit (0.74 [0.62-0.90]). The concurrent presence of fluid overload and inflammation was associated with the highest risk of death. Thus, while pre-dialysis fluid overload was associated with inflammation, even in the absence of inflammation, fluid overload remained a significant risk factor for short-term mortality, even following improvement of fluid status.

Impactfactor: 8.395

Improved survival for sequentially as opposed to concurrently delivered neoadjuvant chemotherapy in non-metastatic breast cancer

Vriens BEPJ, Vriens IJH, Aarts MJB, van Gastel SM, van den Berkmortel FWPJ, Smilde TJ, **van Warmerdam LJC**, van Spronsen DJ, Peer PGM, de Boer M, Tjan-Heijnen VCG; Breast Cancer Trialists' Group of the Netherlands (BOOG).Breast Cancer Res Treat. 2017 Oct;165(3):593-600. Epub 2017 Jul 3

PURPOSE:

The INTENS study was designed to determine whether delivering neoadjuvant chemotherapy at a higher dose in a shorter period of time improves outcome of breast cancer patients.

METHODS:

Women with newly diagnosed breast cancer were randomly assigned to neoadjuvant chemotherapy consisting of four cycles of doxorubicin and cyclophosphamide followed by four cycles of docetaxel (AC 60/600-T 100 mg/m2) or six cycles of TAC as triplet chemotherapy (75/50/500 mg/m2) every 3 weeks. The primary outcome was the pathologic complete response (pCR), with disease-free and overall survival as secondary endpoints.

RESULTS:

In total, 201 patients were included. The pCR rates were 28% for patients treated with AC-T and 19% for patients treated with TAC, with an odds ratio of 1.60 (95% CI 0.90-3.21). With a median follow-up of 6 years (range 0.04-8.41 years), the five-year disease-free survival was 81% for patients treated with sequentially AC-T and 71% for patients treated with concurrent triplet TAC chemotherapy with a stratified hazard ratio (HR) of 0.50 (95% CI 0.29-0.86). Five-year overall survival was 84% versus 76%, respectively, with a stratified HR of 0.55 (95% CI 0.29-1.03).

CONCLUSIONS:

No differences were observed between the two treatment arms with respect to pCR rate, but the sequentially delivered chemotherapy outperformed the triplet combination chemotherapy in terms of survival, despite a lower cumulative dose per agent. GOV nr NCT00314977.

Impactfactor: 3.626

Inflammation and premature aging in advanced chronic kidney disease

Kooman JP, **Dekker MJ**, Usvyat LA, Kotanko P, van der Sande FM, Schalkwijk CG, Shiels PG, Stenvinkel P

Am J Physiol Renal Physiol. 2017 Oct 1;313(4):F938-F950. Epub 2017 Jul 12

Systemic inflammation in end-stage renal disease is an established risk factor for mortality and a catalyst for other complications, which are related to a premature aging phenotype, including muscle wasting, vascular calcification, and other forms of premature vascular disease, depression, osteoporosis, and frailty. Uremic inflammation is also mechanistically related to mechanisms involved in the aging process, such as telomere shortening, mitochondrial dysfunction, and altered nutrient sensing, which can have a direct effect on cellular and tissue function. In addition to uremia-specific causes, such as abnormalities in the phosphate-Klotho axis, there are remarkable similarities between the pathophysiology of uremic inflammation and so-called "inflammaging" in the general population. Potentially relevant, but still somewhat unexplored in this respect, are abnormal or misplaced protein structures, as well as abnormalities in tissue homeostasis, which evoke danger signals through damage-associated molecular patterns, as well as the senescence-associated secretory phenotype. Systemic inflammation, in combination with the loss of kidney function, can impair the resilience of the body to external and internal stressors by reduced functional and structural tissue reserves, and by impairing normal organ crosstalk, thus providing an explanation for the greatly increased risk of homeostatic breakdown in this population. In this review, the relationship between uremic inflammation and a premature aging phenotype, as well as potential causes and consequences, are discussed.

Impactfactor: 3.611

Intelligent dynamic clinical checklists improved checklist compliance in the intensive care unit

De Bie AJ, Nan S, Vermeulen LR, Van Gorp PM, Bouwman RA, Bindels AJ, Korsten HH

Br J Anaesth. 2017 Aug 1;119(2):231-238

Background: Checklists can reduce medical errors. However, the effectiveness of checklists is hampered by lack of acceptance and compliance. Recently, a new type of checklist with dynamic properties has been created to provide more specific checklist items for each individual patient. Our purpose in this simulation-based study was to investigate a newly developed intelligent dynamic clinical checklist (DCC) for the intensive care unit (ICU) ward round.

Methods: Eligible clinicians were invited to participate as volunteers. Highest achievable scores were established for six typical ICU scenarios to determine which items must be checked. The participants 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 requiring a direct intervention.

Results: In total, 20 participants were included, who performed 116 scenarios. The median percentage of checked items was 100.0% with the DCC and 73.6% for the scenarios completed with local standard of care (P <0.001). Critical items remained unchecked in 23.1% of the scenarios performed with local standard of care and 0.0% of the scenarios where the DCC was available (P <0.001). The mean satisfaction score of the DCC was 4.13 out of 5.

Conclusions: This simulation study indicates that an intelligent DCC significantly increases compliance with best practice by reducing the percentage of unchecked items during ICU ward rounds, while the user satisfaction rate remains high. Real-life clinical research is required to evaluate this new type of checklist further.

Impactfactor: 6.238

Let's talk about sex: A qualitative study exploring the experiences of HIV nurses when discussing sexual risk behaviours with HIV-positive men who have sex with men

de Munnik S, den Daas C, **Ammerlaan HS**, Kok G, Raethke MS, Vervoort SC

Int J Nurs Stud. 2017 Sep 6;76:55-61

BACKGROUND:

Despite prevention efforts, the incidence of sexually transmitted infection among HIV-positive men who have sex with men remains high, which is indicative of unchanged sexual risk behaviour. Discussing sexual risk behaviour has been shown to help prevent sexually transmitted infections among HIV-positive men who have sex with men.

OBJECTIVES: The aim of this study was to identify factors that influence whether - and how - specialised HIV nurses discuss sexual risk behaviour with HIV-positive men who have sex with men. Identifying these factors could indicate how best to improve the frequency and quality of discussions about sexual risk behaviour, thereby reducing sexual risk behaviour and sexually transmitted infections.

DESIGN: Qualitative study, focus groups among HIV nurses.

SETTING: Dutch HIV treatment centres.

PARTICIPANTS:

A purposive sample was taken of 25 out of 87 HIV nurses working in one of the 26 specialised HIV treatment centres in the Netherlands. Of the 25 HIV nurses we approached, 22 participate in our study.

METHODS: Three semi-structured focus group interviews were held with 22 HIV nurses from 17 hospitals. Interviews were transcribed verbatim, and thematic analysis was performed.

RESULTS: HIV nurses agreed that discussing sexual risk behaviour is important, but barriers were experienced in relation to doing so. In accordance with the theory of planned behaviour, attitudes, perceived norms and perceived behavioural control were all found to be relevant variables. Barriers to discussing sexual risk behaviour were identified as: dealing with embarrassment, the changing professional role of an HIV nurse, time constraints, and the structure of the consultation.

CONCLUSIONS: To improve the frequency and quality of discussions about sexual risk behaviour with HIV-positive men who have sex with men, our data suggests it would be beneficial to support HIV nurses by developing tools and guidelines addressing what to discuss and how. Using a related topic as a conversational 'bridge' may help nurses to broach this subject with their patients. This would allow HIV nurses to discuss possible risk reduction strategies, such as pre-exposure prophylaxis for HIV-negative partners, condom use, strategic positioning, or sero-sorting.

Impactfactor: 3.755

Lymphoma InterVEntion (LIVE) - patient-reported outcome feedback and a web-based self-management intervention for patients with lymphoma: study protocol for a randomised controlled trial

Arts LPJ, van de Poll-Franse LV, van den Berg SW, Prins JB, Husson O, Mols F, **Brands-Nijenhuis AVM**, Tick L, Oerlemans S

Trials. 2017 Apr 28 18(1):199. doi: 10.1186/s13063-017-1943-2

BACKGROUND:

Patients with lymphoma are at risk of experiencing adverse physical and psychosocial problems from their cancer and its treatment. Regular screening of these symptoms by the use of patient-reported outcomes (PROs) could increase timely recognition and adequate symptom management. Moreover, self-management interventions intend to enhance knowledge and skills and empower patients to better manage their disease and related problems. The objective of the Lymphoma InterVEntion (LIVE) trial is to examine whether feedback to patients on their PROs and access to a web-based, self-management intervention named Living with lymphoma will increase self-management skills and satisfaction with information, and reduce psychological distress.

METHODS/DESIGN:

The LIVE randomised controlled trial consists of three arms: (1) standard care, (2) PRO feedback, and (3) PRO feedback and the Living with lymphoma intervention. Patients who have been diagnosed with Hodgkin lymphoma, non-Hodgkin lymphoma, including chronic lymphocytic leukaemia, as registered in the Netherlands Cancer Registry in various hospitals will be selected for participation. Patients are invited via their haemato-oncologist 6 to 15 months after diagnosis. The PRO feedback includes a graphical overview of patients' own symptom and functioning scores and an option to compare their scores with those of other patients with lymphoma and a normative population of the same age and sex. The Living with lymphoma intervention is based on cognitive behavioural therapy components and includes information, assignments, assessments, and videos. Changes in outcomes from baseline to 16 weeks, 12, and 24 months post intervention will be measured. Primary outcomes are self-management skills, satisfaction with information, and psychological distress. Secondary outcomes are health-related quality of life, illness perceptions, fatigue, and health care use.

DISCUSSION/DESIGN:

The results of the LIVE trial will provide novel insights into whether access to PRO feedback and the Living with lymphoma intervention will be effective in increasing self-management skills and satisfaction with information, and reducing distress. The LIVE trial is embedded in a population-based registry, which provides a unique setting to ascertain information on response, uptake, and characteristics of patients with lymphoma in web-based intervention(s). When effective, PRO feedback and Living with lymphoma could serve as easily and widely accessible interventions for coping with lymphoma.

Impactfactor: 1.969

Maintenance treatment with capecitabine and bevacizumab versus observation in metastatic colorectal cancer: updated results and molecular subgroup analyses of the phase 3 CAIRO3 study

Goey KK, Elias SG, van Tinteren H, Laclé MM, Willems SM, Offerhaus GJ, de Leng WW, Strengman E, Ten Tije AJ, **Creemers GM**, van der Velden A, de Jongh FE, Erdkamp FL, Tanis BC, Punt CJ, Koopman M

Ann Oncol. 2017 Sep 1;28(9):2128-2134

Background: The phase 3 CAIRO3 study showed that capecitabine plus bevacizumab (CAP-B) maintenance treatment after six cycles capecitabine, oxaliplatin, and bevacizumab (CAPOX-B) in metastatic colorectal cancer (mCRC) patients is effective, without compromising quality of life. In this post hoc analysis with updated follow-up and data regarding sidedness, we defined subgroups according to RAS/BRAF mutation status and mismatch repair (MMR) status, and investigated their influence on treatment efficacy.

Patients and methods: A total of 558 patients with previously untreated mCRC and stable disease or better after six cycles CAPOX-B induction treatment were randomised to either CAP-B maintenance treatment (n?=?279) or observation (n?=?279). Upon first progression, patients were to receive CAPOX-B reintroduction until second progression (PFS2, primary end point). We centrally assessed RAS/BRAF mutation status and MMR status, or used local results if central assessment was not possible. Intention-to-treat stratified Cox models adjusted for baseline covariables were used to examine whether treatment efficacy was modified by RAS/BRAF mutation status.

Results: RAS, BRAF mutations, and MMR deficiency were detected in 240/420 (58%), 36/381 (9%), and 4/279 (1%) patients, respectively. At a median follow-up of 87?months (IQR 69-97), all mutational subgroups showed significant improvement from maintenance treatment for the primary end point PFS2

[RAS/BRAF wild-type: hazard ratio (HR) 0.57 (95% CI 0.39-0.84); RAS-mutant: HR 0.74 (0.55-0.98); V600EBRAF-mutant: HR 0.28 (0.12-0.64)] and secondary end points, except for the RAS-mutant subgroup regarding overall survival. Adjustment for sidedness instead of primary tumour location yielded comparable results. Although right-sided tumours were associated with inferior prognosis, both patients with right- and left-sided tumours showed significant benefit from maintenance treatment. Conclusions: CAP-B maintenance treatment after six cycles CAPOX-B is effective in first-line treatment of mCRC across all mutational subgroups. The benefit of maintenance treatment was most pronounced in patients with RAS/BRAF wild-type and V600EBRAF-mutant tumours.

Impactfactor: 11.855

Naar een optimaal beheer van medicatie bij nierpatiënten : zelf doen waar het kan, overnemen waar het moet

Kerskes MC, **Hengst M**

Pil 2017 (4):34-6.

Nierpatiënten zijn kwetsbare patiënten. In deze groep zien we veel multimorbiditeit, meerdere behandelaren en polyfarmacie. In de praktijk blijkt de medicatiebewaking bij deze groep patiënten vaak suboptimaal te zijn door het ontbreken van relevante informatie (zoals nierfunctie of dialysevorm) en hun actuele medicatiegebruik. Tevens blijkt dat niet alle nierpatiënten even therapietrouw zijn. Het Catharina Ziekenhuis in Eindhoven heeft samen met de Nierstichting, Nierpatiëntenvereniging en het Instituut voor Verantwoord Medicijngebruik een checklist ontwikkeld, waarmee het medicatiebeheer van nierpatiënten gestructureerd in kaart kan worden gebracht en mogelijkheden voor verbetering worden aangedragen.

Impactfactor: --

Neutrophil Recovery in Breast Cancer Patients Receiving Docetaxel-Containing Chemotherapy with and without Granulocyte Colony-Stimulating Factor Prophylaxis

Aarts MJ, **Vriens BE**, de Boer M, Peters FP, Mandigers CM, Dercksen MW, Stouthard JM, Tol J, **van Warmerdam LJ**, van de Wouw AJ, Jacobs EM, van der Rijt CCD, Smilde TJ, van der Velden AW, Peer N, Tjan-Heijnen VCG

Oncology. 2017 ;93(5):323-8

OBJECTIVE:

The primary outcome of the current study is, whether there is a protective effect of prior chemotherapy or of prior granulocyte colony-stimulating factor (G-CSF) on the next cycle blood cell counts.

METHODS:

Hematologic toxicity was evaluated, based on a randomized phase III study in breast cancer patients (n = 167) with >20% risk of febrile neutropenia. The primary endpoint was the nadir blood cell counts for patients treated with G-CSF given during all 6 chemotherapy cycles or limited to the first 2 chemotherapy cycles only.

RESULTS:

For the present analyses, 47 patients were eligible. In the G-CSF 1-6 arm, the median white blood cell count (WBC) and absolute neutrophil count (ANC) nadir slowly decreased from 10.8 × 109/L in cycle 1 to 7.5 × 109/L in cycle 6 and from 7.1 × 109/L to 5.5 × 109/L, respectively. The median WBC nadir in the G-CSF 1-2 arm decreased from 1.2 × 109/L in cycle 3 to 0.9 × 109/L in cycle 6 and the ANC nadir showed a grade 4 neutropenia of 0.1 × 109/L in cycles 3-6. All patients had ANC recovery to normal levels (=1.5 × 109/L) without delay on day 1 of the next cycle.

CONCLUSION:

We conclude that there is no protective effect of prior G-CSF or prior chemotherapy use on nadir blood cell counts in subsequent cycles.

Impactfactor: 2.262

Pharmacogenetic analysis of irreversible severe cisplatin-induced nephropathy: a case report of a 27-year-old woman

de Jong C, Sanders S, **Creemers GJ**, Burylo AM, Taks M, Schellens JH, Deenen MJ

Br J Clin Pharmacol. 2017 Sep;83(9):2120-2122

In this report we describe a young patient diagnosed with bulky FIGO stage IIIb squamous cell cervix carcinoma with severe and irreversible nephropathy after three weekly low-doses of cisplatin. Besides several known risk factors such as hypomagnesemia and hypoalbuminemia, the patient also proved to be homozygously polymorphic for two polymorphisms within the COMT gene (c.615 + 310C>T and

c.616-367C>T). As COMT polymorphism has been associated with cisplatin-induced ototoxicity, its effect on nephrotoxicity of cisplatin should be the subject of further investigation.

Impactfactor: 3.493

Physical Activity in End-Stage Renal Disease Patients: The Effects of Starting Dialysis in the First 6 Months after the Transition Period

Broers NJ, Martens RJ, Cornelis T, van der Sande FM, Diederen NM, Hermans MM, Wirtz JJ, Stifft F, **Konings CJ**, Dejagere T, Canaud B, Wabel P, Leunissen KM, Kooman JP

Nephron. 2017;137(1):47-56

OBJECTIVES:

Physical inactivity in end-stage renal disease (ESRD) patients is associated with increased mortality, and might be related to abnormalities in body composition (BC) and physical performance. It is uncertain to what extent starting dialysis influences the effects of ESRD on physical activity (PA). This study aimed to compare PA and physical performance between stage 5 chronic kidney disease (CKD-5) non-dialysis and dialysis patients, and healthy controls, to assess alterations in PA during the transition from CKD-5 non-dialysis to dialysis, and to relate PA to BC.

METHODS:

For the cross-sectional analyses 44 CKD-5 non-dialysis patients, 29 dialysis patients, and 20 healthy controls were included. PA was measured by the SenseWear™ pro3. Also, the walking speed and handgrip strength (HGS) were measured. BC was measured by the Body Composition Monitor©. Longitudinally, these parameters were assessed in 42 CKD-5 non-dialysis patients (who were also part of the cross-sectional analysis), before the start of dialysis and 6 months thereafter.

RESULTS:

PA was significantly lower in CKD-5 non-dialysis patients as compared to that in healthy controls but not as compared to that in dialysis patients. HGS was significantly lower in dialysis patients as compared to that in healthy controls. Walking speed was significantly lower in CKD-5 non-dialysis patients as compared to that in healthy controls but not as compared to that in dialysis patients. Six months after starting dialysis, activity related energy expenditure (AEE) and walking speed significantly increased.

CONCLUSIONS:

PA is already lower in CKD-5 non-dialysis patients as compared to that in healthy controls and does not differ from that of dialysis patients. However, the transition

Impactfactor: 1.939

Practical Value of Anti-Xa Activity in the Evaluation of Extracorporeal Circuit Anticoagulation during Haemodialysis: Results of a Cross-Sectional Single-Centre Study

Coene KL, **Dekker MJ**, Kerskes MC, **Hengst M**, **Schonck MJ**, **Konings CJ**, Scharnhorst V

Nephron. 2017;137(3):205-211

BACKGROUND/AIMS: Anticoagulation of the extracorporeal circuit is essential for adequate haemodialysis (HD). Low molecular weight heparins (LMWHs) are safe and sufficient towards achieving this goal. In the Netherlands, dosage is based on bodyweight and adjusted based on clinical events. LMWH levels during dialysis can be quantified through measurement of the anti-Xa activity and a target range of 0.5-1.0 IU/mL has been proposed. We aimed to evaluate the practical value of the anti-Xa activity to guide LMWH dosage in HD patients. Additionally, the value of the activated partial thromboplastin time (APTT) was investigated.

METHODS: All prevalent adult HD patients of our dialysis clinic were included. APTT and anti-Xa activity were measured before, during and after 2 dialysis sessions. Clinical and dialysis characteristics, including LMWH dosage, were derived from digital patient charts.

RESULTS: Our final study cohort consisted of 83 patients. LMWH dosage during dialysis was appropriate for bodyweight in 61% of cases, of which 50% reached an anti-Xa activity within the putative target range of 0.5-1.0 IU/mL. Forty-six percent of patients had an anti-Xa activity >1.0 IU/mL. Anti-Xa levels during and after dialysis were significantly correlated ($r = 0.803$, $p < 0.01$). No thrombotic or haemorrhagic complications were observed in this study. Correlation of APTT with anti-Xa activity was poor.

CONCLUSION: Anti-Xa activity measurements during dialysis can identify patients in whom LMWH dosage should be lowered in a subsequent dialysis session. Whether such an intervention leads to a decrease in haemorrhagic complications needs to be evaluated in prospective studies.

Impactfactor: 1.939

Randomized phase III trial of S-1 versus capecitabine in the first-line treatment of metastatic colorectal cancer: SALTO study by the Dutch Colorectal Cancer Group

Kwakman JJM, Simkens LH, van Rooijen JM, van de Wouw AJ, Ten Tije AJ, **Creemers GJ**, Hendriks MP, Los M, van Alphen RJ, Polée MB, Muller EW, van der Velden AM, van Voorthuizen T, Koopman M, Mol L, van Werkhoven E, Punt CJ

Ann Oncol. 2017 Jun 1 28(6):1288-1293

Background:

Hand-foot syndrome (HFS) is a common side-effect of capecitabine. S-1 is an oral fluoropyrimidine with comparable efficacy to capecitabine in gastrointestinal cancers but associated with a lower incidence of HFS in Asian patients. This study compares the incidence of HFS between S-1 and capecitabine as first-line treatment in Western metastatic colorectal cancer (mCRC) patients.

Patients and methods:

Patients with previously untreated mCRC and planned treatment with fluoropyrimidine monochemotherapy were randomized 1 : 1 to receive either capecitabine (1250?mg/m2 orally for patients?<70 years; 1000?mg/m2 for patients =70 years, twice daily on days 1-14) or S-1 (30?mg/m2 orally twice daily on days 1-14) in 3-weekly cycles, with bevacizumab optional in both groups. The primary endpoint was the incidence of any grade HFS, as assessed by both physicians and patients (diaries). Secondary endpoints included grade 3 HFS, other toxicities, relative dose intensity, progression-free survival, response rate and overall survival.

Results:

A total of 161 patients were randomized in 27 centres. The incidence of any grade HFS as assessed by physicians was 73% in the capecitabine group (n?=?80) and 45% in the S-1 group (n?=?80) [odds ratio (95% confidence interval) 0.31 (0.16-0.60), P?=?0.0005]. The incidence of grade 3 HFS was 21% and 4% (P?=?0.003), respectively. Patient-assessed any grade HFS was 84% and 58%, respectively (P?=?0.004). Grade 3 anorexia was more common in the S-1 group (3% versus 13%, P?=?0.03). Median relative dose intensity was 88% in the capecitabine group and 95% in the S-1 group (P?=?0.026). There were no statistically significant differences in median progression-free survival, response rate and overall survival rates.

Conclusion:

Treatment with S-1 in Western mCRC patients is associated with a significantly lower incidence of HFS compared with capecitabine, with comparable efficacy.

Impactfactor: 11.855

Recurrence-free and overall survival among elderly stage III colon cancer patients treated with CAPOX or capecitabine monotherapy

van Erning FN, Janssen-Heijnen ML, **Creemers GJ**, Pruijt JF, Maas HA, Lemmens VE

Int J Cancer. 2017 Jan 1; 140(1):224-233. Epub 2016 Sep 22

The aim of this study is to investigate the effects of CAPOX and capecitabine on recurrence-free survival (RFS) and overall survival (OS) among elderly stage III colon cancer patients and to evaluate the effect of (non-)completion. Patients aged =70 years who underwent resection only or who were subsequently treated with CAPOX or capecitabine in 10 large non-academic hospitals were included. RFS and OS were analyzed with Kaplan-Meier curves and multivariable Cox regression adjusted for patient and tumor characteristics. 982 patients were included: 630 underwent surgery only, 191 received CAPOX and 161 received capecitabine. Five-year RFS and OS did not differ between capecitabine and CAPOX (RFS: 63% vs. 60% (p?=?0.91), adjusted HR?=?0.99 (95%CI 0.68-1.44); OS: 66% vs. 66% (p?=?0.76), adjusted HR?=?0.93 (95%CI 0.64-1.34)). After resection only, RFS was 38% and OS 37%. Completion rates were 48% for CAPOX and 68% for capecitabine. Three-year RFS and OS did not differ between patients who discontinued CAPOX early and patients who completed treatment with CAPOX (RFS: 61% vs. 69% (p?=?0.21), adjusted HR?=?1.42 (95%CI 0.85-2.37); OS: 68% vs. 78% (p?=?0.41), adjusted HR?=?1.17 (95%CI 0.70-1.97)). Three-year RFS and OS differed between patients who discontinued capecitabine early and patients who completed treatment with capecitabine (RFS: 54% vs. 72% (p?=?0.01), adjusted HR?=?2.07 (95%CI 1.11-3.84); OS: 65% vs. 80% (p?=?0.01), adjusted HR?=?2.00 (95%CI 1.12-3.59)). Receipt of CAPOX or capecitabine is associated with improved RFS and OS. The advantage does not differ by regimen. The addition of oxaliplatin might not be justified in elderly stage III colon cancer patients.

Impactfactor: 1.846

Safety and tolerability of subcutaneous trastuzumab for the adjuvant treatment of human epidermal growth factor receptor 2-positive early breast cancer: SafeHer phase III study's primary analysis of 2573 patients

J. Gligorov, M. Verrill, M. De Laurentiis, K.H. Jung, H.A. Azim, N. Al-Sakaff, S. Lauer, M. Shing, X. Pivot on behalf of show the SafeHer Study Group: **Warmerdam LJ**

European journal of cancer, 2017;82;237-46

Aim

To assess the safety and tolerability of adjuvant subcutaneous trastuzumab (Herceptin® SC, H SC), delivered from an H SC Vial via hand-held syringe (Cohort A) or single-use injection device (Cohort B), with or without chemotherapy, for human epidermal growth factor receptor 2 (HER2)-positive stage I to IIIC early breast cancer (EBC) in the phase III SafeHer study (NCT01566721).

Methods

Patients received 600 mg fixed-dose H SC every 3 weeks for 18 cycles. The chemotherapy partner was at the investigators' discretion (H SC monotherapy was limited to =10% of the population). Data from the first H SC dose until 28 days (plus a 5-day window) after the last dose are presented. Results are descriptive.

Results

In the overall population, 2282/2573 patients (88.7%) experienced adverse events (AEs). Of the above, 128 (5.0%) patients experienced AEs leading to study drug discontinuation; 596 (23.2%) experienced grade = 3 AEs and 326 (12.7%) experienced serious AEs. Grade = 3 cardiac disorders were reported in 24 patients (0.9%), including congestive heart failure in eight (0.3%).

As expected, the AE rates varied according to the timing of chemotherapy in both cohorts, with higher rates in concurrent versus sequential chemotherapy subgroups. In the concurrent chemotherapy subgroup, AEs were more common during the actual period of concurrent chemotherapy compared with the period when patients did not receive concurrent chemotherapy.

Conclusion

SafeHer confirms the safety and tolerability of the H SC 600 mg fixed dose for 1 year (every 3 weeks for 18 cycles) as adjuvant therapy with concurrent or sequential chemotherapy for HER2-positive EBC. These primary analysis results are consistent with the known safety profile for intravenous H and H SC.

Impactfactor: 6.029

Salt intake and blood pressure response to percutaneous renal denervation in resistant hypertension

de Beus E, de Jager RL, Beeftink MM, Sanders MF, Spiering W, Vonken EJ, Voskuil M, Bots ML, Blankestijn PJ; SYMPATHY study group: Tonino WA, Brueren BR, **Konings CJ**

J Clin Hypertens (Greenwich). 2017 Nov;19(11):1125-1133

The effect of lowering sympathetic nerve activity by renal denervation (RDN) is highly variable. With the exception of office systolic blood pressure (BP), predictors of the BP-lowering effect have not been identified. Because dietary sodium intake influences sympathetic drive, and, conversely, sympathetic activity influences salt sensitivity in hypertension, we investigated 24-hour urinary sodium excretion in participants of the SYMPATHY trial. SYMPATHY investigated RDN in patients with resistant hypertension. Both 24-hour ambulatory and office BP measurements were end points. No relationship was found for baseline sodium excretion and change in BP 6 months after RDN in multivariable-adjusted regression analysis. Change in the salt intake-measured BP relationships at 6 months vs baseline was used as a measure for salt sensitivity. BP was 8 mm Hg lower with similar salt intake after RDN, suggesting a decrease in salt sensitivity. However, the change was similar in the control group, and thus not attributable to RDN.

Impactfactor: 3.242

Synchronous peritoneal metastases of small bowel adenocarcinoma: Insights into an underexposed clinical phenomenon

Legué LM, Simkens GA, **Creemers GJ**, Lemmens VE, de Hingh IH

Eur J Cancer. 2017 Nov 10;87:84-91

BACKGROUND:

The aim of this population-based study was to provide insight into the incidence, risk factors and treatment-related survival of patients with peritoneal metastases (PM) of small bowel adenocarcinoma (SBA).

METHODS:

Data from the Netherlands Cancer Registry were used. All patients diagnosed with SBA between 2005 and 2014 were included. The influence of patient and tumour characteristics on the odds of developing PM was analysed. Subsequently, for all further analyses, patients without synchronous PM of SBA were excluded. The log-rank test and Kaplan-Meier analyses were conducted to estimate survival, and the Cox proportional hazards model was used to evaluate the risk of death.

RESULTS:

Of the 1428 included patients diagnosed with SBA, 181 (13%) presented with synchronous PM. Synchronous PM was found in 9% of the duodenal tumours and in 17% of the more distal tumours. Median overall survival of all patients with PM was 5.9 months, whereas survival of both 11 months was observed in patients treated with primary tumour resection or palliative chemotherapy and 32 months after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Poor prognostic factors for survival were age =70 years (hazard ratio [HR] 1.6, 95% confidence interval [CI] 1.1-2.2), systemic metastases other than PM (HR 2.0, 95% CI 1.4-2.9) and an advanced (HR 1.9, 95% CI 1.3-3.0) or unknown T-stage (HR 2.1, 95% CI 1.2-3.5).

CONCLUSIONS:

Synchronous PM was frequently encountered in SBA. Without treatment, prognosis was extremely poor. Survival was higher after primary tumour resection, palliative chemotherapy and CRS+HIPEC, but selection bias probably played a significant role calling for further clinical research.

Impactfactor: 6.029

The Clinical Course of Minimal Change Nephrotic Syndrome With Onset in Adulthood or Late Adolescence: A Case Series

Maas RJ, Deegens JK, Beukhof JR, Reichert LJ, Ten Dam MA, Beutler JJ, van den Wall Bake AWL, Rensma PL, **Konings CJ**, Geerse DA, Feith GW, Van Kuijk WH, Wetzels JF

Am J Kidney Dis. 2017 May;69(5):637-646

BACKGROUND:

Few studies have examined the treatment and outcome of adult-onset minimal change nephrotic syndrome (MCNS). We retrospectively studied 125 patients who had MCNS with onset in either adulthood or late adolescence. Presenting characteristics, duration of initial treatment and response to treatment, relapse patterns, complications, and long-term outcome were studied.

STUDY DESIGN:

Case series.

SETTING & PARTICIPANTS:

Patients with new-onset nephrotic syndrome 16 years or older and a histologic diagnosis of MCNS in 1985 to 2011 were identified from pathology records of 10 participating centers.

OUTCOMES:

Partial and complete remission, treatment resistance, relapse, complications, renal survival.

RESULTS:

Corticosteroids were given as initial treatment in 105 (84%) patients. After 16 weeks of corticosteroid treatment, 92 (88%) of these patients had reached remission. Median time to remission was 4 (IQR, 2-7) weeks. 7 (6%) patients initially received cyclophosphamide with or without corticosteroids, and all attained remission after a median of 4 (IQR, 3-11) weeks. 13 (10%) patients reached remission without immunosuppressive treatment. One or more relapses were observed in 57 (54%) patients who received initial corticosteroid treatment. Second-line cyclophosphamide resulted in stable remission in 57% of patients with relapsing MCNS. Acute kidney injury was observed in 50 (40%) patients. Recovery of kidney function occurred almost without exception. Arterial or venous thrombosis occurred in 11 (9%) patients. At the last follow-up, 113 (90%) patients were in remission and had preserved kidney function. 3 patients with steroid-resistant MCNS progressed to end-stage renal disease, which was associated with focal segmental glomerulosclerosis lesions on repeat biopsy.

LIMITATIONS: Retrospective design, variable treatment protocols.

CONCLUSIONS:

The large majority of patients who had MCNS with onset in adulthood or late adolescence were treated with corticosteroids and reached remission, but many had relapses. Cyclophosphamide resulted in stable remission in many patients with relapses. Significant morbidity was observed due to acute kidney injury and other complications. Progression to end-stage renal disease occurred in a few patients and was explained by focal segmental glomerulosclerosis.

Impactfactor: 7.623

The impact of age on first-line systemic therapy in patients with metachronous metastases from colorectal cancer

Razenberg LG, van Erning FN, Pruijt HF, Ten Tije AJ, van Riel JM, **Creemers GJ**, Lemmens VE

J Geriatr Oncol. 2017 Jan; 8(1):37-43. Epub 2016 Sep 19

OBJECTIVES: The paucity of evidence for the optimal use of systemic therapy in elderly patients with metastatic colorectal cancer (mCRC) poses significant challenges to cancer specialists. The present population-based study provides insight into the impact of age on palliative systemic therapy in patients with metachronous metastases from CRC, in order to optimize the decision-making process.

METHODS: Data on the development and treatment of metachronous metastases were collected for patients with primary resected CRC diagnosed between 2003 and 2008 in the Eindhoven area of the Netherlands Cancer Registry. Patients undergoing surgery for metastases were excluded, resulting in a study population treated with palliative intent, with or without systemic therapy (n=746).

RESULTS: 385 patients received palliative systemic therapy (52%). Patients aged =75years were less likely to receive systemic therapy (31% =75years vs 73% <60years) and more likely to receive single-agent chemotherapy than combination-chemotherapy. Elderly patients (=75years) treated with capecitabine-oxaliplatin (CAPOX) received fewer cycles (51% =3 oxaliplatin cycles, 43% =3 capecitabine cycles) and lower cumulative dosages compared to patients aged <75years, although initial dosages were similar. If capecitabine monotherapy (CapMono) was administered, starting dosages were 2414mg/m2/d<75years and 1992mg/m2/d=75years ($p<0.05$), but no differences in number of received cycles or cumulative dosages were observed.

CONCLUSION: Age beginning at 75years significantly influenced palliative systemic therapy. Even in selected elderly patients, first-line treatment with CAPOX was associated with less cycles and lower cumulative dosages compared to younger patients. With single-agent fluoropyrimidine therapy, however, no such results were observed.

Impactfactor: 2.852

The truth on current peritoneal dialysis: state of the art

Krediet RT, Abrahams AC, de Fijter CW, Betjes MG, Boer WH, van Jaarsveld BC, **Konings CJ**, Dekker FW

Neth J Med. 2017 Jun;75(5):179-189

The share of peritoneal dialysis (PD) in the spectrum of chronic dialysis has decreased markedly in the Netherlands in the last 15 years. Consequently, the knowledge of nephrologists and nursing staff on PD has declined leading to a negative spiral in which loss of experience resulted in loss of enthusiasm to offer PD to patients and also in less interest in the new PD developments. All these changes took place while the results of PD improved and patient survival was at least similar to that on haemodialysis. The aim of this review is first to give a summary of the principles and practice of patient and staff education and to describe the role of the medical contribution in decision-making. On this basis, the second aim is to update internist-nephrologists on a number of issues that have been underexposed in the past. Recent patient and technique survival data of PD patients is reviewed, and also the new insights into dialysis adequacy. The presence of residual renal function is the main determinant of patient survival together with prevention of overhydration. Urea and creatinine removal are not important at all when patients are still passing urine. Many early problems with PD are due to the peritoneal catheter and suggestions are made for improvement of its function. The prevention and management of infections is reviewed, and also the regular assessment of peritoneal function. Free water transport is a predictor of encapsulating peritoneal sclerosis (EPS), which should be assessed regularly. The pathogenesis of EPS, treatment and the decreasing incidence are discussed.

Impactfactor: 1.244

Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery

Haanschoten MC, **Kreeftenberg HG**, Arthur Bouwman R, van Straten AH, Buhre WF, Soliman Hamad MA

J Cardiothorac Vasc Anesth. 2017 Feb;31(1):45-53. Epub 2016 Apr 22

OBJECTIVES:

In the present study, the authors investigated the predictive value of postoperative peak arterial lactate levels for early and late mortality after cardiac surgery.

DESIGN:

Retrospective analysis of prospectively collected data.

SETTING:

Single-center study in an academic hospital.

PARTICIPANTS:
Adult patients who underwent cardiac surgery between 2004 and 2014 (n = 16,376).
INTERVENTIONS:
Different cardiac surgical procedures.
MEASUREMENTS AND RESULTS:
Patients were classified according to the peak arterial lactate level (PALL) within 3 days postoperatively. Logistic regression analysis and Cox regression analysis were performed to identify postoperative peak arterial lactate level as a predictor for early and late mortality respectively. In 8460 patients (51.7%), lactate was not measured postoperatively because these patients were managed according to the fast-track protocol. These patients constituted group 1 in our population but were excluded from the regression analysis. The remaining patients (n = 7,916; 48.3%) were divided according to the postoperative peak arterial lactate level (PALL): PALL<5 mmol/L (group 2), PALL 5 to 10 mmol/L (group 3), and PALL of>10 mmol/L (group 4). Early mortality was 3.7%, 20.4%, and 62.9% in groups 2, 3, and 4 respectively (p<0.0001). This mortality rate was significantly higher than that of group 1 (1.6%); p<0.0001. Multivariate regression analyses revealed postoperative peak arterial lactate as a significant predictor of 30-day mortality (odds ratio = 1.44 [1.39-1.48], p<0.001) as well as for late mortality (hazard ratio = 1.05 [1.01-1.10], p<0.025).
CONCLUSIONS:
Postoperative peak arterial lactate level in patients undergoing cardiac surgery is an independent predictor for both early and late mortality.

Impactfactor: 1.519

Vitamin D and type 2 diabetes

Lips P, Eekhoff M, van Schoor N, **Oosterwerff M**, de Jongh R, Krul-Poel Y, Simsek S
J Steroid Biochem Mol Biol. 2017 Oct;173:280-285. Epub 2016 Dec 5

Vitamin D deficiency is associated with a decreased insulin release, insulin resistance and type 2 diabetes in experimental and epidemiological studies. Animal studies show that 1a,25-dihydroxyvitamin D3 (1,25(OH)2D3) stimulates the pancreatic ß-cell to secrete insulin. The relationship between vitamin D deficiency and insulin resistance could develop through inflammation, as vitamin D deficiency is associated with increased inflammatory markers. In addition, genetic polymorphisms of vitamin D - related genes may predispose to impaired glycemic control and type 2 diabetes. Epidemiologic studies showed an association between low serum 25-hydroxyvitamin D3 (25(OH)D3) concentration and an increased risk for the metabolic syndrome and type 2 diabetes. This may be partly explained by an increased fat mass. A possible causal relationship between vitamin D deficiency and type 2 diabetes should be proven by randomized clinical trials showing that either type 2 diabetes can be prevented or insulin release and insulin sensitivity can be improved by vitamin D supplements. The results of randomized clinical trials on the effect of vitamin D versus placebo, sometimes combined with calcium, in patients with impaired glucose tolerance ("prediabetes") or type 2 diabetes are inconsistent. Some studies showed a slight decrease of fasting plasma glucose or improvement of insulin resistance, but often only in posthoc analyses. These effects are mainly visible in patients with vitamin D deficiency and impaired glucose tolerance at baseline. Meta-analyses of randomized clinical trials in general did not show significant effects of vitamin D supplementation on glycemic control. Currently, several large scale randomized clinical trials with vitamin D supplementation in doses of 1600-4000IU/d are ongoing with glycemic control or incidence of diabetes mellitus as outcome. Vitamin D deficiency needs to be prevented or cured, but until the results of these trials are published, high-dose vitamin D supplementation cannot be recommended for prevention or amelioration of type 2 diabetes.

Impactfactor: 4.561

Volume-outcome relation in palliative systemic treatment of metastatic oesophagogastric cancer

Haj Mohammad N, **Bernards N**, van Putten M, Lemmens VEPP, van Oijen MGH, van Laarhoven HWM
Eur J Cancer. 2017 Jun 78:28-36. Epub 2017 Apr 14

INTRODUCTION:
Palliative systemic therapy has been shown to improve survival in metastatic oesophagogastric cancer. Administration of palliative systemic therapy in metastatic oesophagogastric cancer varies between hospitals. We aimed to explore the association between the annual hospital volume of oesophagogastric cancer patients and survival.
METHODS:

Patients diagnosed in the Netherlands between 2005 and 2013 with metastatic oesophagogastric cancer were identified in the Netherlands Cancer Registry. Patients were attributed according to three definitions of high volume: (1) high-volume incidence centre, (2) high-volume treatment centre and (3) high-volume surgical centre. Independent predictors for administration of palliative chemotherapy were evaluated by means of multivariable logistic regression analysis, and multivariable Cox proportional hazard regression analysis was performed to assess the impact of high-volume centres on survival.
RESULTS:
Our data set comprised 4078 patients with metastatic oesophageal cancer, and 5425 patients with metastatic gastric cancer, with a median overall survival of 20 weeks (95% confidence interval [CI] 19-21 weeks) and 16 weeks (95% CI 15-17 weeks), respectively. Patients with oesophageal cancer treated in a high-volume surgical centre (adjusted hazard ratio [HR] 0.80, 95% CI 0.70-0.91) and a high-volume treatment centre (adjusted HR 0.88, 95% CI 0.78-0.99) exhibited a decreased risk of death. For gastric cancer, patients treated in a high-volume surgical centre (adjusted HR 0.83, 95% CI 0.74-0.92) had a superior outcome.
CONCLUSION:
Improved survival in patients undergoing palliative systemic therapy for oesophagogastric cancer was associated with treatment in high-volume treatment and surgical centres. Further research should be implemented to explore which specific factors of high-volume centres are associated with improved outcomes.
Impactfactor: 6.029

Kindergeneeskunde

A neonate with a unique non-Down syndrome transient proliferative megakaryoblastic disease

Bertrums EJ, Buijs A, van Grotel M, **Dors N**, de Rooij JD, de Haas V, Hopman S, Jongmans MC, Zwaan CM, van den Heuvel-Eibrink MM.

Pediatr Blood Cancer. 2017 Mar; 64(3).

Transient myeloproliferative disorder (TMD) is a leukemia type that occurs typically in newborns. In Down syndrome, TMD is referred to as transient abnormal myelopoiesis (TAM).32 Recently, transientness has also been reported in acute myeloid leukemia patients with germline trisomy 21 mosaicism, and even in cases with somatic trisomy 21, with or without GATA1 mutations. TMD cases without trisomy 21 are rare, and recurrent genetic aberrations that aid in clinical decision-making are scarcely described. We describe here a TMD patient without

trisomy 21 or GATA1 mutation in whom single-nucleotide polymorphism analysis of leukemic blasts revealed a novel combined submicroscopic deletion (5q31.1-5q31.3 and 8q23.2q24).

Impactfactor: 2.513

ACAN Gene Mutations in Short Children Born SGA and Response to Growth Hormone Treatment

van der Steen M, Pfundt R, Maas SJWH, Bakker-van Waarde WM, **Odink RJ**, Hokken-Koelega AC

J Clin Endocrinol Metab. 2017 May 1; 102(5):1458-1467

Background: Some children born small for gestational age (SGA) show advanced bone age (BA) maturation during growth hormone (GH) treatment. ACAN gene mutations have been described in children with short stature and advanced BA.

Objective: To determine the presence of ACAN gene mutations in short SGA children with advanced BA and assess the response to GH treatment.

Methods: BA assessment in 290 GH-treated SGA children. ACAN sequencing in 29 children with advanced BA =0.5 years compared with calendar age.

Results: Four of 29 SGA children with advanced BA had an ACAN gene mutation (13.8%). Mutations were related to additional characteristics: midface hypoplasia (P = 0.003), joint problems (P = 0.010), and broad great toes (P = 0.003). Children with one or fewer additional characteristic had no mutation. Of children with two additional characteristics, 50% had a mutation. Of children with three additional characteristics, 100% had a mutation. All GH-treated children with a mutation received gonadotropin-releasing hormone analog (GnRHa) treatment for 2

years from onset of puberty. At adult height, one girl was 5 cm taller than her mother and one boy was 8 cm taller than his father with the same ACAN gene mutation.

Conclusion: This study expands the differential diagnosis of genetic variants in children born SGA and proposes a clinical scoring system for identifying subjects most likely to have an ACAN gene mutation. ACAN sequencing should be considered in children born SGA with persistent short stature, advanced BA, and midface hypoplasia, joint problems, or broad great toes. Our findings suggest that children with an ACAN gene mutation benefit from GH treatment with 2 years of GnRHa.

Impactfactor: 5.455

Diet and ADHD, Reviewing the Evidence: A Systematic Review of Meta-Analyses of Double-Blind Placebo-Controlled Trials Evaluating the Efficacy of Diet Interventions on the Behavior of Children with ADHD

Pelsser LM, Frankena K, **Toorman J**, Rodrigues Pereira R

PLoS One. 2017 Jan 25;12(1):e0169277

INTRODUCTION: Attention-deficit/hyperactivity disorder (ADHD) is a debilitating mental health problem hampering the child's development. The underlying causes include both genetic and environmental factors and may differ between individuals. The efficacy of diet treatments in ADHD was recently evaluated in three reviews, reporting divergent and confusing conclusions based on heterogeneous studies and subjects. To address this inconsistency we conducted a systematic review of meta-analyses of double-blind placebo-controlled trials evaluating the effect of diet interventions (elimination and supplementation) on ADHD.

METHODS: Our literature search resulted in 14 meta-analyses, six of which confined to double-blind placebo-controlled trials applying homogeneous diet interventions, i.e. artificial food color (AFC) elimination, a few-foods diet (FFD) and poly-unsaturated fatty acid (PUFA) supplementation. Effect sizes (ES) and Confidence intervals (CI) of study outcomes were depicted in a forest plot. I2 was calculated to assess heterogeneity if necessary and additional random effects subgroup meta-regression was conducted if substantial heterogeneity was present.

RESULTS: The AFC ESs were 0.44 (95% CI: 0.16-0.72, I2 = 11%) and 0.21 (95% CI: -0.02-0.43, I2 = 68%) [parent ratings], 0.08 (95% CI: -0.07-0.24, I2 = 0%) [teacher ratings] and 0.11 (95% CI: -0.13-0.34, I2 = 12%) [observer ratings]. The FFD ESs were 0.80 (95% CI: 0.41-1.19, I2 = 61%) [parent ratings] and 0.51 (95% CI: -0.02-1.04, I2 = 72%) [other ratings], while the PUFA ESs were 0.17 (95% CI: -0.03-0.38, I2 = 38%) [parent ratings], -0.05 (95% CI: -0.27-0.18, I2 = 0%) [teacher ratings] and 0.16 (95% CI: 0.01-0.31, I2 = 0%) [parent and teacher ratings]. Three meta-analyses (two FFD and one AFC) resulted in high I2 without presenting subgroup results. The FFD meta-analyses provided sufficient data to perform subgroup analyses on intervention type, resulting in a decrease of heterogeneity to 0% (diet design) and 37.8% (challenge design).

CONCLUSION: Considering the small average ESs PUFA supplementation is unlikely to provide a tangible contribution to ADHD treatment, while further research is required for AFC elimination before advising this intervention as ADHD treatment. The average FFD ES is substantial, offering treatment opportunities in subgroups of children with ADHD not responding to or too young for medication. Further FFD research should focus on establishing the underlying mechanisms of food (e.g. incrimination of gut microbiota) to simplify the FFD approach in children with ADHD.

Impactfactor: 2.806

Growth and prevalence of feeding difficulties in children with Robin sequence: a retrospective cohort study

Paes EC, de Vries IAC, Penris WM, Hanny KH, **Lavrijsen SW***, van Leerdam EK, Rademaker MM, Veldhoen ES, Eijkemans RMJC, Kon M, Breugem CC

Clin Oral Investig. 2017 Jul;21(6):2063-2076.Epub 2016 Nov 21

OBJECTIVES:

In addition to breathing problems, patients with Robin sequence (RS) often encounter feeding difficulties (FD). Data regarding the occurrence of FD and possible influencing factors are scarce. The study aim was to elucidate these factors to improve treatment strategies.

MATERIAL AND METHODS:

A retrospective comparative cohort study was conducted, consisting of 69 infants diagnosed with both RS and a cleft palate and 64 isolated cleft palate only (iCPO) infants. Data regarding FD, growth, and airway intervention were collected during the first 2 years of life. A systematic review of the literature was conducted to identify reported FD in RS patients.

RESULTS:

RS patients had more FD (91 %) than iCPO patients (72 %; p = 0.004). Also, nasogastric (NG)-tube feeding was necessary more frequently and for a longer period (both p < 0.001). Growth was lower in RS than iCPO infants (p = 0.008) and was not affected by the kind of airway management (conservative/surgical; p = 0.178), cleft palate grade (p = 0.308), or associated disorders (p = 0.785). By contrast, surgical intervention subtype did significantly affect growth. Mean reported FD for RS in the literature is 80 % (range = 47-100 %), and 55 % (range = 11-100 %) of infants need NG-tube feeding.

CONCLUSIONS:

FD is present in a large proportion of infants with RS, which indicates the need for early recognition and proper treatment to ensure optimal growth. Growth during the first 2 years of life is significantly lower in RS patients than iCPO patients, which indicates the need for careful attention and long-term follow-up.

CLINICAL RELEVANCE:

This study indicates the need for early recognition and proper treatment of FD in RS to ensure optimal growth. In addition, growth needs careful attention and long-term follow-up.

** = ten tijde van publicatie verbonden aan: Department of Pediatrics, Wilhelmina Children's Hospital, Utrecht, The Netherlands*

Impactfactor: 2.308

Variation in baseline factor VIII concentration in a retrospective cohort of mild/moderate hemophilia A patients carrying identical F8 mutations

Loomans JI, van Velzen AS, Eckhardt CL, Peters M, Mäkipernaa A, Holmstrom M, Brons PP, **Dors N**, Haya S, Voorberg J, van der Bom JG, Fijnvandraat K

J Thromb Haemost. 2017 Feb;15(2):246-254. Feb 3

Essentials Factor VIII levels vary in mild and moderate hemophilia A (MHA) patients with the same mutation. We aimed to estimate the variation and determinants of factor VIII levels among MHA patients. Age and genotype explain 59% of the observed inter-individual variation in factor VIII levels. Intra-individual variation accounted for 45% of the variation in the three largest mutation groups.

SUMMARY:

Background The bleeding phenotype in patients with mild/moderate hemophilia A (MHA) is inversely associated with the residual plasma concentration of factor VIII (FVIII:C). Within a group of patients with the same F8 missense mutation, baseline FVIII:C may vary, because, in healthy individuals, von Willebrand factor (VWF) levels, ABO blood group and age are also known to influence baseline FVIII:C. Our understanding of the pathophysiologic process of the causative genetic event leading to reduced baseline FVIII:C in MHA patients is still limited. Objectives To estimate the variation and determinants of baseline FVIII:C among MHA patients with the same F8 missense mutation. Methods Three hundred and forty-six patients carrying mutations that were present in at least 10 patients in the cohort were selected from the INSIGHT and the RISE studies, which are cohort studies including data of 3534 MHA patients from Europe, Canada, and Australia. Baseline FVIII:C was measured with a one-stage clotting assay. We used Levene's test, univariate and multivariate linear regression, and mixed-model analyses. Results For 59% of patients, the observed variation in baseline FVIII:C was explained by age and genotype. Compared to FVIII:C in patients with Arg612Cys, FVIII:C was significantly different in patients with eight other F8 missense mutations. Intra-individual variation explained 45% of the observed variance in baseline FVIII:C among patients with the same mutation. Conclusion Our results indicate that baseline FVIII:C levels are not exclusively determined by F8 genotype in MHA patients. Insights into other factors may provide potential novel targets for the treatment of MHA.

Impactfactor: 5.287

Klinische Fysica

A virtual dosimetry audit - Towards transferability of gamma index analysis between clinical trial QA groups

Hussein M, Clementel E, Eaton DJ, Greer PB, Haworth A, Ishikura S, Kry SF, Lehmann J, Lye J, Monti AF, Nakamura M, **Hurkmans C**, Clark CH; Global Quality Assurance of Radiation Therapy Clinical Trial Harmonisation Group

Radiother Oncol. 2017 Dec;125(3):398-404

PURPOSE:

Quality assurance (QA) for clinical trials is important. Lack of compliance can affect trial outcome. Clinical trial QA groups have different methods of dose distribution verification and analysis, all with the ultimate aim of ensuring trial compliance. The aim of this study was to gain a better understanding of different processes to inform future dosimetry audit reciprocity.

MATERIALS:

Six clinical trial QA groups participated. Intensity modulated treatment plans were generated for three different cases. A range of 17 virtual 'measurements' were generated by introducing a variety of simulated perturbations (such as MLC position deviations, dose differences, gantry rotation errors, Gaussian noise) to three different treatment plan cases. Participants were blinded to the 'measured' data details. Each group analysed the datasets using their own gamma index (?) technique and using standardised parameters for passing criteria, lower dose threshold, ? normalisation and global ?

RESULTS:

For the same virtual 'measured' datasets, different results were observed using local techniques. For the standardised ?, differences in the percentage of points passing with ??<?1 were also found, however these differences were less pronounced than for each clinical trial QA group's analysis. These variations may be due to different software implementations of ?.

CONCLUSIONS:

This virtual dosimetry audit has been an informative step in understanding differences in the verification of measured dose distributions between different clinical trial QA groups. This work lays the foundations for audit reciprocity between groups, particularly with more clinical trials being open to international recruitment.

Impactfactor: 2.568

Cone-Beam CT-based position verification for oesophageal cancer: Evaluation of registration methods and anatomical changes during radiotherapy

van Nunen A, van der Sangen MJ, van Boxtel M, **van Haaren PM**

Technical Innovations & Patient Support in Radiation Oncology 2017;(3-4):30–36.

Purpose: To evaluate different registration methods, setup margins and number of corrections for CBCT-based position verification for oesophageal cancer and to evaluate anatomical changes during the course of radiotherapy treatment.

Methods: From 50 patients, 440 CBCT-scans were registered automatically using a soft tissue or bone registration algorithm and compared to the clinical match. Moreover, relevant anatomical changes were monitored. A sub-analysis was performed to evaluate if tumour location influenced setup variations.Margin calculation was performed and the number of setup corrections was estimated. Results were compared to a patient group previously treated with MV-EPID based position verification.

Results: CBCT-based setup variations were smaller than EPID-based setup variations, resulting in smaller setup margins of 5.9 mm (RL), 7.5 mm (CC) and 4.7 mm (AP) versus 6.0 mm, 7.8 mm and 5.5 mm, respectively.

A reduction in average number of setup corrections per patient was found from 0.75 to 0.36. From all automatically registered CBCT-scans, a clipbox around PTV and vertebras combined with soft tissue registration resulted in the smallest setup margins of 5.9 mm (RL), 7.7 mm (CC), 4.8 mm (AP) and smallest average number of corrections of 0.38. For distally located tumours, a setup margin of 7.7 mm (CC) was required compared to 5.6 mm for proximal tumours. Reduction of GTV volume, heart volume and change in diaphragm position were observed in 16, 10 and 15 patients, respectively.

Conclusions: CBCT-based set-up variations are smaller than EPID-based variations and vary according to tumour location. When using kV-CBCT a large variety of anatomical changes is revealed, which cannot be observed with MV-EPID.

Impactfactor: --

De rol van PET/CT bij oligometastatische ziekte

Roef MJ, van der Sangen MJ, **Hurkmans CW**

NTVO : Ned Tijdschr Oncol 2017;14(7):256-64

De diagnostiek en behandeling van oligometastatische ziekte staat de laatste jaren toenemend in de belangstelling. PET/CT is een 'total body' beeldvormende techniek met een relatief goede opbrengst in de detectie van zowel regionale lymfogene metastasen als van metastasen op afstand en heeft daarom vaak de voorkeur boven andere modaliteiten. Zo wordt PET/CT steeds vaker ingezet bij de (re)stadiëring, radiotherapieplanning en follow-up. Bij het gebruik van PET/CT dient men zich bewust te zijn van de beperkingen van het onderzoek. Zowel apparatuur-als patiëntgebonden factoren liggen hieraan ten grondslag.

Impactfactor: --

Elective breast radiotherapy including level I and II lymph nodes: A planning study with the humeral head as planning risk volume

Surmann K, van der Leer J, Branje T, van der Sangen M, van Lieshout M, **Hurkmans CW**

Radiat Oncol. 2017 Jan 18;12(1):22

BACKGROUND:

The aim of this study was to assess the dose to the humeral head planning risk volume with the currently used high tangential fields (HTF) and compare different planning techniques for breast radiotherapy including axillary level I and II lymph nodes (PTVn) while sparing the humeral head.

METHODS:

Ten patients with left-sided breast cancer were enrolled in a planning study with 16 fractions of 2.66 Gy. Four planning techniques were compared: HTF, HTF with sparing of the humeral head, 6-field IMRT with sparing of the humeral head and VMAT with sparing of the humeral head. The humeral head?+?10 mm was spared by restricting V40Gy?<?1 cc.

RESULTS:

The dose to the humeral head was too high with HTF (V40Gy on average 20.7 cc). When sparing the humeral head in HTF, PTVn V90% decreased significantly from 97.9% to 89.4%. 6-field IMRT and VMAT had a PTVn V90% of 98.2% and 99.5% respectively. However, dose to the lungs, heart and especially the contralateral breast increased with VMAT.

CONCLUSIONS:

The humeral head is rarely spared when using HTF. When sparing the humeral head, the 6-field IMRT technique leads to adequate PTV coverage while not increasing the dose to the OARs.

Impactfactor: 2.568

ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer

Guckenberger M, Andratschke N, Dieckmann K, Hoogeman MS, Hoyer M, **Hurkmans C**, Tanadini-Lang S, Lartigau E, Méndez Romero A, Senan S, Verellen D

Radiother Oncol. 2017 Jul;124(1):11-17

BACKGROUND:

Stereotactic body radiotherapy (SBRT) has become the standard of care for medically inoperable patients with peripherally located, early stage non-small cell lung cancer (NSCLC), and for those refusing surgical resection. Despite the availability of national and international guidelines, there exists substantial variability in many aspects of SBRT practice.

METHODS:

The ESTRO ACROP guideline is based on a questionnaire covering all aspects of SBRT implementation and practice (n=114 items). The questionnaire was answered by the 11 faculty members of the ESTRO course "Clinical practice and implementation of image-guided SBRT" and their 8 institutions.

RESULTS:

Agreement by >50% of the institutions was achieved in 72% of all items. Only 8/57 technologies and techniques were identified as mandatory for SBRT while 32/57 were considered as optional. In contrast, quality-assurance related elements were considered as mandatory in 12/24 items. A consensus of risk-adapted SBRT fractionation was achieved with 3×15Gy for peripherally located lesions and 4×12Gy (PTV D95-D99; Dmax <125% to <150%) for lesions with broad chest wall contact. For patients free from severe comorbidities and with favourable long-term OS expectancy, use of the maximum tolerated dose of 3×18Gy should be considered.

CONCLUSIONS:

This ACROP guideline achieved detailed recommendations in all aspects of SBRT implementation and practice, which will contribute to further standardization of SBRT for peripherally located early stage NSCLC.

Impactfactor: 4.328

European Organization for Research and Treatment of Cancer (EORTC) recommendations for planning and delivery of high-dose, high precision radiotherapy for lung cancer

De Ruysscher D, Faivre-Finn , Moeller D, Nestle U, **Hurkmans CW**, Le Péchoux C, Belderbos J, Guckenberger M, Senan S; Lung Group and the Radiation Oncology Group of the European Organization for Research and Treatment of Cancer (EORTC)

Radiother Oncol. 2017 Jul;124(1):1-10

PURPOSE:

To update literature-based recommendations for techniques used in high-precision thoracic radiotherapy for lung cancer, in both routine practice and clinical trials.

METHODS:

A literatue search was performed to identify published articles that were considered clinically relevant and practical to use. Recommendations were categorised under the following headings: patient positioning and immobilisation, Tumour and nodal changes, CT and FDG-PET imaging, target volumes definition, radiotherapy treatment planning and treatment delivery. An adapted grading of evidence from the Infectious Disease Society of America, and for models the TRIPOD criteria, were used.

RESULTS:

Recommendations were identified for each of the above categories.

CONCLUSION:

Recommendations for the clinical implementation of high-precision conformal radiotherapy and stereotactic body radiotherapy for lung tumours were identified from the literature. Techniques that were considered investigational at present are highlighted.

Impactfactor: 4.328

Heart position variability during voluntary moderate deep inspiration breath-hold radiotherapy for breast cancer determined by repeat CBCT scans

van Haaren P, Claassen-Janssen F, van de Sande I, Boersma L, van der Sangen M, **Hurkmans C**

Phys Med. 2017 Aug;40:88-94

Voluntary moderate deep inspiration breath hold (vmDIBH) in left-sided breast cancer radiotherapy reduces cardiac dose. The aim of this study was to investigate heart position variability in vmDIBH using CBCT and to compare this variability with differences in heart position between vmDIBH and free breathing (FB). For 50 patients initial heart position with respect to the field edge (HP-FE) was measured on a vmDIBH planning CT scan. Breath-hold was monitored using an in-house developed vertical plastic stick. On pre-treatment CBCT scans, heart position variability with respect to the field edge (?HP-FE) was measured, reflecting heart position variability when using an offline correction protocol. After registering the CBCT scan to the planning CT, heart position variability with respect to the chest wall (?HP-CW) was measured, reflecting heart position variability when using an online correction protocol. As a control group, vmDIBH and FB computed tomography (CT) scans were acquired for 30 patients and registering both scans on the chest wall. For 34 out of 50 patients, the average HP-FE and HP-CW increased over the treatment course in comparison to the planning CT. Averaged over all patients and all treatment fractions, the ?HP-FE and the ?HP-CW was 0.8±4.2mm (range -9.4-+10.6mm) and 1.0±4.4mm (range -8.3-+10.4mm) respectively. The average gain in heart to chest wall distance was 11.8±4.6mm when using vmDIBH instead of FB. In conclusion, substantial variability in heart position using vmDIBH was observed during the treatment course.

Impactfactor: 1.990

Individualized early death and long-term survival prediction after stereotactic radiosurgery for brain metastases of non-small cell lung cancer: Two externally validated nomograms

Zindler JD, Jochems A, Lagerwaard FJ, Beumer R, Troost EGC, Eekers DBP, Compter I, van der Toorn PP, Essers M, Oei B, **Hurkmans CW**, Bruynzeel AME, Bosmans G, Swinnen A, Leijenaar RTH, Lambin P.

Radiother Oncol. 2017 May 123(2):189-194. Epub 2017 Feb 23

INTRODUCTION:

Commonly used clinical models for survival prediction after stereotactic radiosurgery (SRS) for brain metastases (BMs) are limited by the lack of individual risk scores and disproportionate prognostic groups. In this study, two nomograms were developed to overcome these limitations.
METHODS:
495 patients with BMs of NSCLC treated with SRS for a limited number of BMs in four Dutch radiation oncology centers were identified and divided in a training cohort (n=214, patients treated in one hospital) and an external validation cohort n=281, patients treated in three other hospitals). Using the training cohort, nomograms were developed for prediction of early death (<3months) and long-term survival (>12months) with prognostic factors for survival. Accuracy of prediction was defined as the area under the curve (AUC) by receiver operating characteristics analysis for prediction of early death and long term survival. The accuracy of the nomograms was also tested in the external validation cohort.
RESULTS:
Prognostic factors for survival were: WHO performance status, presence of extracranial metastases, age, GTV largest BM, and gender. Number of brain metastases and primary tumor control were not prognostic factors for survival. In the external validation cohort, the nomogram predicted early death statistically significantly better ($p<0.05$) than the unfavorable groups of the RPA, DS-GPA, GGS, SIR, and Rades 2015 (AUC=0.70 versus range AUCs=0.51-0.60 respectively). With an AUC of 0.67, the other nomogram predicted 1year survival statistically significantly better ($p<0.05$) than the favorable groups of four models (range AUCs=0.57-0.61), except for the SIR (AUC=0.64, $p=0.34$). The models are available on www.predictcancer.org.
CONCLUSION:
The nomograms predicted early death and long-term survival more accurately than commonly used prognostic scores after SRS for a limited number of BMs of NSCLC. Moreover these nomograms enable individualized probability assessment and are easy into use in routine clinical practice.

Impactfactor: 4.328

Quality assurance of radiotherapy in the ongoing EORTC 1219-DAHANCA-29 trial for HPV/p16 negative squamous cell carcinoma of the head and neck: Results of the benchmark case procedure

Christiaens M, Collette S, Overgaard J, Gregoire V, Kazmierska J, Castadot P, Giralt J, Grant W, Tomsej M, Bar-Deroma R, Monti AF, **Hurkmans CW**, Weber DC.

Radiother Oncol. 2017 Jun; 123(3):424-430. Epub 2017 May 4

BACKGROUND AND PURPOSE:
The phase III EORTC 1219-DAHANCA 29 intergroup trial evaluates the influence of nimorazole in patients with locally advanced head and neck cancer when treated with accelerated radiotherapy (RT) in combination with chemotherapy. This article describes the results of the RT Benchmark Case (BC) performed before patient inclusion.
MATERIALS AND METHODS:
The participating centers were asked to perform a 2-step BC, consisting of (1) a delineation and (2) a planning exercise according to the protocol guidelines. Submissions were prospectively centrally reviewed and feedback was given to the submitting centers. Sørensen-Dice similarity index (DSI) and the 95th percentile Hausdorff distance (HD) were retrospectively used to evaluate the agreement between the centers and the expert contours.
RESULTS:
Fifty-four submissions (34 delineation and 20 planning exercises) from 19 centers were reviewed. Nine (47%) centers needed to perform the delineation step twice and three (16%) centers 3 times before receiving an approval. An increase in DSI-value and a decrease in HD, in particular for the prophylactic Clinical Target Volume (pCTV), could be found for the resubmitted cases. No unacceptable variations could be found for the planning exercise.
CONCLUSIONS:
These BC-results highlight the need for effective and prospective RTQA in clinical trials. Even with clearly defined protocol guidelines, delineation and not planning remain the main reason for unacceptable protocol variations. The introduction of more objective quantitative analysis methods, such as the HD and DSI, in future trials might strengthen the evaluation by experts.

Impactfactor: 4.328

Quantification, improvement, and harmonization of small lesion detection with state-of-the-art PET

van der Vos CS, Koopman D, Rijnsdorp S, **Arends AJ**, Boellaard R, van Dalen JA, Lubberink M, Willemsen AT, Visser EP

Eur J Nucl Med Mol Imaging. 2017 Aug;44(Suppl 1):4-16

In recent years, there have been multiple advances in positron emission tomography/computed tomography (PET/CT) that improve cancer imaging. The present generation of PET/CT scanners introduces new hardware, software, and acquisition methods. This review describes these new developments, which include time-of-flight (TOF), point-spread-function (PSF), maximum-a-posteriori (MAP) based reconstruction, smaller voxels, respiratory gating, metal artefact reduction, and administration of quadratic weight-dependent 18F-fluorodeoxyglucose (FDG) activity. Also, hardware developments such as continuous bed motion (CBM), (digital) solid-state photodetectors and combined PET and magnetic resonance (MR) systems are explained. These novel techniques have a significant impact on cancer imaging, as they result in better image quality, improved small lesion detectability, and more accurate quantification of radiopharmaceutical uptake. This influences cancer diagnosis and staging, as well as therapy response monitoring and radiotherapy planning. Finally, the possible impact of these developments on the European Association of Nuclear Medicine (EANM) guidelines and EANM Research Ltd. (EARL) accreditation for FDG-PET/CT tumor imaging is discussed.

Impactfactor: 7.277

The role of dosimetry audit in lung SBRT multi-centre clinical trials

Clark CH, **Hurkmans CW**, Kry SF Global Quality Assurance of Radiation Therapy Clinical Trials Harmonisation Group

Phys Med. 2017 Dec;44:171-176. Epub 2017 Apr 5

Stereotactic Body Radiotherapy (SBRT) in the lung is a challenging technique which requires high quality clinical trials to answer the un-resolved clinical questions. Quality assurance of these clinical trials not only ensures the safety of the treatment of the participating patients but also minimises the variation in treatment, thus allowing the lowest number of patient treatments to answer the trial question. This review addresses the role of dosimetry audits in the quality assurance process and considers what can be done to ensure the highest accuracy of dose calculation and delivery and it's assessment in multi-centre trials.

Impactfactor: 1.990

Whole brain radiotherapy versus stereotactic radiosurgery for 4-10 brain metastases: a phase III randomised multicentre trial

Zindler JD, Bruynzeel AME, Eekers DBP, **Hurkmans CW**, Swinnen A, Lambin P

BMC Cancer. 2017 Jul 25;17(1):500

BACKGROUND: Maintenance of quality of life is the primary goal during treatment of brain metastases (BM). This is a protocol of an ongoing phase III randomised multicentre study. This study aims to determine the exact additional palliative value of stereotactic radiosurgery (SRS) over whole brain radiotherapy (WBRT) in patients with 4-10 BM.

METHODS: The study will include patients with 4-10 BM from solid primary tumours diagnosed on a high-resolution contrast-enhanced MRI scan with a maximum lesional diameter of 2.5 cm in any direction and a maximum cumulative lesional volume of 30 cm3. Patients will be randomised between WBRT in five fractions of 4 Gy to a total dose of 20 Gy (standard arm) and single dose SRS to the BMs (study arm) in the range of 15-24 Gy. The largest BM or a localisation in the brainstem will determine the prescribed SRS dose. The primary endpoint is difference in quality of life (EQ5D EUROQOL score) at 3 months after radiotherapy with regard to baseline. Secondary endpoints are difference in quality of life (EQ5D EUROQOL questionnaire) at 6, 9 and 12 months after radiotherapy with regard to baseline. Other secondary endpoints are at 3, 6, 9 and 12 months after radiotherapy survival, Karnofsky = 70, WHO performance status, steroid use (mg), toxicity according to CTCAE V4.0 including hair loss, fatigue, brain salvage during follow-up, type of salvage, time to salvage after randomisation and Barthel index. Facultative secondary endpoints are neurocognition with the Hopkins verbal learning test revised, quality of life EORTC QLQ-C30, quality of life EORTC BN20 brain module and fatigue scale EORTC QLQ-FA13.

DISCUSSION: Worldwide, most patients with more than 4 BM will be treated with WBRT. Considering the potential advantages of SRS over WBRT, i.e. limiting radiation doses to uninvolved brain and a high

rate of local tumour control by just a single treatment with fewer side effects, such as hair loss and fatigue, compared to WBRT, SRS might be a suitable alternative for patients with 4-10 B

Impactfactor: 3.288

Kwaliteit

Use of an intraoperative checklist to decrease the incidence of re-exploration for postoperative bleeding after cardiac surgery

van Boxtel AG, van Veghel D, Soliman Hamad MA, **Schulz DN**, Stepaniak PS, van Straten AH

Interact Cardiovasc Thorac Surg. 2017 Oct 1;25(4):555-558

OBJECTIVES: We have implemented an intraoperative checklist aiming to reduce the incidence of re-exploration for bleeding after cardiac surgery. The present report addresses the results of adopting such a checklist regarding the incidence of postoperative bleeding.

METHODS: The checklist was implemented by presenting it in several staff meetings of the Catharina Heart Center. Copies of the checklist were presented in every operating room. Data were collected by the Catharina Heart Center, aligned with the 'Meetbaar Beter' data manual and validated by 'Meetbaar Beter' through their data quality system. The incidence of re-exploration for bleeding was analysed in a variable life-adjusted display curve. The patient population operated after the implementation of the checklist was compared with a recent historical population before its implementation.

RESULTS: From January 2013 through April 2016, 4817 cardiac surgical procedures were performed in our institution. Before May 2015, 3210 procedures were performed (Group 1), complicated by 112 re-exploration for bleeding (3.5%). The 'reoperation for bleeding checklist' was implemented on 1 May 2015. After this date, the number of re-explorations for bleeding decreased to 29 (1.8%) of the 1607 cardiac surgical procedures (Group 2) (P?<?0.05).

CONCLUSIONS: An intraoperative checklist is feasible to implement, low cost, quick and simple to measure with a significant reduction in the incidence of re-exploration for bleeding. This report shows an example of the positive effects of transparency in publishing outcomes' data in cardiac surgery.

Impactfactor: 1.329

Longgeneeskunde

Analysis of nocturnal actigraphic sleep measures in patients with COPD and their association with daytime physical activity

Spina G, Spruit MA, Alison J, Benzo RP, Calverley PMA, Clarenbach CF, Costello RW, Donaire-Gonzalez D, Dürr S, Garcia-Aymerich J, van Gestel AJR, Gramm M, Hernandes NA, Hill K, Hopkinson NS, Jarreta D, Kohler M, Kirsten AM, Leuppi JD, Magnussen H, Maltais F, Man WD, McKeough ZJ, Mesquita R, Miedinger D, Pitta F, Singh SJ, **Smeenk FW**, Tal-Singer R, Vagaggini B, Waschki B, Watz H, Wouters EFM, Zogg S, den Brinker AC

Thorax. 2017 Aug 72(8):694-701.. Epub 2017 Jan 12

BACKGROUND:

Sleep disturbances are common in patients with chronic obstructive pulmonary disease (COPD) with a considerable negative impact on their quality of life. However, factors associated with measures of sleep in daily life have not been investigated before nor has the association between sleep and the ability to engage in physical activity on a day-to-day basis been studied.

AIMS:

To provide insight into the relationship between actigraphic sleep measures and disease severity, exertional dyspnoea, gender and parts of the week; and to investigate the association between sleep measures and next day physical activity.

METHODS:

Data were analysed from 932 patients with COPD (66% male, 66.4±8.3 years, FEV1% predicted=50.8±20.5). Participants had sleep and physical activity continuously monitored using a multisensor activity monitor for a median of 6 days. Linear mixed effects models were applied to investigate the factors associated with sleep impairment and the association between nocturnal sleep and patients' subsequent daytime physical activity.

RESULTS:

Actigraphic estimates of sleep impairment were greater in patients with worse airflow limitation and worse exertional dyspnoea. Patients with better sleep measures (ie, non-fragmented sleep, sleeping bouts =225 min, sleep efficiency =91% and time spent awake after sleep onset <57 min) spent significantly more time in light ($p<0.01$) and moderate-to-vigorous physical activity ($p<0.01$).

CONCLUSIONS:

There is a relationship between measures of sleep in patients with COPD and the amount of activity they undertake during the waking day. Identifying groups with specific sleep characteristics may be useful information when designing physical activity-enhancing interventions.

Impactfactor: 8.272

Changes in pathogens and pneumococcal serotypes causing community-acquired pneumonia in The Netherlands

Vestjens SM, Wagenvoort GH, Grutters JC, Meek B, **Aldenkamp AF**, Vlaminckx BJ, Bos WJ, Rijkers GT, van de Garde EM

Vaccine. 2017 Jul 24;35(33):4112-4118

BACKGROUND:

In 2006 a 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the immunisation programme for infants in The Netherlands and replaced by PCV10 in 2011. Limited data exist about the impact of PCV on the aetiology of CAP as a whole. The aim of the present study is to describe the overall changes in microbial aetiology, pneumococcal burden (including non-bacteraemic pneumococcal pneumonia) and its serotypes in adult community-acquired pneumonia (CAP) after the introduction of these PCVs.

METHODS:

Hospitalised adult CAP patients who participated in three consecutive trials were studied (2004-2006 (n=201), 2007-2009 (n=304) and 2012-2016 (n=300) and considered as pre-PCV7, PCV7 and PCV10 period). Extensive conventional microbiological testing was applied for all patients. In addition, patients with a serotype-specific pneumococcal antibody response were diagnosed with pneumococcal CAP. Changes in proportions of causative pathogens and distributions of pneumococcal serotypes were calculated.

RESULTS:

The proportion of pneumococcal CAP decreased from 37% (n=74/201) to 26% (n=77/300) comparing the pre-PCV7 period with the PCV10 period ($p=0.01$). For other pathogens, including Legionella spp., Mycoplasma pneumoniae, S. aureus, H. influenzae, and respiratory viruses, no sustained shifts were observed in their relative contribution to the aetiology of CAP. Within the pneumococcal CAP patients,

we observed a decrease in PCV7 and an increase in non-PCV10 serotype disease. PCV10-extra type disease did not decrease significantly comparing the PCV10 period with the pre-PCV7 and PCV7 period, respectively. Notably, PCV7 type disease decreased both in bacteraemic and non-bacteraemic patients.

CONCLUSIONS:

Our findings confirm that PCV introduction in infants impact the microbial aetiology of adult CAP and suggest herd effects in adults with CAP after introduction of PCVs in children.

Impactfactor: 3.235

Dichotomous ALK-IHC Is a Better Predictor for ALK Inhibition Outcome than Traditional ALK-FISH in Advanced Non-Small Cell Lung Cancer

van der Wekken AJ, Pelgrim R, 't Hart N, Werner N, Mastik MF, Hendriks L, van der Heijden EH, Looijen-Salamon M, de Langen AJ, Staal-van den Brekel J, Riemersma S, **van den Borne BE**, Speel EJ, Dingemans AC, Hiltermann TJ, van den Berg A, Timens W, Schuuring E, Groen HJ

Clin Cancer Res. 2017 Aug 1 23(15):4251-4258. Epub 2017 Feb 9

Purpose: ALK rearrangement detection using FISH is the standard test to identify patients with non-small cell lung carcinoma (NSCLC) eligible for treatment with ALK inhibitors. Recently, ALK protein expression in resectable NSCLC showed predictive value. We evaluated tumor response rate and survival after crizotinib treatment of patients with advanced NSCLC with ALK activation using both dichotomous immunohistochemical (IHC) staining and FISH.Experimental Design: Patients with stage IV NSCLC treated with crizotinib were selected. Tumor response was assessed. ALK rearrangements were detected by FISH (Vysis ALK-break-apart FISH-Probe KIT) and IHC [Ventana ALK (D5F3) CDx assay]. Cohorts of patients with ALK-FISH-positive advanced NSCLC from four other hospitals were used for validation.Results: Twenty-nine consecutive patients with ALK-positive advanced NSCLC diagnosed by FISH and/or IHC on small biopsies or fine-needle aspirations (FNA) were treated with ALK inhibitors. All ALK-IHC-positive patients responded to crizotinib except three with primary resistance. No tumor response was observed in 13 ALK-FISH-positive but ALK-IHC-negative patients. This was confirmed in an external cohort of 16 patients. Receiver operator characteristic (ROC) curves for ALK-IHC and ALK-FISH compared with treatment outcome showed that dichotomous ALK-IHC outperforms ALK-FISH [tumor response area under the curve: (AUC), 0.86 vs. 0.64, P = 0.03; progression-free survival (PFS): AUC 0.86 vs. 0.36, P = 0.005; overall survival (OS): AUC, 0.78 vs. 0.41, P = 0.01, respectively].Conclusions: Dichotomous ALK-IHC is superior to ALK-FISH on small biopsies and FNA to predict tumor response and survival to crizotinib for patients with advanced NSCLC. Our data strongly suggest adapting the guidelines and using dichotomous ALK-IHC as standard companion diagnostic test to select patients with NSCLC who benefit from ALK-targeting therapy.

Impactfactor: 9.619

Nasal gene expression differentiates COPD from controls and overlaps bronchial gene expression

Boudewijn IM, Faiz A, Steiling K, van der Wiel E, Telenga ED, Hoonhorst SJM, Ten Hacken NHT, Brandsma CA, Kerstjens HAM, Timens W, Heijink IH, Jonker MR, de Bruin HG, Sebastiaan Vroegop J, Pasma HR, Boersma WG, **Wielders P**, van den Elshout F, Mansour K, Spira A, Lenburg ME, Guryev V, et al

Respir Res. 2017 Dec 21;18(1):213

BACKGROUND:

Nasal gene expression profiling is a promising method to characterize COPD non-invasively. We aimed to identify a nasal gene expression profile to distinguish COPD patients from healthy controls. We investigated whether this COPD-associated gene expression profile in nasal epithelium is comparable with the profile observed in bronchial epithelium.

METHODS:

Genome wide gene expression analysis was performed on nasal epithelial brushes of 31 severe COPD patients and 22 controls, all current smokers, using Affymetrix Human Gene 1.0 ST Arrays. We repeated the gene expression analysis on bronchial epithelial brushes in 2 independent cohorts of mild-to-moderate COPD patients and controls.

RESULTS:

In nasal epithelium, 135 genes were significantly differentially expressed between severe COPD patients and controls, 21 being up- and 114 downregulated in COPD (false discovery rate?<?0.01). Gene Set Enrichment Analysis (GSEA) showed significant concordant enrichment of COPD-associated nasal and bronchial gene expression in both independent cohorts (FDRGSEA <?0.001).

CONCLUSION: We identified a nasal gene expression profile that differentiates severe COPD patients from controls. Of interest, part of the nasal gene expression changes in COPD mimics differentially expressed genes in the bronchus. These findings indicate that nasal gene expression profiling is potentially useful as a non-invasive biomarker in COPD.

Impactfactor: 3.841

Physical activity patterns and clusters in 1001 patients with COPD

Mesquita R, Spina G, Pitta F, Donaire-Gonzalez D, Deering BM, Patel M, Mitchell KE, Alison J, van Gestel AJ, Zogg S, Gagnon P, Abascal-Bolado B, Vagaggini B, Garcia-Aymerich J, Jenkins SC, **Romme EA**, Kon SS, Albert PS, Waschki B, Shrikrishna D, Singh SJ, Hopkinson NS, Miedinger D, Benzo RP, Maltais F, Paggiaro P, McKeough ZJ, Polkey MI, Hill K, Man WD, Clarenbach CF, Hernandes NA, Savi D, Wootton S, Furlanetto KC, Cindy Ng LW, Vaes AW, Jenkins C, Eastwood PR, Jarreta D, Kirsten A, Brooks D, Hillman DR, Sant'Anna T, Meijer K, Dürr S, Rutten EP, Kohler M, Probst VS, Tal-Singer R, Gil EG, den Brinker AC, Leuppi JD, Calverley PM, **Smeenk FW**, Costello RW, Gramm M, Goldstein R31, Groenen MT, Magnussen H, Wouters EF, ZuWallack RL, Amft O, Watz H, Spruit MA

Chron Respir Dis. 2017 Aug;14(3):256-269

We described physical activity measures and hourly patterns in patients with chronic obstructive pulmonary disease (COPD) after stratification for generic and COPD-specific characteristics and, based on multiple physical activity measures, we identified clusters of patients. In total, 1001 patients with COPD (65% men; age, 67 years; forced expiratory volume in the first second [FEV1], 49% predicted) were studied cross-sectionally. Demographics, anthropometrics, lung function and clinical data were assessed. Daily physical activity measures and hourly patterns were analysed based on data from a multisensor armband. Principal component analysis (PCA) and cluster analysis were applied to physical activity measures to identify clusters. Age, body mass index (BMI), dyspnoea grade and ADO index (including age, dyspnoea and airflow obstruction) were associated with physical activity measures and hourly patterns. Five clusters were identified based on three PCA components, which accounted for 60% of variance of the data. Importantly, couch potatoes (i.e. the most inactive cluster) were characterised by higher BMI, lower FEV1, worse dyspnoea and higher ADO index compared to other clusters ($p < 0.05$ for all). Daily physical activity measures and hourly patterns are heterogeneous in COPD. Clusters of patients were identified solely based on physical activity data. These findings may be useful to develop interventions aiming to promote physical activity in COPD.

Impactfactor: 1.818

Re-certification of respiratory professionals: current practice and the future - educational forum report

Sehlbach C, Thomson C, Bennett J, Perez de Llano L, **Smeenk F**, Yokoyama A, Horváth I, Driessen E,

Rohde GBreathe (Sheff). 2017 Jun;13(2):77-80

Re-certification of respiratory professionals: a report of an @ERStalk education forum held at #ERSLDN16 http://ow.ly/pUKY30bzcrK.

Impactfactor: --

Talking about end-of-life care in a timely manner

Smeenk FW, Schrijver LA, van Bavel HC, van de Laar EF

Breathe 2017; 3(4): e95-e102

Geen abstract beschikbaar

Impactfactor: --

The contribution of an asthma diagnostic consultation service in obtaining an accurate asthma diagnosis for primary care patients: results of a real-life study

Gillis RM, **van Litsenburg W**, **van Balkom RH**, Muris JW, **Smeenk FW**.

NPJ Prim Care Respir Med. 2017 May 19; 27(1):35

Previous studies showed that general practitioners have problems in diagnosing asthma accurately, resulting in both under and overdiagnosis. To support general practitioners in their diagnostic process, an asthma diagnostic consultation service was set up. We evaluated the performance of this asthma diagnostic consultation service by analysing the (dis)concordance between the general practitioners working hypotheses and the asthma diagnostic consultation service diagnoses and possible consequences this had on the patients' pharmacotherapy. In total 659 patients were included in this study. At this service the patients' medical history was taken and a physical examination and a histamine challenge test were carried out. We compared the general practitioners working hypotheses with the

asthma diagnostic consultation service diagnoses and the change in medication that was incurred. In 52% (n?=?340) an asthma diagnosis was excluded. The diagnosis was confirmed in 42% (n?=?275). Furthermore, chronic rhinitis was diagnosed in 40% (n?=?261) of the patients whereas this was noted in 25% (n?=?163) by their general practitioner. The adjusted diagnosis resulted in a change of medication for more than half of all patients. In 10% (n?=?63) medication was started because of a new asthma diagnosis. The 'one-stop-shop' principle was met with 53% of patients and 91% (n?=?599) were referred back to their general practitioner, mostly within 6 months. Only 6% (n?=?41) remained under control of the asthma diagnostic consultation service because of severe unstable asthma. In conclusion, the asthma diagnostic consultation service helped general practitioners significantly in setting accurate diagnoses for their patients with an asthma hypothesis. This may contribute to diminish the problem of over and underdiagnosis and may result in more appropriate treatment regimens.

ASTHMA:

SERVICE HELPS GENERAL PRACTITIONERS MAKE ACCURATE DIAGNOSES: A consultation service can help general practitioners more accurately diagnose asthma and select the appropriate treatments for their patients. Researchers in The Netherlands, led by Frank Smeenk from Catharina Hospital in Eindhoven, describe an asthma diagnostic consultation service they created to support GPs in their diagnostic process for patients suspected of having asthma. Over a four-year period, the service received a total of 659 referrals and only confirmed the diagnosis of asthma in 275 cases. Another 20 patients had asthma overlapping with chronic obstructive pulmonary syndrome. The service also picked up other diseases, such as rhinitis, that general practitioners had missed. Overall, because of the consultation service and its revised diagnoses, more than half of all patients adjusted their medications. Most patients required only a single consultation and could then be referred back to their physicians.

Impactfactor: 2.793

The SQ House Dust Mite SLIT-Tablet Is Well Tolerated in Patients with House Dust Mite Respiratory Allergic Disease

Emminger W, Hernández MD, Cardona V, **Smeenk F**, Fogh BS, Calderon MA, de Blay F, Backer V

Int Arch Allergy Immunol. 2017;174(1):35-44

BACKGROUND:

The SQ house dust mite (HDM) SLIT-tablet (ALK, Denmark) addresses the underlying cause of HDM respiratory allergic disease, and a clinical effect has been demonstrated for both HDM allergic rhinitis and allergic asthma. Here, we present pooled safety data from an adult population with HDM respiratory allergy, with particular focus on the impact of asthma on the SQ HDM SLIT-tablet tolerability profile.

METHODS:

Safety data from 2 randomised double-blind, placebo-controlled clinical trials were included: MT-04: 834 adults with HDM allergic asthma not well controlled by inhaled corticosteroids and with HDM allergic rhinitis, and MT-06: 992 adults with moderate-to-severe HDM allergic rhinitis despite the use of allergy pharmacotherapy and with or without asthma.

RESULTS:

The proportion of subjects experiencing adverse events (AEs) was greater in the active treatment group (12 SQ-HDM; 73% of subjects) compared to placebo (53%). The most common treatment-related AEs were local allergic reactions. No AEs were reported as systemic allergic reactions. Regardless of asthma status, most AEs were mild or moderate (>97% of AEs) and the frequency of serious AEs was low. Subgroup analysis revealed no statistically significant difference in the risk of experiencing moderate or severe treatment-related AEs for subjects with asthma compared to subjects without asthma (p = 0.88). In addition, subjects with partly controlled or uncontrolled asthma were no more likely to experience moderate or severe treatment-related AEs than subjects with controlled asthma (p = 0.42).

CONCLUSION:

The SQ HDM SLIT-tablet is well tolerated, and the safety profile was comparable for subjects with HDM respiratory allergic disease irrespective of asthma status.

Impactfactor: 2.72

Maag- Darm- Leverziekten

An unexpected cause of nausea and vomiting in a patient with metastasised lung cancer

Bouma HR, **Schreuder RM**

Neth J Med. 2017 Jun;75(5):215

Geen abstract beschikbaar

Ten tijde van publicatie verbonden aan: Department of Gastroenterology, University Medical Center Groningen

Impactfactor: 1.244

Computer-aided detection of early Barrett's neoplasia using volumetric laser endomicroscopy

Swager AF, van der Sommen F, Klomp SR, Zinger S, Meijer SL, **Schoon EJ**, Bergman JJGHM, de With PH, **Curvers WL**

Gastrointest Endosc. 2017 Nov 86(5):839-846. Epub 2017 Mar 16

BACKGROUND AND AIMS:

Volumetric laser endomicroscopy (VLE) is an advanced imaging system that provides a near-microscopic resolution scan of the esophageal wall layers up to 3-mm deep. VLE has the potential to improve detection of early neoplasia in Barrett's esophagus (BE). However, interpretation of VLE images is complex because of the large amount of data that need to be interpreted in real time. The aim of this study was to investigate the feasibility of a computer algorithm to identify early BE neoplasia on ex vivo VLE images.

METHODS:

We used 60 VLE images from a database of high-quality ex vivo VLE-histology correlations, obtained from BE patients ± neoplasia (30 nondysplastic BE [NDBE] and 30 high-grade dysplasia/early adenocarcinoma images). VLE features from a recently developed clinical VLE prediction score for BE neoplasia served as input for the algorithm: (1) higher VLE surface than subsurface signal and (2) lack of layering. With this input, novel clinically inspired algorithm features were developed, based on signal intensity statistics and grayscale correlations. For comparison, generic image analysis methods were examined for their performance to detect neoplasia. For classification of the images in the NDBE or neoplastic group, several machine learning methods were evaluated. Leave-1-out cross-validation was used for algorithm validation.

RESULTS:

Three novel clinically inspired algorithm features were developed. The feature "layering and signal decay statistics" showed the optimal performance compared with the other clinically features ("layering" and "signal intensity distribution") and generic image analyses methods, with an area under the receiver operating characteristic curve (AUC) of .95. Corresponding sensitivity and specificity were 90% and 93%, respectively. In addition, the algorithm showed a better performance than the clinical VLE prediction score (AUC .81).

CONCLUSIONS:

This is the first study in which a computer algorithm for BE neoplasia was developed based on VLE images with direct histologic correlates. The algorithm showed good performance to detect BE neoplasia in ex vivo VLE images compared with the performance of a recently developed clinical VLE prediction score. This study suggests that an automatic detection algorithm has the potential to assist endoscopists in detecting early neoplasia on VLE. Future studies on in vivo VLE scans are needed to further validate the algorithm.

Impactfactor: 6.501

Double-Balloon Endoscopy in Overt and Occult Small Bowel Bleeding: Results, Complications, and Correlation with Prior Videocapsule Endoscopy in a Tertiary Referral Center

Hermans C, **Stronkhorst A**, Tjhie-Wensing A, Kamphuis J, Balkom BV, Dahlmans R, **Gilissen L**

Clin Endosc. 2017 Jan 50(1):69-75. doi: 10.5946/ce.2016.079. Epub 2017 Jan 12

BACKGROUND/AIMS:

Videocapsule endoscopy (VCE) and double-balloon endoscopy (DBE) allow deep exploration in patients with suspected small bowel pathology. VCE is often performed as an initial small bowel examination to explore whether an intervention by DBE is indicated and to determine insertion route. The study aim was to evaluate the correlation between DBE and VCE in patients with obscure or overt bleeding or anemia, as well as intervention frequency, and complications.

METHODS:

Retrospective observational study.

RESULTS:

DBE procedures (n=205) showed small bowel lesions in 64% cases. Antegrade DBE showed positive results in 79% cases, mostly angiodysplasias (63%). Retrograde DBE showed positive results in 22% cases. An intervention was performed in 64% of DBE procedures. The major complication rate was 0.5%, which was one case of perforation. Pancreatitis did not occur. The overall diagnostic agreement was 66% among the 134 DBEs with preceded VCE.

CONCLUSIONS:

In cases of overt or occult bleeding or anemia, DBE was positive in 64%, with only a few complications. Positive correlation was 66% among initially performed VCEs and DBEs. Owing to the time-consuming and invasive character of DBE, performing VCE before DBE might still be clinically relevant.

Impactfactor: --

Early prediction of thiopurine-induced hepatotoxicity in inflammatory bowel disease

Wong DR, Coenen MJ, Derijks LJ, Vermeulen SH, van Marrewijk CJ, Klungel OH, Scheffer H, Franke B, Guchelaar HJ, de Jong DJ, Engels LG, Verbeek AL, Hooymans PM; TOPIC Recruitment Team: **Stronkhorst A, Gilissen LP, Schoon EJ**

Aliment Pharmacol Ther. 2017 Feb;45(3):391-402

BACKGROUND:

Hepatotoxicity, gastrointestinal complaints and general malaise are common limiting adverse reactions of azathioprine and mercaptopurine in IBD patients, often related to high steady-state 6-methylmercaptopurine ribonucleotide (6-MMPR) metabolite concentrations.

AIM:

To determine the predictive value of 6-MMPR concentrations 1 week after treatment initiation (T1) for the development of these adverse reactions, especially hepatotoxicity, during the first 20 weeks of treatment.

METHODS:

The cohort study consisted of the first 270 IBD patients starting thiopurine treatment as part of the Dutch randomised-controlled trial evaluating pre-treatment thiopurine S-methyltransferase genotype testing (ClinicalTrials.gov NCT00521950). Blood samples for metabolite assessment were collected at T1. Hepatotoxicity was defined by alanine aminotransaminase elevations >2 times the upper normal limit or a ratio of alanine aminotransaminase/alkaline phosphatase =5.

RESULTS:

Forty-seven patients (17%) presented hepatotoxicity during the first 20 weeks of thiopurine treatment. A T1 6-MMPR threshold of 3615 pmol/8 × 108 erythrocytes was defined. Analysis of patients on stable thiopurine dose (n = 174) showed that those exceeding the 6-MMPR threshold were at increased risk of hepatotoxicity: OR = 3.8 (95% CI: 1.8-8.0). Age, male gender and BMI were significant determinants. A predictive algorithm was developed based on these determinants and the 6-MMPR threshold to assess hepatotoxicity risk [AUC = 0.83 (95% CI: 0.75-0.91)]. 6-MMPR concentrations above the threshold also correlated with gastrointestinal complaints: OR = 2.4 (95% CI: 1.4-4.3), and general malaise: OR = 2.0 (95% CI: 1.1-3.7).

CONCLUSIONS:

In more than 80% of patients, thiopurine-induced hepatotoxicity could be explained by elevated T1 6-MMPR concentrations and the independent risk factors age, gender and BMI, allowing personalised thiopurine treatment in IBD to prevent early failure.

Impactfactor: *7.286*

Eradication of Barrett's neoplasia: endoscopy vs. laparoscopy

Schoon E

Endoscopy. 2017 Jul;49(7):629-630

Geen abstract beschikbaar

Impactfactor: *6.107*

Evaluation of image features and classification methods for Barrett's cancer detection using VLE imaging

Klomp S, van der Sommen F, Swager A, Zinger S, **Schoon EJ, Curvers WL**, Bergman JJ, de With PN

Proc SPIE 10134, Medical Imaging 2017: Computer-Aided Diagnosis, 101340D March 3

Volumetric Laser Endomicroscopy (VLE) is a promising technique for the detection of early neoplasia in Barrett’s Esophagus (BE). VLE generates hundreds of high resolution, grayscale, cross-sectional images of

the esophagus. However, at present, classifying these images is a time consuming and cumbersome effort performed by an expert using a clinical prediction model. This paper explores the feasibility of using computer vision techniques to accurately predict the presence of dysplastic tissue in VLE BE images. Our contribution is threefold. First, a benchmarking is performed for widely applied machine learning techniques and feature extraction methods. Second, three new features based on the clinical detection model are proposed, having superior classification accuracy and speed, compared to earlier work. Third, we evaluate automated parameter tuning by applying simple grid search and feature selection methods. The results are evaluated on a clinically validated dataset of 30 dysplastic and 30 non-dysplastic VLE images. Optimal classification accuracy is obtained by applying a support vector machine and using our modified Haralick features and optimal image cropping, obtaining an area under the receiver operating characteristic of 0.95 compared to the clinical prediction model at 0.81. Optimal execution time is achieved using a proposed mean and median feature, which is extracted at least factor 2.5 faster than alternative features with comparable performance.

Impactfactor: --

Feasibility of laser marking in Barrett's esophagus with volumetric laser endomicroscopy: first-in-man pilot study

Swager AF, de Groof AJ, Meijer SL, Weusten BL, **Curvers WL**, Bergman JJ

Gastrointest Endosc. 2017 Sep;86(3):464-472. Epub 2017 Feb 2

BACKGROUND AND AIM:

Volumetric laser endomicroscopy (VLE) provides a circumferential scan of the esophageal wall layers and has potential to improve detection of neoplasia in Barrett's esophagus (BE). The novel VLE laser marking system enables direct in vivo marking of suspicious areas as identified on VLE. These laser marked areas can subsequently be targeted for biopsies. The aim was to evaluate the visibility and positional accuracy of laser marks (LMs) in different esophageal tissue types on white light endoscopy (WLE) and VLE.

METHODS:

Patients with BE with or without neoplasia underwent imaging with VLE. Protocol refinements were practiced in a learning phase. In the second phase, visibility of LMs was assessed by random marking in squamous, BE, and gastric tissue. In phase 3, positional accuracy of the LMs was tested by identifying and laser marking surrogate targets (endoscopically placed cautery marks). In the final phase, the most suspicious areas for neoplasia were identified in each patient using VLE, targeted by LMs, and biopsy samples subsequently obtained.

RESULTS:

Sixteen patients with BE were included (14 men; median age, 68 years), 1 of whom was included twice in different study phases. Worst histologic diagnoses were 9 non-dysplastic Barrett's esophagus (NDBE), 3 low-grade dysplasia (LGD), 4 high-grade dysplasia (HGD), and 1 early adenocarcinoma (EAC). In total, 222 LMs were placed, of which 97% was visible on WLE. All LMs were visible on VLE directly after marking, and 86% could be confirmed during post hoc analysis. LM targeting was successful with positional accuracy in 85% of cautery marks. Inaccurate targeting was caused by system errors or difficult cautery mark visualization on VLE. In the final phase (5 patients), 18 areas suspicious on VLE were identified, which were all successfully targeted by LMs (3 EAC, 3 HGD, 1 LGD, and 11 NDBE). Mean VLE procedure time was 22 minutes (±6 minutes standard deviation); mean endoscopy time was 56 minutes (±17 minutes). No adverse events were reported.

CONCLUSIONS:

This first-in-human study of VLE-guided laser marking was found to be feasible and safe in 17 procedures. Most LMs were visible on WLE and VLE. Targeting VLE areas of interest proved to be highly successful. VLE-guided laser marking may improve the detection and delineation of Barrett's neoplasia in the future.

Impactfactor: *6.501*

Identification of volumetric laser endomicroscopy features predictive for early neoplasia in Barrett's esophagus using high-quality histological correlation

Swager AF, Tearney GJ, Leggett CL, van Oijen MG, Meijer SL, Weusten BL, **Curvers WL**, Bergman JJ

Gastrointest Endosc. 2017 May; 85(5):918-926.e7. Epub 2016 Sep 19

BACKGROUND AND AIMS: Volumetric laser endomicroscopy (VLE) provides a circumferential scan that enables visualization of the subsurface layers of the esophageal wall at 7 μm resolution. The aims of this study were to identify VLE features of Barrett's esophagus (BE) neoplasia and to develop a VLE

prediction
score.
METHODS: A database of VLE images from endoscopic resection specimens, precisely correlated with histology, from patients with BE with and without neoplasia was used. Features potentially predictive for early BE neoplasia were identified by unblinded evaluation of 25 VLE-histology images. In a learning phase, 20 VLE images with or without BE neoplasia were scored by 2 VLE experts, blinded to histology. A prediction score was created by using multivariable logistic regression analyses and validated by scoring 40 VLE images (50% neoplastic) by using area under receiver operating characteristic (ROC) curve (AUC) analysis.
RESULTS: Three VLE features independently predictive for BE neoplasia were identified: (1) lack of layering; (2) higher surface than subsurface signal; (3) presence of irregular, dilated glands/ducts. A VLE neoplasia prediction score was developed with the following: (1) 6 points; (2) 6 or 8 points for equal or higher
surface signal; and (3) 5 points. The ROC curve of this prediction score showed an AUC of 0.81 (95% confidence interval, 0.71-0.90). A cut-off value of =8 wasassociated with sensitivity and specificity of 83% and 71%, respectively.
CONCLUSIONS: When high-quality ex vivo VLE-histology correlation was used, the VLE features of layering, surface signal, and irregular glands/ducts were independently and significantly associated with BE neoplasia. A VLE prediction score for BE neoplasia was developed and validated, with promising accuracy.

Impactfactor: 6.501

Percutaneous endoscopic gastrostomy under conscious sedation in patients with amyotrophic lateral sclerosis is safe: an observational study

Strijbos D, Hofstede J, Keszthelyi D, Masclee AAM, **Gilissen LP**

Eur J Gastroenterol Hepatol. 2017 Nov;29(11):1303-1308

OBJECTIVES:
Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease that causes muscle weakness with respiratory and swallowing dysfunction, eventually leading to death. Permanent enteral feeding is indicated in almost all patients. A percutaneous endoscopic gastrostomy (PEG) tube is considered the first choice, usually performed under conscious sedation (intravenous midazolam). Guidelines are very cautious with respect to sedation in ALS because of the risk for respiratory complications. In our tertiary referral hospital, conscious sedation has been used for many years.Our aim was to review 30-day complications in PEG performed under conscious sedation in ALS patients (without noninvasive positive pressure ventilation during the procedure).
PATIENTS AND METHODS:
A retrospective review, including all ALS patients undergoing PEG under conscious sedation from October 2009 to April 2016, was performed.
RESULTS:
Analyis included 45 (44% men) patients receiving intravenous midazolam sedation (mean dose 5?mg) during PEG placement, age 36-91 years (mean: 68.7 years). Forced vital capacity (FVC) was 24-116% (mean 68%), of which mild to moderate dysfunction (FVC 50-69%) was present in 42.2% of patients and (very) severe dysfunction (FVC <50%) in 8.8%. No respiratory complications (e.g. aspiration pneumonia) were observed. Other complications, for example, infection, bleeding and peritonitis occurred in, respectively, 8.9, 2.2 and 0%. Mean survival after PEG placement was 13.4 months (range: 1-45 months).
CONCLUSION:
Conscious sedation during PEG insertion in ALS patients did not lead to respiratory complications or to an increase in other complications. Our data indicate that conscious sedation can be used safely in ALS patients with mild to moderate pulmonary dysfunction.

Impactfactor: 1.968

Pit pattern analysis with high-definition chromoendoscopy and narrow-band imaging for optical diagnosis of dysplasia in patients with ulcerative colitis

Bisschops R, Bessissow T, Dekker E, East JE, Para-Blanco A, Ragunath K, Bhandari P, Rutter M, **Schoon E**, Wilson A, John JM, Van Steen K, Baert F, Ferrante M

Gastrointest Endosc. 2017 Dec;86(6):1100-1106.e1

BACKGROUND AND AIMS:
Patients with longstanding ulcerative colitis (UC) are at increased risk of developing colorectal neoplasia. Chromoendoscopy (CE) increases detection of lesions, and Kudo pit pattern classification I and II have been suggested to be predictive of benign polyps in UC. Little is known on the use of this classification in nonmagnified high-definition (HD) (virtual) CE and narrow-band Imaging (NBI) or on the interobserver agreement. The aim of this pilot study was to assess the diagnostic accuracy and the interobserver agreement of the Kudo pit pattern classification in UC patients undergoing surveillance with methylene blue CE or NBI in a multicenter study.
METHODS:
Fifty images of lesions identified in 27 UC patients (13 neoplastic) either with classical CE (methylene blue .1%; n = 24) or NBI (n = 26) were selected by an independent investigator. Images were selected from a randomized controlled trial to compare CE and NBI. All nonmagnified images were obtained with a processor and mounted in a PowerPoint file in a standardized way (same size; black background). Ten endoscopists with extensive experience in NBI/CE were asked to assess the lesions for the predominant Kudo pit pattern (I, II, IIIL, IIIS, IV, and V) to indicate if they believed the lesion was neoplastic and how confident they were about the diagnosis. Histology was used as the criterion standard.
RESULTS:
Median sensitivity, specificity, negative predictive value, and positive predictive value for diagnosing neoplasia based on the presence of pit pattern other than I or II was 77%, 68%, 88%, and 46%, respectively. Diagnostic accuracy was significantly higher when a diagnosis was made with a high level of confidence (77% vs 21%, P < .001). The overall interobserver agreement for any pit pattern was only fair (? = .282), with CE being significantly better than NBI (.322 vs .224, P < .001). From a clinical viewpoint the difference between neoplastic and non-neoplastic lesions is important. The agreement for differentiation between non-neoplastic patterns (I, II) and neoplastic patterns (IIIL, IIIS, IV, or V) was moderate (? = .587) and even significantly better for NBI in comparison with CE (? = .653 vs .495, P < .001).
CONCLUSIONS:
Differentiation between non-neoplastic and neoplastic pit patterns in UC lesions shows a moderate to substantial agreement among expert endoscopists. The agreement for differentiating neoplastic from non-neoplastic lesions is significantly better for NBI in comparison with HD CE. The assessment of pit pattern I or II with nonmagnified HD CE or NBI has a high negative predictive value to rule out neoplasia.
Impactfactor: 6.501

Quantitative attenuation analysis for identification of early Barrett's neoplasia in volumetric laser endomicroscopy

Swager AF, Faber DJ, de Bruin DM, Weusten BL, Meijer SL, Bergman JJ, **Curvers WL**, van Leeuwen TG
J Biomed Opt. 2017 Aug 1;22(8):86001

Early neoplasia in Barrett's esophagus (BE) is difficult to detect. Volumetric laser endomicroscopy (VLE) incorporates optical coherence tomography, providing a circumferential scan of the esophageal wall layers. The attenuation coefficient (μVLE) quantifies decay of detected backscattered light versus depth, and could potentially improve BE neoplasia detection. The aim is to investigate feasibility of μVLE for identification of early BE neoplasia. In vivo and ex vivo VLE scans with histological correlation from BE patients ± neoplasia were used. Quantification by μVLE was performed manually on areas of interest (AoIs) to differentiate neoplasia from nondysplastic (ND)BE. From ex vivo VLE scans from 16 patients (13 with neoplasia), 68 AoIs were analyzed. Median μVLE values (mm-1) were 3.7 [2.1 to 4.4 interquartile range (IQR)] for NDBE and 4.0 (2.5 to 4.9 IQR) for neoplasia, not statistically different (p=0.82). Fourteen in vivo scans were used: nine from neoplastic and five from NDBE patients. Median μVLE values were 1.8 (1.5 to 2.6 IQR) for NDBE and 2.1 (1.9 to 2.6 IQR) for neoplasia, with no statistically significant difference (p=0.37). In conclusion, there was no significant difference in μVLE values in VLE scans from early neoplasia versus NDBE. Future studies with a larger sample size should explore other quantitative methods for detection of neoplasia during BE surveillance.
Impactfactor: 2.530

Short article: The effect of implementation of a treatment algorithm for infliximab on remission rates and drug costs in inflammatory bowel disease patients

Taks M, **Pijls PA**, Derijks LJ, Ten Broeke R, Grouls RJ, Curvers J, **Gilissen LP**
Eur J Gastroenterol Hepatol. 2017 Feb;29(2):169-173

INTRODUCTION:
The effective, but expensive, drug infliximab is used in patients with inflammatory bowel disease (IBD). Monitoring infliximab trough levels and anti-infliximab antibody (ATI) formation can lead to a more cost-effective use of infliximab therapy. The aim of our study was to investigate the effect of implementation of a treatment algorithm for infliximab in a single-centre IBD cohort, focussing on remission rates and drug costs.
METHODS:
IBD patients aged 18 years or older treated with infliximab were asked to participate in this study. Remission rates were assessed using faecal calprotectin levels and a validated questionnaire. Infliximab trough levels and ATIs were determined at baseline and at the third infliximab infusion. According to the advice given by the treatment algorithm, infliximab dosage adjustments were performed at the second infliximab infusion.
RESULTS:
Between January and December 2015 a total of 62 IBD patients in our centre were treated with infliximab, of whom 33 (53%) patients agreed to participate in this study. The number of patients in remission was 28 (85%) at baseline and there were 13 dose adaptations suggested by the treatment algorithm for the successive second infusion. Four patients possessed undetectable infliximab levels and positive ATI status at baseline. After the second infusion, there were 29 (88%) patients in remission at the third infusion. All of this resulted in an annual drug cost reduction of &OV0556;47?026 (7.4%).
CONCLUSION:
Our developed treatment algorithm of infliximab led to optimization of infliximab therapy in IBD patients by increasing remission rates and reducing drug costs.

Impactfactor: 2.093

The cost-effectiveness of radiofrequency ablation for Barrett's esophagus with low-grade dysplasia: results from a randomized controlled trial (SURF trial)

Phoa KN, Rosmolen WD, Weusten BLAM, Bisschops R, **Schoon EJ**, Das S, Ragunath K, Fullarton G, DiPietro M, Ravi N, Tijssen JGP, Dijkgraaf MGW, Bergman JJGHM,SURF investigators

Gastrointest Endosc. 2017 Jul 86(1):120-129.e2. Epub 2016 Dec 9

BACKGROUND AND AIMS: The Surveillance versus Radiofrequency Ablation (SURF) trial randomized 136 patients with Barrett's esophagus (BE) containing low-grade dysplasia (LGD), to receive radiofrequency ablation (ablation, n = 68) or endoscopic surveillance (control, n = 68). Ablation reduced the risk of neoplastic progression to high-grade dysplasia and esophageal adenocarcinoma (EAC) by 25% over 3 years (1.5% for ablation vs 26.5% for control). We performed a cost-effectiveness analysis from a provider perspective alongside this trial.
METHODS: Patients were followed for 3 years to quantify their use of health care services, including therapeutic and surveillance endoscopies, treatment of adverse events, and medication. Costs for treatment of progression were analyzed separately. Incremental cost-effectiveness ratios (ICER) were calculated by dividing the difference in costs (excluding and including the downstream costs for treatment of progression) by the difference in prevented events of progression. Bootstrap analysis (1000 samples) was used to construct 95% confidence intervals (CIs).
RESULTS: Patients who underwent ablation generated mean costs of U.S.$13,503 during the trial versus $2236 for controls (difference $11,267; 95% CI, $9996-$12,378), with an ICER per prevented event of progression of $45,066. Including the costs for treatment of progression, ablation patients generated mean costs of $13,523 versus $4,930 for controls (difference $8593; 95% CI, $6881-$10,153) with an ICER of $34,373. Based on the various ICER estimates derived from the bootstrap analysis, one can be reasonably certain (>75%) that ablation is efficient at a willingness to pay of $51,664 per prevented event of progression or $40,915 including downstream costs of progression.
CONCLUSIONS: Ablation for patients with confirmed BE-LGD is more effective and more expensive than endoscopic surveillance in reducing the risk of progression to high-grade dysplasia/EAC. The increase in costs of ablation can be justified to avoid a serious event such as neoplastic progression. At a willingness to pay of $40,915 per prevented event of progression, one can be reasonably certain that ablation is efficient.

Impactfactor: 6.501

Neurologie

Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands)

Mulder MJ, Ergezen S, Lingsma HF, Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lycklama À, Nijeholt G, Emmer BJ, van der Worp HB, Nederkoorn PJ, Roos YB, van Oostenbrugge RJ, van Zwam WH, Majoie CB, van der Lugt A, Dippel DW; Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) Investigators: **Keizer K,** Tielbeek AV

Stroke. 2017 Jul;48(7):1869-1876

BACKGROUND AND PURPOSE:

High blood pressure (BP) is associated with poor outcome and the occurrence of symptomatic intracranial hemorrhage in acute ischemic stroke. Whether BP influences the benefit or safety of intra-arterial treatment (IAT) is not known. We aimed to assess the relation of BP with functional outcome, occurrence of symptomatic intracranial hemorrhage and effect of IAT.

METHODS:

This is a post hoc analysis of the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands). BP was measured at baseline, before IAT or stroke unit admission. We estimated the association of baseline BP with the score on the modified Rankin Scale at 90 days and safety parameters with ordinal and logistic regression analysis. Effect of BP on the effect of IAT was tested with multiplicative interaction terms.

RESULTS:

Systolic BP (SBP) had the best correlation with functional outcome. This correlation was U-shaped; both low and high baseline SBP were associated with poor functional outcome. Higher SBP was associated with symptomatic intracranial hemorrhage (adjusted odds ratio, 1.25 for every 10 mm Hg higher SBP [95% confidence interval, 1.09-1.44]). Between SBP and IAT, there was no interaction for functional outcome, symptomatic intracranial hemorrhage, or other safety parameters; the absolute benefit of IAT was evident for the whole SBP range. The same was found for diastolic BP.

CONCLUSIONS:

BP does not affect the benefit or safety of IAT in patients with acute ischemic stroke caused by proximal intracranial vessel occlusion. Our data provide no arguments to withhold or delay IAT based on BP.

Impactfactor: 6.032

Cerebellar Disease Mimicking Cerebrotendinous Xanthomatosis: Langerhans Cell Histiocytosis

Stelten BM, van der Knaap MS, Wevers RA, Verrips A

Pediatr Neurol. 2017 Aug;73:98-100

BACKGROUND:

This report highlights the differential diagnosis of predominant cerebellar white matter abnormalities with dentate nuclei involvement.

PATIENT DESCRIPTION:

We describe two individuals with Langerhans cell histiocytosis in whom the diagnosis of cerebrotendinous xanthomatosis was initially considered. The clinical picture consisted of a progressive cerebellar syndrome with typical magnetic resonance imaging abnormalities. In both individuals, the cerebellar syndrome preceded the diagnosis of Langerhans cell histiocytosis.

CONCLUSIONS:

The magnetic resonance imaging abnormalities and neurological features in patients with Langerhans cell histiocytosis can be strikingly similar to those with cerebrotendinous xanthomatosis. In cerebrotendinous xanthomatosis, the cerebellar symptoms and cerebellar white matter abnormalities are usually seen in adult patients. In a pediatric patient with a cerebellar syndrome, showing these cerebellar white matter abnormalities a diagnosis of Langerhans cell histiocytosis is more likely.

Ten tijde van het onderzoek verbonden aan het Canisius Wilhelmina Ziekenhuis

Impactfactor: 2.018

Comparison of 2D (RANO) and volumetric methods for assessment of recurrent glioblastoma treated with bevacizumab-a report from the BELOB trial

Gahrmann R, van den Bent M, van der Holt B, Vernhout RM, Taal W, Vos M, de Groot JC, Beerepoot LV, Buter J, Flach ZH, **Hanse M**, Jasperse B, Smits M

Neuro Oncol. 2017 Jun 1 19(6):853-861

Background:
The current method for assessing progressive disease (PD) in glioblastoma is according to the Response Assessment in Neuro-Oncology (RANO) criteria. Bevacizumab-treated patients may show pseudo-response on postcontrast T1-weighted (T1w) MRI, and a more infiltrative non-enhancing growth pattern on T2w/fluid attenuated inversion recovery (FLAIR) images. We investigated whether the RANO criteria remain the method of choice for assessing bevacizumab-treated recurrent glioblastoma when compared with various volumetric methods.
Methods:
Patients with assessable MRI data from the BELOB trial (n = 148) were included. Patients were treated with bevacizumab, lomustine, or both. At first and second radiological follow-up (6 and 12 wk), PD was determined using the 2D RANO criteria and various volumetric methods based on enhancing tumor only and enhancing plus non-enhancing tumor. Differences in overall survival (OS) between PD and non-PD patients were assessed with the log-rank test and a Cox model. Hazard ratios (HRs) and their 95% CIs were determined.
Results:
For all patients together, all methods (except subtraction of non-enhancing from enhancing volume at first follow-up) showed significant differences in OS between PD and non-PD patients ($P < .001$). The largest risk increase for death in case of PD at both first and second follow-up was found with the RANO criteria: HR = 2.81 (95% CI, 1.92-4.10) and HR = 2.80 (95% CI, 1.75-4.49), respectively. In the bevacizumab-treated patients, all methods assessed showed significant differences in OS between PD and non-PD patients. There were no significant differences between methods.
Conclusions:
In the first 12 weeks, volumetric methods did not provide significant improvement over the RANO criteria as a posttreatment prognostic marker.

Impactfactor: 7.786

Controversies in MS: All relapsing multiple sclerosis patients should be managed at a specialist clinic - Combine the best of two worlds!

Hengstman GJ

Mult Scler. 2017 Jun; 23(7):1041. Epub 2016 Sep 21

Geen abstract beschikbaar

Impactfactor: 4.840

Hyperglycemia predicts poststroke infections in acute ischemic stroke

Zonneveld TP, Nederkoorn PJ, Westendorp WF, Brouwer MC, van de Beek D, Kruyt ND; PASS Investigators:

Keizer K

Neurology. 2017 Apr 11;88(15):1415-1421

OBJECTIVE:
To investigate whether admission hyperglycemia predicts poststroke infections and, if so, whether poststroke infections modify the effect of admission hyperglycemia on functional outcome in ischemic stroke.
METHODS:
We used data from acute ischemic stroke patients in the Preventive Antibiotics in Stroke Study (PASS), a multicenter randomized controlled trial (n = 2,550) investigating the effect of preventive antibiotics on functional outcome. Admission hyperglycemia was defined as blood glucose =7.8 mmol/L and poststroke infection as any infection during admission judged by an expert adjudication committee. Functional outcome at 3 months was assessed with the modified Rankin Scale.
RESULTS:
Of 1,676 nondiabetic ischemic stroke patients, 338 (20%) had admission hyperglycemia. After adjustment for potential confounding variables, admission hyperglycemia was associated with poststroke infection (adjusted odds ratio [aOR] 2.31, 95% CI 1.31-4.07), worse 3-month functional outcome (common aOR 1.40, 95% CI 1.12-1.73), and 3-month mortality (aOR 2.11, 95% CI 1.40-3.19). Additional adjustment for poststroke infection in the functional outcome analysis, done to assess poststroke infection as an intermediate in the pathway from admission hyperglycemia to functional outcome, did not substantially change the model. In patients with recorded diabetes mellitus (n = 418), admission hyperglycemia was not associated with poststroke infection (aOR 0.49, 95% CI 0.15-1.58).

CONCLUSIONS:

In nondiabetic acute ischemic stroke patients, admission hyperglycemia is associated with poststroke infection and worse functional outcome. Poststroke infections did not modify the effect of admission hyperglycemia on functional outcome in ischemic stroke.

Impactfactor: *8.320*

[Neurogenic thoracic outlet syndrome] - Neurogeen thoracic-outletsyndroom

Teijink JA, Pesser N, van Grinsven R, van Suijlekom H, van Sambeek MR, **van Nuenen BF**

Ned Tijdschr Geneeskd. 2017;161(0):D1385

Neurogenic thoracic outlet syndrome (nTOS) is a type of thoracic outlet syndrome (TOS) where compression of the brachial plexus is responsible for development of upper-extremity, head and neck symptoms. We present a 16-year-old and a 34-year-old patient with nTOS. Diagnosis in both cases was done by following the recently published reporting standards for (n)TOS. After this multidisciplinary diagnostic work-up we performed a transaxillary thoracic outlet decompression (TOD). Due to lack of literature, difficult nomenclature and complexity of diagnosis and treatment, diagnosis of nTOS is often delayed. Recent experience shows that treatment of nTOS is safe and effective, both in the short term and the long term.

Impactfactor: --

Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma

Perry JR, Laperriere N, O'Callaghan CJ, Brandes AA, Menten J, Phillips C, Fay M, Nishikawa R, Cairncross JG, Roa W, Osoba D, Rossiter JP, Sahgal A, Hirte H, Laigle-Donadey F, Franceschi E, Chinot O, Golfinopoulos V, Fariselli L, Wick A, Feuvret L, Back M, Tills M, Winch C, Baumert BG, Wick W, Ding K, Mason WP; Trial Investigators:

Hanse MC

N Engl J Med. 2017 Mar 16;376(11):1027-1037

BACKGROUND:

Glioblastoma is associated with a poor prognosis in the elderly. Survival has been shown to increase among patients 70 years of age or younger when temozolomide chemotherapy is added to standard radiotherapy (60 Gy over a period of 6 weeks). In elderly patients, more convenient shorter courses of radiotherapy are commonly used, but the benefit of adding temozolomide to a shorter course of radiotherapy is unknown.

METHODS:

We conducted a trial involving patients 65 years of age or older with newly diagnosed glioblastoma. Patients were randomly assigned to receive either radiotherapy alone (40 Gy in 15 fractions) or radiotherapy with concomitant and adjuvant temozolomide.

RESULTS:

A total of 562 patients underwent randomization, 281 to each group. The median age was 73 years (range, 65 to 90). The median overall survival was longer with radiotherapy plus temozolomide than with radiotherapy alone (9.3 months vs. 7.6 months; hazard ratio for death, 0.67; 95% confidence interval [CI], 0.56 to 0.80; P<0.001), as was the median progression-free survival (5.3 months vs. 3.9 months; hazard ratio for disease progression or death, 0.50; 95% CI, 0.41 to 0.60; P<0.001). Among 165 patients with methylated O6-methylguanine-DNA methyltransferase (MGMT) status, the median overall survival was 13.5 months with radiotherapy plus temozolomide and 7.7 months with radiotherapy alone (hazard ratio for death, 0.53; 95% CI, 0.38 to 0.73; P<0.001). Among 189 patients with unmethylated MGMT status, the median overall survival was 10.0 months with radiotherapy plus temozolomide and 7.9 months with radiotherapy alone (hazard ratio for death, 0.75; 95% CI, 0.56 to 1.01; P=0.055; P=0.08 for interaction). Quality of life was similar in the two trial groups.

CONCLUSIONS:

In elderly patients with glioblastoma, the addition of temozolomide to short-course radiotherapy resulted in longer survival than short-course radiotherapy alone.

Impactfactor: *72.406*

Topographic distribution of cerebral infarct probability in patients with acute ischemic stroke: mapping of intra-arterial treatment effect

Boers AM, Berkhemer OA, Slump CH, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Yoo AJ, Dippel DW, Marquering HA, Majoie CB1; MR CLEAN trial investigators: **Keizer K,** Tielbeek AV

J Neurointerv Surg. 2017 May;9(5):431-436. doi: 10.1136/neurintsurg-2016-012387. Epub 2016 Apr 25

BACKGROUND:

Since proof emerged that IA treatment (IAT) is beneficial for patients with acute ischemic stroke, it has become the standard method of care. Despite these positive results, recovery to functional independence is established in only about one-third of treated patients. The effect of IAT is commonly assessed by functional outcome, whereas its effect on brain tissue salvage is considered a secondary outcome measure (at most). Because patient and treatment selection needs to be improved, understanding the treatment effect on brain tissue salvage is of utmost importance.

OBJECTIVE:

To introduce infarct probability maps to estimate the location and extent of tissue damage based on patient baseline characteristics and treatment type.

METHODS:

Cerebral infarct probability maps were created by combining automatically segmented infarct distributions using follow-up CT images of 281 patients from the MR CLEAN trial. Comparison of infarct probability maps allows visualization and quantification of probable treatment effects. Treatment impact was calculated for 10 Alberta Stroke Program Early CT Score (ASPECTS) and 27 anatomical regions.

RESULTS:

The insular cortex had the highest infarct probability in both control and IAT populations (47.2% and 42.6%, respectively). Comparison showed significant lower infarct probability in 4 ASPECTS and 17 anatomical regions in favor of IAT. Most salvaged tissue was found within the ASPECTS M2 region, which was 8.5% less likely to infarct.

CONCLUSIONS:

Probability maps intuitively visualize the topographic distribution of infarct probability due to treatment, which makes it a promising tool for estimating the effect of treatment.

Impactfactor: 3.551

Two-Year Outcome after Endovascular Treatment for Acute Ischemic Stroke

van den Berg LA, Dijkgraaf MG, Berkhemer OA, Fransen PS, Beumer D, Lingsma HF, Majoie CB, Dippel DW, van der Lugt A, van Oostenbrugge RJ van Zwam WH, Roos YB; MR CLEAN Investigators*: **Keizer K**, Tielbeek AV

N Engl J Med. 2017 Apr 6;376(14):1341-1349

BACKGROUND:

Several trials involving patients with acute ischemic stroke have shown better functional outcomes with endovascular treatment than with conventional treatment at 90 days after initiation of treatment. However, results on long-term clinical outcomes are lacking.

METHODS:

We assessed clinical outcomes 2 years after patients were randomly assigned to receive either endovascular treatment (intervention group) or conventional treatment (control group) for acute ischemic stroke. The primary outcome was the score on the modified Rankin scale at 2 years; this scale measures functional outcome, with scores ranging from 0 (no symptoms) to 6 (death). Secondary outcomes included all-cause mortality and the quality of life at 2 years, as measured by means of a health utility index that is based on the European Quality of Life-5 Dimensions questionnaire (scores range from -0.329 to 1, with higher scores indicating better health).

RESULTS:

Of the 500 patients who underwent randomization in the original trial, 2-year data for this extended follow-up trial were available for 391 patients (78.2%) and information on death was available for 459 patients (91.8%). The distribution of outcomes on the modified Rankin scale favored endovascular treatment over conventional treatment (adjusted common odds ratio, 1.68; 95% confidence interval [CI], 1.15 to 2.45; P=0.007). There was no significant difference between the treatment groups in the percentage of patients who had an excellent outcome (i.e., a modified Rankin scale score of 0 or 1). The mean quality-of-life score was 0.48 among patients randomly assigned to endovascular treatment as compared with 0.38 among patients randomly assigned to conventional treatment (mean difference, 0.10; 95% CI, 0.03 to 0.16; P=0.006). The cumulative 2-year mortality rate was 26.0% in the intervention group and 31.0% in the control group (adjusted hazard ratio, 0.9; 95% CI, 0.6 to 1.2; P=0.46).

CONCLUSIONS:

In this extended follow-up trial, the beneficial effect of endovascular treatment on functional outcome at 2 years in patients with acute ischemic stroke was similar to that reported at 90 days in the original trial.

Impactfactor: 72.406

Nucleaire Geneeskunde

De rol van PET/CT bij oligometastatische ziekte

Roef MJ, van der Sangen MJ, Hurkmans CW

NTVO : Ned Tijdschr Oncol 2017;14(7):256-64

De diagnostiek en behandeling van oligometastatische ziekte staat de laatste jaren toenemend in de belangstelling. PET/CT is een 'total body' beeldvormende techniek met een relatief goede opbrengst in de detectie van zowel regionale lymfogene metastasen als van metastasen op afstand en heeft daarom vaak de voorkeur boven andere modaliteiten. Zo wordt PET/CT steeds vaker ingezet bij de (re)stadiëring, radiotherapieplanning en follow-up. Bij het gebruik van PET/CT dient men zich bewust te zijn van de beperkingen van het onderzoek. Zowel apparatuur- als patiëntgebonden factoren liggen hieraan ten grondslag

Impactfactor: --

Onderwijs & Onderzoek

Fetal heart rate abnormalities during and after external cephalic version: Which fetuses are at risk and how are they delivered?

Kuppens SM, Smailbegovic I, **Houterman S**, de Leeuw I, Hasaart TH

BMC Pregnancy Childbirth. 2017 Oct 17;17(1):363

BACKGROUND: Fetal heart rate abnormalitie (FHR) during and after external cephalic version (ECV) are relatively frequent. They may raise concern about fetal wellbeing. Only occasionally they may lead to an emergency cesarean section.

METHODS: Prospective cohort study in 980 women (>?34 weeks gestation) with a singleton fetus in breech presentation. During and after external cephalic version (ECV) FHR abnormalities were recorded. Obstetric variables and delivery outcome were evaluated. Primary outcome was to identify which fetuses are at risk for FHR abnormalities. Secondary outcome was to identify a possible relationship between FHR abnormalities during and after ECV and mode of delivery and fetal distress during subsequent labor.

RESULTS: The overall success rate of ECV was 60% and in 9% of the attempts there was an abnormal FHR pattern. In two cases FHR abnormalities after ECV led to an emergency CS. Estimated fetal weight per 100 g (OR 0.90, CI: 0.87-0.94) and longer duration of the ECV-procedure (OR 1.13, CI: 1.05-1.21) were factors significantly associated with the occurrence of FHR abnormalities. FHR abnormalities were not associated with the mode of delivery or the occurrence of fetal distress during subsequent labor.

CONCLUSIONS: FHR abnormalities during and after ECV are more frequent with lower estimated fetal weight and longer duration of the procedure. FHR abnormalities during and after ECV have no consequences for subsequent mode of delivery. They do not predict whether fetal distress will occur during labor.

Impactfactor: 2.180

Improved and more effective algorithms to screen for nutrient deficiencies after bariatric surgery

Bazuin I, Pouwels S, **Houterman S**, Nienhuijs SW, Smulders JF, Boer AK

Eur J Clin Nutr. 2017 Feb 71(2):198-202

BACKGROUND/OBJECTIVES:

Most bariatric guidelines recommend frequent lab monitoring of patients to detect nutrient and vitamin deficiencies as early as possible. The aim of this study was to optimize the cost effectiveness of the nutrient panel, by developing an algorithm, which detects nutrient deficiencies at lower costs.

SUBJECTS/METHODS:

In this retrospective study, 2055 patients who had undergone Laparoscopic Roux-Y Gastric Bypass (LRYGB) and Laparoscopic Sleeve Gastrectomy (LSG) surgery at Catharina Hospital Eindhoven between January 2009 and December 2013 were included. Perioperative biochemical measurements (7 days before and 127 days after surgery) and measurements >549 days before surgery were excluded. For analysis, the most recent preoperative and postoperative measurements were selected for each biochemical parameter separately. First, the amount of moderate and severe deficiencies were calculated. Second, we investigated whether each variable (vitamins A, B1, B6, B12, D, folate, ferritin, zinc and magnesium) could predict the presence of deficiency.

RESULTS:

In total, 561 (LRYGB) and 831 (LSG) patients had at least preoperative and postoperative values of vitamin A, B1, B6, B12, D, folate, ferritin, zinc or magnesium. The algorithm reduces vitamin D, B12, B6, B1 and ferritin examinations by 15, 11, 28, 28 and 38%, respectively, without missing clinically relevant deficiencies. The corresponding potential cost savings was 14%.

CONCLUSIONS:

This study identified substantial cost savings in laboratory test for both LRYGB and LSG procedures. The potential cost reduction of 14% might even be increased to 42% when less frequent moderate deficiencies are not screened anymore, whereas >99.0 of moderate deficiencies will be detected.

Impactfactor: 3.057

Self-assessment in laparoscopic surgical skills training: Is it reliable?

Ganni S, Chmarra MK, Goossens RHM, Jakimowicz JJ

Surg Endosc. 2017 Jun; 31(6):2451-2456. Epub 2016 Sep 21

BACKGROUND: The concept of self-assessment has been widely acclaimed for its role in the professional development cycle and self-regulation. In the field of medical education, self-assessment has been most used to evaluate the cognitive knowledge of students. The complexity of training and evaluation in

laparoscopic surgery has previously acted as a barrier in determining the benefits self-assessment has to offer in comparison with other fields of medical education.
METHODS: Thirty-five surgical residents who attended the 2-day Laparoscopic Surgical Skills Grade 1 Level 1 curriculum were invited to participate from TheNetherlands, India and Romania. The competency assessment tool (CAT) for laparoscopic cholecystectomy was used for self- and expert-assessment and the resulting distributions assessed.
RESULTS: A comparison between the expert- and self-assessed aggregates of scores from the CAT agreed with previous studies. Uniquely to this study, the aggregates of individual sub-categories-'use of instruments'; 'tissue handling'; and errors 'within the component tasks' and the 'end product' from both self- and expert-assessments-were investigated. There was strong positive correlation ($r_s > 0.5$; $p < 0.001$) between the expert- and self-assessment in all categories with only the 'tissue handling' having a weaker correlation ($r_s = 0.3$; $p = 0.04$). The distribution of the mean of the differences between self-assessment and expert-assessment suggested no significant difference between the scores of experts and the residents in all categories except the 'end product' evaluation where the difference was significant ($W = 119$, $p = 0.03$).
CONCLUSION: Self-assessment using the CAT form gives results that are consistently not different from expert-assessment when assessing one's proficiency in surgical skills. Areas where there was less agreement could be explained by variations in the level of training and understanding of the assessment criteria.
Impactfactor: 3.747

Operatiekamers

Balancing demand and supply in the operating room: A study for the cardiothoracic department in a large teaching hospital

Stepaniak PS, Pouwels S

J Clin Anesth. 2017 Nov;42:7-8

Geen abstract beschikbaar

Impactfactor: 1.284

Use of an intraoperative checklist to decrease the incidence of re-exploration for postoperative bleeding after cardiac surgery

van Boxtel AG, van Veghel D, Soliman Hamad MA, Schulz DN, **Stepaniak PS**, van Straten AH

Interact Cardiovasc Thorac Surg. 2017 Oct 1;25(4):555-558

OBJECTIVES: We have implemented an intraoperative checklist aiming to reduce the incidence of re-exploration for bleeding after cardiac surgery. The present report addresses the results of adopting such a checklist regarding the incidence of postoperative bleeding.

METHODS: The checklist was implemented by presenting it in several staff meetings of the Catharina Heart Center. Copies of the checklist were presented in every operating room. Data were collected by the Catharina Heart Center, aligned with the 'Meetbaar Beter' data manual and validated by 'Meetbaar Beter' through their data quality system. The incidence of re-exploration for bleeding was analysed in a variable life-adjusted display curve. The patient population operated after the implementation of the checklist was compared with a recent historical population before its implementation.

RESULTS: From January 2013 through April 2016, 4817 cardiac surgical procedures were performed in our institution. Before May 2015, 3210 procedures were performed (Group 1), complicated by 112 re-exploration for bleeding (3.5%). The 'reoperation for bleeding checklist' was implemented on 1 May 2015. After this date, the number of re-explorations for bleeding decreased to 29 (1.8%) of the 1607 cardiac surgical procedures (Group 2) (P?<?0.05).

CONCLUSIONS: An intraoperative checklist is feasible to implement, low cost, quick and simple to measure with a significant reduction in the incidence of re-exploration for bleeding. This report shows an example of the positive effects of transparency in publishing outcomes' data in cardiac surgery.

Impactfactor: 1.329

Orthopedie

Antibiotic prophylaxis is not indicated prior to dental procedures for prevention of periprosthetic joint infections

Rademacher WM, Walenkamp GH, Moojen DJ, **Hendriks JG**, Goedendorp TA, Rozema FR

Acta Orthop. 2017 Oct;88(5):568-574

Background and purpose - To minimize the risk of hematogenous periprosthetic joint infection (HPJI), international and Dutch guidelines recommended antibiotic prophylaxis prior to dental procedures. Unclear definitions and contradictory recommendations in these guidelines have led to unnecessary antibiotic prescriptions. To formulate new guidelines, a joint committee of the Dutch Orthopaedic and Dental Societies conducted a systematic literature review to answer the following question: can antibiotic prophylaxis be recommended for patients (with joint prostheses) undergoing dental procedures in order to prevent dental HPJI? Methods - The Medline, Embase, and Cochrane databases were searched for randomized controlled trials (RCTs), reviews, and observational studies up to July 2015. Studies were included if they involved patients with joint implants undergoing dental procedures, and either considered HPJI as an outcome measure or described a correlation between HPJI and prophylactic antibiotics. A guideline was formulated using the GRADE method and AGREE II guidelines. Results - 9 studies were included in this systematic review. All were rated "very low quality of evidence". Additional literature was therefore consulted to address clinical questions that provide further insight into pathophysiology and risk factors. The 9 studies did not provide evidence that use of antibiotic prophylaxis reduces the incidence of dental HPJI, and the additional literature supported the conclusion that antibiotic prophylaxis should be discouraged in dental procedures. Interpretation - Prophylactic antibiotics in order to prevent dental HPJI should not be prescribed to patients with a normal or an impaired immune system function. Patients are recommended to maintain good oral hygiene and visit the dentist regularly.

Impactfactor 3.446

Guideline on the diagnosis and treatment of primary idiopathic clubfoot

Besselaar AT, Sakkers RJB, Schuppers HA, Witbreuk MMEH, Zeegers EVCM, Visser JD, Boekestijn RA, Margés SD, **Van der Steen MCM**, Burger KNJ

Acta Orthop. 2017 Jun 88(3):305-309. Epub 2017 Mar 7

A delegation of 6 pediatric orthopedic surgeons from the Dutch Orthopedic Association (NOV) and 2 members of the board of the Dutch Parents' Association for children with clubfoot created the guideline "The diagnosis and treatment of primary idiopathic clubfeet" between April 2011 and February 2014. The development of the guideline was supported by a professional methodologist from the Dutch Knowledge Institute of Medical Specialists. This evidence-based guideline process was new and unique, in the sense that the process was initiated by a parents' association. This is the first official guideline in pediatric orthopedics in the Netherlands, and to our knowledge it is also the first evidence-based guideline on clubfoot worldwide. The guideline was developed in accordance with the criteria of the international AGREE instrument (AGREE II: Appraisal of Guidelines for Research and Evaluation II). The scientific literature was searched and systematically analyzed. In the second phase, conclusions and recommendations in the literature were formulated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method. Recommendations were developed considering the balance of benefits and harms, the type and quality of evidence, the values and preferences of the people involved, and the costs. The guideline is a solid foundation for standardization of clubfoot treatment in the Netherlands, with a clear recommendation of the Ponseti method as the optimal method of primary clubfoot treatment. We believe that the format used in the current guideline sets a unique example for guideline development in pediatric orthopedics that may be used worldwide. Our format ensured optimal collaboration between medical specialists and parents, and resulted in an important change in clubfoot care in the Netherlands, to the benefit of medical professionals as well as parents and patients. In this way, it is possible to improve professional collaboration between medical specialists and parents, resulting in an important change in clubfoot care in the Netherlands that will benefit medical professionals, parents, and patients. The guideline was published online, and is freely available from the Dutch Guideline Database (www.richtlijnendatabase.nl).

Impactfactor 3.446

Kniesimulator voor het oefenen van schuifladentesten

Voorn S, van de Vrande H, de Cock B, van den Brand J, Bender T, Cuijpers J, van den Eijnde M, **van der Steen MC**, Reijman M, Janssen RP

FysioPraxis 2017(4):20-21.

Impactfactor --

Risks, consequences, and prevention of falls of older people in oral healthcare centers

de Baat C, **de Baat P**, Gerritsen AE, Flohil KA, van der Putten GJ, van der Maarel-Wierink CD.

Spec Care Dentist. 2017 Mar; 37(2):71-77. Epub 2016 Oct 22.

One-third of community-dwelling people older than 65 years of age fall each year, and half of them fall at least twice a year. Older care home residents are approximately three times more likely to fall when compared to community-dwelling older people. Risk indicators for falls are related to the older people's body, environment, behavior, and activities. An important health risk indicator is (orthostatic or postprandial) hypotension, which may induce cerebral hypoperfusion. Although the majority of falls remain without major consequences, 10% to 25% of falls in care homes result in bodily trauma. Prevalent fall-related injuries are brain injury, lower extremity fracture including hip fracture and forearm/wrist fracture, facial fracture, humeral fracture, and rib/scapular fracture. As fall accidents by older people can have severe consequences, prevention of falls is of paramount importance. Healthcare providers, including oral healthcare providers, should inform older people on risks of falling and draw attention to potentially hazardous arrangements.

Impactfactor: --

Total Knee Arthroplasty: What to Expect? A Survey of the Members of the Dutch Knee Society on Long-Term Recovery after Total Knee Arthroplasty

Tolk JJ, **van der Steen MC**, Janssen RPA, Reijman M J

Knee Surg. 2017 Jul;30(6):612-616. Epub 2016 Nov 23

The rate of satisfaction after total knee arthroplasty (TKA) is consistently reported around 80%, leaving one in five patients unsatisfied to some extent. Fulfillment of expectations is reported as the strongest predictor of treatment satisfaction. In this study, we aimed to evaluate what Dutch orthopedic surgeons assume are realistic expectations for recovery 1?year after TKA. We invited the members of the Dutch Knee Society (DKS) to fill out a web-based questionnaire. For expectation measurement, the validated Dutch version of the Hospital for Special Surgery (HSS) knee replacement expectations survey was used. A total of 150 invitations were successfully sent; 84 orthopedic surgeons responded (56%). The overall HSS knee replacement expectation score was 66.0 (standard deviation, 14.0) on a 0 to 100 scale. Most improvement was predicted for the items "pain relief" and "walking short distances." Expectations related to patients' ability to kneel or squat after TKA were scored poorly. To the opinion of the members of the DKS, after TKA improvement can be expected in domains of pain, function, activities, and psychological wellbeing. Return to normal is not likely to occur, especially in demanding physical activities.

Impactfactor: 1.657

Pamm

Acenocoumarol as a risk factor for calciphylaxis: a feature clinicians should be aware of

Wenstedt EF, **Huysentruyt CJ,** Konings CJ

Neth J Med. 2017 May; 75(4):161-164

In contrast with uraemic calciphylaxis in end-stage renal disease, causes of and risk factors for non-uraemic calciphylaxis are relatively unknown to clinicians and have yet to become fully established. This report describes a case of non-uraemic calciphylaxis, in which the use of acenocoumarol might have been a risk factor. It is important to raise awareness about this association among clinicians, as vitamin K antagonists have to be stopped for an optimal treatment of this severe condition.

Impactfactor: 1.244

Acute toxicity and surgical complications after preoperative (chemo)radiation therapy for rectal cancer in patients with inflammatory bowel disease

Bosch SL, van Rooijen SJ, Bökkerink GM, Braam HJ, Derikx LA, Poortmans P, Marijnen CA, Nagtegaal ID, de Wilt JH

Radiother Oncol. 2017 Apr;123(1):147-153.

PURPOSE:

Preoperative therapy reduces local recurrences and may facilitate surgery in rectal cancer patients. However, in patients with inflammatory bowel disease (IBD) this treatment is often withheld due to the perceived risk of excessive side-effects, even though evidence is limited. The purpose of this study is to investigate the effects of preoperative therapy on acute toxicity and post-operative complications in IBD patients with rectal cancer.

METHODS:

The Dutch pathology registry (PALGA) was searched for patients with IBD and rectal cancer treated between January 1991 and May 2010. Histopathology and clinical charts were reviewed to confirm IBD diagnosis and evaluate clinical and pathological characteristics.

RESULTS:

Out of 161 patients, 66 received preoperative therapy (41%), including short-course radiation therapy (SC-RT), long course radiation therapy (LC-RT), and chemoradiation therapy (CRT) in 32, 13, and 21 patients respectively. Grade=3 acute toxicity occurred in 0 patients (0.0%), 1 patient (7.7%), and 6 patients (28.6%) respectively (p=0.004). Systemic corticosteroids were used by 10.5% of patients at time of treatment. Grade=3 post-operative 30-day complication rate (28.1% overall) was not associated with type of preoperative therapy.

CONCLUSION:

Results did not show excessive rates of toxicity or post-operative complications and support the use of standard preoperative therapies for rectal cancer (especially SC-RT) in IBD patients with relatively indolent disease. Caution is warranted in patients with active IBD, since the exact impact of active bowel inflammation could not be determined retrospectively. Prospective studies should investigate the influence of active IBD on acute and late toxicity in patients receiving pelvic irradiation.

Impactfactor: 4.328

NDRG4, an early detection marker for colorectal cancer, is specifically expressed in enteric neurons

Vaes N, **Lentjes MH**, Gijbels MJ, Rademakers G, Daenen KL, Boesmans W, Wouters KA, Geuzens A, Qu X, Steinbusch HP, Rutten BP, Baldwin SH, Sharkey KA, Hofstra RM, van Engeland M, Vanden Berghe P, Melotte V

Neurogastroenterol Motil. 2017 Sep;29(9):e13095 .

BACKGROUND:

Promoter methylation of N-myc Downstream-Regulated Gene 4 (NDRG4) in fecal DNA is an established early detection marker for colorectal cancer (CRC). Despite its connection to CRC, NDRG4 is predominantly studied in brain and heart, with little to no knowledge about its expression or role in other organs. In this study, we aimed to determine the whole-body expression of NDRG4, with a focus on the intestinal tract.

METHODS:

We investigated NDRG4 expression throughout the body by immunohistochemistry, Western Blotting and in situ mRNA hybridization using tissues from NDRG4 wild-type, heterozygous and knockout mice and humans. In addition, we explored cell-specific expression of NDRG4 in murine whole-mount gut preparations using immunofluorescence and confocal microscopy.

KEY RESULTS:

NDRG4 is specifically expressed within nervous system structures throughout the body. In the intestinal tract of both mouse and man, NDRG4 immunoreactivity was restricted to the enteric nervous system (ENS), where it labeled cell bodies of the myenteric and submucosal plexuses and interconnecting nerve fibers. More precisely,

NDRG4 expression was limited to neurons, as NDRG4 always co-localized with HuC/D (pan-neuronal marker) but never with GFAP (an enteric glial cell marker). Furthermore, NDRG4 was expressed in various neuropeptide Y positive neurons, but was only found in a minority (~10%) of neurons expressing neuronal nitric oxide synthase.
CONCLUSIONS AND INFERENCES:
NDRG4 is exclusively expressed by central, peripheral and enteric neurons/nerves, suggesting a neuronal-specific role of this protein. Our findings raise the question whether NDRG4, via the ENS, an understudied component of the tumor microenvironment, supports CRC development and/or progression.
Impactfactor: 3.617

Notice of Retraction and Replacement: Oostdijk et al. Effects of Decontamination of the Oropharynx and Intestinal Tract on Antibiotic Resistance in ICUs: A Randomized Clinical Trial
JAMA. 2014;312(14):1429-1437
Oostdijk EA, Kesecioglu J, Schultz MJ, Visser CE, de Jonge E, van Essen EH, Bernards AT, Purmer I, Brimicombe R, Bergmans D, van Tiel F, Bosch FH, Mascini E, van Griethuysen A, Bindels A, **Jansz A**, van Steveninck FA, van der Zwet WC, Fijen JW, Thijsen S, de Jong R, Oudbier J, Raben A, van der Vorm E, Koeman M, Rothbarth P, Rijkeboer A, Gruteke P, Hart H, Peerbooms P, Winsser LJ, van Elsacker-Niele AW, Demmendaal K, Brandenburg A, de Smet AM, Bonten MJ JAMA. 2017 Apr 18;317(15):1583-1584.
Geen abstract beschikbaar
Impactfactor: 44.405

Plastische Chirurgie

Carpal Ligaments: A Functional Classification
Garcia-Elias M, Puig de la Bellacasa I, **Schouten C**
Hand Clin. 2017 Aug;33(3):511-520

Recent laboratory research has disclosed that carpal ligaments exhibit different kinetic behaviors depending on the direction and point of application of the forces being applied to the wrist. The so-called helical antipronation ligaments are mostly active when the wrist is axially loaded, whereas the helical antisupination ligaments constrain supination torques to the distal row. This novel way of interpreting the function of the carpal ligaments may help in developing better strategies to treat carpal instabilities.

Impactfactor: 0.904

Covering of an exposed vascular graft in the groin with an external oblique muscle rotational flap
Vierhout BP, **Smit JM**, Zeebregts CJ
J Surg Case Rep. 2017 Feb 4 2017(2):rjx009. eCollection 2017 Feb

Abdominal muscles, such as the oblique- and transverse muscles, find their blood supply from multiple segmental pedicles from the iliac artery. Besides its superior vascularization, its release is simple, leaving two abdominal muscles for securing abdominal wall strength. The release of the muscle and coverage of the graft requires partial muscle mobilization and is a minor reconstruction, but extension of the mobilization cranially enables coverage of larger defects. We present a case of an infected vascular graft in the groin successfully preserved through coverage with an external oblique muscle flap.

Impactfactor: --

Limitation of ischaemic tissue response in a reconstruction with short ischaemia time during free flap surgery
van Onna MA, Visser J, van der Hulst RR
J Plast Reconstr Aesthet Surg. 2017 Aug;70(8):e17-e18.
Geen abstract beschikbaar
Impactfactor: 2.048

Patient Reported Outcome Measures van post-bariatrische plastische chirurgie met behulp van de BODY-Q.
Geerards, A.B. Mink van der Molen, V.M. Monpellier, S. Klein, E.S.J. van der Beek, **M.M. Hoogbergen**
Nederlands Tijdschrift voor Plastische Chirurgie, 2017;8(1):7-9
Impactfactor: --

Psychiatrie

Mild cognitive impairment and risk of depression and anxiety: A population-based study

Mirza SS, Ikram MA, Bos D, **Mihaescu R**, Hofman A, Tiemeier H

Alzheimers Dement. 2017 Feb;13(2):130-139

INTRODUCTION:

Many people with mild cognitive impairment (MCI) suffer from concomitant depression or anxiety. Whether MCI increases the risk of future depression or anxiety is unknown.

METHODS:

In the Rotterdam Study, cross-sectional (n = 4168) and longitudinal associations (n = 2967) of MCI with Diagnostic and Statistical Manual of Mental Disorders-depressive and anxiety disorders-were assessed (2002-2005 to 2009-2011).

RESULTS:

At baseline, 413 persons had MCI; 125 (22 MCI and 103 non-MCI) had a depressive disorder and 330 had an anxiety disorder (46 MCI and 284 non-MCI). In longitudinal depression analysis, of the 212 persons with prevalent MCI, 6 (2.8%) developed depression compared with 29 (1%) in the nonexposed group. In longitudinal anxiety analysis, 11 (7.3%) of the 151 with prevalent MCI developed anxiety, compared with 75 (3.4%) in nonexposed group. Persons with MCI had more depressive and anxiety disorders and also a higher risk of developing depressive disorder, odds ratio (OR) 3.13 (95% confidence interval [CI]: 1.26, 7.77), and anxiety disorder, OR 2.59 (95% CI: 1.31, 5.12).

DISCUSSION:

MCI is a risk factor for dementia and for depressive and anxiety disorders, suggesting common pathological pathways for cognitive and psychiatric outcomes.

Impactfactor: 9.478

Psychologie

Functional status in patients with medically unexplained physical symptoms: Coping styles and their relationship with depression and anxiety

Sempértegui GA, Karreman A, **van Hout GC**, Bekker MH

J Health Psychol. 2017 Nov;22(13):1743-1754. Epub 2016 Mar 29

This study examined how coping styles are related to functional status in patients with medically unexplained physical symptoms and to what extent depression and anxiety account for this relationship. In 90 Dutch adult patients presenting medically unexplained physical symptoms, coping styles, health-related functional status, anxiety, and depression were measured. Multiple regression analyses and mediation analysis showed that coping styles were directly and indirectly related to functional status. In this relationship, depression and anxiety played an important role. The findings highlight the relevance of addressing coping styles, depression, and anxiety when targeting the functional status of patients with medically unexplained physical symptoms in clinical practice.

Impactfactor --

Radiologie

Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands)

Mulder MJ, Ergezen S, Lingsma HF, Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lycklama À, Nijeholt G, Emmer BJ, van der Worp HB, Nederkoorn PJ, Roos YB, van Oostenbrugge RJ, van Zwam WH, Majoie CB, van der Lugt A, Dippel DW; Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) Investigators*: Keizer K, **Tielbeek AV**

Stroke. 2017 Jul;48(7):1869-1876

BACKGROUND AND PURPOSE:
High blood pressure (BP) is associated with poor outcome and the occurrence of symptomatic intracranial hemorrhage in acute ischemic stroke. Whether BP influences the benefit or safety of intra-arterial treatment (IAT) is not known. We aimed to assess the relation of BP with functional outcome, occurrence of symptomatic intracranial hemorrhage and effect of IAT.
METHODS:
This is a post hoc analysis of the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands). BP was measured at baseline, before IAT or stroke unit admission. We estimated the association of baseline BP with the score on the modified Rankin Scale at 90 days and safety parameters with ordinal and logistic regression analysis. Effect of BP on the effect of IAT was tested with multiplicative interaction terms.
RESULTS:
Systolic BP (SBP) had the best correlation with functional outcome. This correlation was U-shaped; both low and high baseline SBP were associated with poor functional outcome. Higher SBP was associated with symptomatic intracranial hemorrhage (adjusted odds ratio, 1.25 for every 10 mm Hg higher SBP [95% confidence interval, 1.09-1.44]). Between SBP and IAT, there was no interaction for functional outcome, symptomatic intracranial hemorrhage, or other safety parameters; the absolute benefit of IAT was evident for the whole SBP range. The same was found for diastolic BP.
CONCLUSIONS:
BP does not affect the benefit or safety of IAT in patients with acute ischemic stroke caused by proximal intracranial vessel occlusion. Our data provide no arguments to withhold or delay IAT based on BP.

Impactfactor: 6.032

Case report. Infarction of a testis in a patient suffering from sickle cell anaemia / Case report. Infarcering van een testis bij een patiënt met sikkelcelanemie

Beulens, AJW, Kuenen MBG , **Yo LSF** , Koldewijn EL

Of all patients who visit the Emergency Room (ER) with scrotal pain, only a small number is diagnosed with testicular torsion. After physical examination and ultrasound with colour doppler of the scrotum the majority of these patients are diagnosed with another condition, in most cases an epididymo-orchitis. However, in some cases there a less common cause for the pain is found. We present the case of a 20-year-old Haitian male in our ER, suffering from an acute painful left testicle, caused by testicular infarction based on sickle cell anaemia.

Impactfactor: --

Comparison of cardiac magnetic resonance imaging and bio-impedance spectroscopy for the assessment of fluid displacement induced by external leg compression

Saporito S, Dovancescu S, Herold IH, **van den Bosch HC**, van Assen HC, Aarts RM, Korsten HH, Mischi M

Physiol Meas. 2017 Jan;38(1):15-32. Epub 2016 Dec 12

Heart failure is marked by frequent hospital admissions, often as a consequence of pulmonary congestion. Current gold standard techniques for thoracic fluid measurement require invasive heamodynamic access and therefore they are not suitable for continuous monitoring. Changes in thoracic impedance (TI) may enable non-invasive early detection of congestion and prevention of unplanned hospitalizations. However, the usefulness of TI to assess thoracic fluid status is limited by inter-subject variability and by the lack of reliable normalization methods. Indicator dilution methods allow absolute fluid volume estimation; cardiac magnetic resonance (CMR) has been recently proposed to apply indicator dilution methods in a minimally-invasive manner. In this study, we aim to compare bio-impedance spectroscopy (BIS) and CMR for the assessment of thoracic fluid status, and to determine their ability to detect fluid displacement induced by a leg compression procedure in healthy volunteers. A pressure gradient was applied across each subject's legs for 5?min (100-60 mmHg, distal to proximal). Each subject underwent a continuous TI-BIS measurement during the procedure, and repeated CMR-

based indicator dilution measurements on a 1.5 T scanner at baseline, during compression, and after pressure release. The Cole-Cole and the local density random walk models were used for parameter extraction from TI-BIS and indicator dilution measurements, respectively. Intra-thoracic blood volume index (ITBI) derived from CMR, and extracellular fluid resistance (R E) from TI-BIS, were considered as thoracic fluid status measures. Eight healthy volunteers were included in this study. An increase in ITBI of 45.2??±??47.2?ml m-2 was observed after the leg inflation (13.1??±??15.1% w.r.t. baseline, p??<??0.05), while a decrease of??-0.84??±??0.39 O in R E (-1.7??±??0.9% w.r.t. baseline, p??<??0.05) was observed. ITBV and R E normalized by body mass index were strongly inversely correlated (r??=??-0.93, p??<??0.05). In conclusion, an acute fluid displacement to the thoracic circulation was induced in healthy volunteers. Significant changes were observed in the considered thoracic fluid measures derived from BIS and CMR. Good correlation was observed between the two measurement techniques. Further clinical studies will be necessary to prospectively evaluate the value of a combination of the two techniques for prediction of re-hospitalizations after admission for heart failure.

Impactfactor: 2.058

Interval breast cancer characteristics before, during and after the transition from screen-film to full-field digital screening mammography

van Bommel RMG, Weber R, Voogd AC, **Nederend J**, Louwman MWJ, Venderink D, Strobbe LJA, Rutten MJC, Plaisier ML, Lohle PN, Hooijen MJH, Tjan-Heijnen VCG, Duijm LEM

BMC Cancer. 2017 May 5; 17(1):315

BACKGROUND:

To determine the proportion of "true" interval cancers and tumor characteristics of interval breast cancers prior to, during and after the transition from screen-film mammography screening (SFM) to full-field digital mammography screening (FFDM).

METHODS:

We included all women with interval cancers detected between January 2006 and January 2014. Breast imaging reports, biopsy results and breast surgery reports of all women recalled at screening mammography and of all women with interval breast cancers were collected. Two experienced screening radiologists reviewed the diagnostic mammograms, on which the interval cancers were diagnosed, as well as the prior screening mammograms and determined whether or not the interval cancer had been missed on the most recent screening mammogram. If not missed, the cancer was considered an occult ("true") interval cancer.

RESULTS:

A total of 442 interval cancers had been diagnosed, of which 144 at SFM with a prior SFM (SFM-SFM), 159 at FFDM with a prior SFM (FFDM-SFM) and 139 at FFDM with a prior FFDM (FFDM-FFDM). The transition from SFM to FFDM screening resulted in the diagnosis of more occult ("true") interval cancers at FFDM-SFM than at SFM-SFM (65.4% (104/159) versus 49.3% (71/144), $P < 0.01$), but this increase was no longer statistically significant in women who had been screened digitally for the second time (57.6% (80/139) at FFDM-FFDM versus 49.3% (71/144) at SFM-SFM). Tumor characteristics were comparable for the three interval cancer cohorts, except of a lower porportion (75.7 and 78.0% versus 67.2% af FFDM-FFDM, $P < 0.05$) of invasive ductal cancers at FFDM with prior FFDM.

CONCLUSIONS:

An increase in the proportion of occult interval cancers is observed during the transition from SFM to FFDM screening mammography. However, this increase seems temporary and is no longer detectable after the second round of digital screening. Tumor characteristics and type of surgery are comparable for interval cancers detected prior to, during and after the transition from SFM to FFDM screening mammography, except of a lower proportion of invasive ductal cancers after the transition.

Impactfactor: 3.288

Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms

van Schaik TG, Yeung KK, Verhagen HJ, de Bruin JL, van Sambeek MR*, Balm R, Zeebregts CJ, van Herwaarden JA, Blankensteijn JD; DREAM trial participants: **Tielbeek AV**

J Vasc Surg. 2017 Nov;66(5):1379-1389

OBJECTIVE: andomized trials have shown an initial survival benefit of endovascular over conventional open abdominal aortic aneurysm repair but no long-term difference up to 6 years after repair. Longer

follow-up may be required to demonstrate the cumulative negative impact on survival of higher reintervention rates associated with endovascular repair.

METHODS: We updated the results of the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, a multicenter, randomized controlled trial comparing open with endovascular aneurysm repair, up to 15 years of follow-up. Survival and reinterventions were analyzed on an intention-to-treat basis. Causes of death and secondary interventions were compared by use of an events per person-year analysis.

RESULTS: There were 178 patients randomized to open and 173 to endovascular repair. Twelve years after randomization, the cumulative overall survival rates were 42.2% for open and 38.5% for endovascular repair, for a difference of 3.7 percentage points (95% confidence interval, -6.7 to 14.1; P = .48). The cumulative rates of freedom from reintervention were 78.9% for open repair and 62.2% for endovascular repair, for a difference of 16.7 percentage points (95% confidence interval, 5.8-27.6; P = .01). No differences were observed in causes of death. Cardiovascular and malignant disease account for the majority of deaths after prolonged follow-up.

CONCLUSIONS: During 12 years of follow-up, there was no survival difference between patients who underwent open or endovascular abdominal aortic aneurysm repair, despite a continuously increasing number of reinterventions in the endovascular repair group. Endograft durability and the need for continued endograft surveillance remain key issues.

Impactfactor: 3.536

Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years

Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, Greenhalgh RM; EVAR-1, DREAM, OVER and ACE Trialists: Teijink JA, Cuypers PhW, **Tielbeek AV**, Sambeek MR

Br J Surg. 2017 Feb;104(3):166-178

BACKGROUND: The erosion of the early mortality advantage of elective endovascular aneurysm repair (EVAR) compared with open repair of abdominal aortic aneurysm remains without a satisfactory explanation.

METHODS: An individual-patient data meta-analysis of four multicentre randomized trials of EVAR versus open repair was conducted to a prespecified analysis plan, reporting on mortality, aneurysm-related mortality and reintervention.

RESULTS: The analysis included 2783 patients, with 14?245 person-years of follow-up (median 5·5?years). Early (0-6 months after randomization) mortality was lower in the EVAR groups (46 of 1393 versus 73 of 1390 deaths; pooled hazard ratio 0·61, 95 per cent c.i. 0·42 to 0·89; P = 0·010), primarily because 30-day operative mortality was lower in the EVAR groups (16 deaths versus 40 for open repair; pooled odds ratio 0·40, 95 per cent c.i. 0·22 to 0·74). Later (within 3 years) the survival curves converged, remaining converged to 8 years. Beyond 3 years, aneurysm-related mortality was significantly higher in the EVAR groups (19 deaths versus 3 for open repair; pooled hazard ratio 5·16, 1·49 to 17·89; P = 0·010). Patients with moderate renal dysfunction or previous coronary artery disease had no early survival advantage under EVAR. Those with peripheral artery disease had lower mortality under open repair (39 deaths versus 62 for EVAR; P?=?0·022) in the period from 6 months to 4 years after randomization.

CONCLUSION: The early survival advantage in the EVAR group, and its subsequent erosion, were confirmed. Over 5?years, patients of marginal fitness had no early survival advantage from EVAR compared with open repair. Aneurysm-related mortality and patients with low ankle?:?brachial pressure index contributed to the erosion of the early survival advantage for the EVAR group. Trial registration numbers: EVAR-1, ISRCTN55703451; DREAM?(Dutch Randomized Endovascular Aneurysm Management), NCT00421330; ACE (Anévrysme de l'aorte abdominale, Chirurgie versus Endoprothèse), NCT00224718; OVER (Open Versus Endovascular Repair Trial for Abdominal Aortic Aneurysms).

Impactfactor: 5.899

MRI for Local Staging of Colon Cancer: Can MRI Become the Optimal Staging Modality for Patients With Colon Cancer?

Nerad E, Lambregts DM, **Kersten EL**, Maas M, Bakers FC, **van den Bosch HC**, Grabsch HI, Beets-Tan RG, Lahaye MJ

Dis Colon Rectum. 2017 Apr;60(4):385-392

BACKGROUND: Colon cancer is currently staged with CT. However, MRI is superior in the detection of colorectal liver metastasis, and MRI is standard in local staging of rectal cancer. Optimal (local) staging of

colon cancer could become crucial in selecting patients for neoadjuvant treatment in the near future (Fluoropyrimidine Oxaliplatin and Targeted Receptor Preoperative Therapy trial).
OBJECTIVE: The purpose of this study was to evaluate the diagnostic performance of MRI for local staging of colon cancer.
DESIGN: This was a retrospective study.
SETTINGS: The study was conducted at the Maastricht University Medical Centre.
PATIENTS: In total, 55 patients with biopsy-proven colon carcinoma were included.
MAIN OUTCOME MEASURES:
All of the patients underwent an MRI (1.5-tesla; T2 and diffusion-weighted imaging) of the abdomen and were retrospectively analyzed by 2 blinded, independent readers. Histopathology after resection was the reference standard. Both readers evaluated tumor characteristics, including invasion through bowel wall (T3/T4 tumors), invasion beyond bowel wall of =5?mm and/or invasion of surrounding organs (T3cd/T4), serosal involvement, extramural vascular invasion, and malignant lymph nodes (N+). Interobserver agreement was compared using ? statistics.
RESULTS: MRI had a high sensitivity (72%-91%) and specificity (84%-89%) in detecting T3/T4 tumors (35/55) and a low sensitivity (43%-67%) and high specificity (75%-88%) in detecting T3cd/T4 tumors (15/55). For detecting serosal involvement and extramural vascular invasion, MRI had a high sensitivity and moderate specificity, as well as a moderate sensitivity and specificity in the detection of nodal involvement. Interobserver agreements were predominantly good; the more experienced reader achieved better results in the majority of these categories.
LIMITATIONS:
The study was limited by its retrospective nature and moderate number of inclusions.
CONCLUSIONS: MRI has a good sensitivity for tumor invasion through the bowel wall, extramural vascular invasion, and serosal involvement. In addition, together with its superior liver imaging, MRI might become the optimal staging modality for colon cancer. However, more research is needed to confirm this. See Video Abstract at http://links.lww.com/DCR/A309.

Impactfactor: 3.519

Screening outcome in women repeatedly recalled for the same mammographic abnormality before, during and after the transition from screen-film to full-field digital screening mammography

van Bommel R, Voogd AC, Louwman MW, Strobbe LJ, Venderink D, Duijm LE

Eur Radiol. 2017 Feb;27(2):553-561

OBJECTIVE:
The aim of this study was to retrospectively determine screening outcome in women recalled twice for the same mammographic lesion before, during, and after transition from screen-film (SFM) to full-field digital screening mammography (FFDM).
METHODS:
We included women with a repeated recall for the same mammographic abnormality (37 at subsequent SFM-screening, obtained between January 2000-April 2010; respectively 54 and 65 women with a prior SFM-screen or FFDM-screen followed by subsequent FFDM-screening, obtained between May 2009-July 2013).
RESULTS:
At SFM-screening, repeated recalls for the same lesion comprised 1.2 % of recalls (37/3217), including 13 malignancies (positive predictive value (PPV), 35.1 %). During the SFM to FFDM transition (SFM-screen followed by FFDM-screen), FFDM recalls comprised more repeated recalls for the same lesion (2.2 %, P?=?0.002), with a lower PPV (14.8 %, P?=?0.02). This proportion increased to 2.8 % after transition to FFDM (i.e., two successive FFDM-screens), with 16 malignancies (PPV, 24.6 %). Invasive cancers at repeated recall were smaller than interval cancers (T1a-c, 79.4 versus 46.8 %, P?=?0.001), with less lymph node involvement (20.6 versus 46.5 %, P?=?0.007).
CONCLUSIONS:
More women are repeatedly recalled for the same mammographic abnormality during and after the transition from SFM to FFDM-screening, with comparable cancer risks before and after the transition. These cancers show better prognostic characteristics than interval cancers.
KEY POINTS:
• FFDM-screening increases the number of repeated recalls for the same mammographic abnormality. • The PPV of these recalls is comparable before and after transition to FFDM-screening. • Cancers

diagnosed after a repeated recall are smaller than interval cancers. • These cancers also show less lymph node involvement than interval cancers.

Impactfactor: 3.967

Topographic distribution of cerebral infarct probability in patients with acute ischemic stroke: mapping of intra-arterial treatment effect

Boers AM, Berkhemer OA, Slump CH, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Yoo AJ, Dippel DW, Marquering HA, Majoie CB1; MR CLEAN trial investigators: Keizer K, **Tielbeek AV**

J Neurointerv Surg. 2017 May;9(5):431-436. doi: 10.1136/neurintsurg-2016-012387. Epub 2016 Apr 25

BACKGROUND:

Since proof emerged that IA treatment (IAT) is beneficial for patients with acute ischemic stroke, it has become the standard method of care. Despite these positive results, recovery to functional independence is established in only about one-third of treated patients. The effect of IAT is commonly assessed by functional outcome, whereas its effect on brain tissue salvage is considered a secondary outcome measure (at most). Because patient and treatment selection needs to be improved, understanding the treatment effect on brain tissue salvage is of utmost importance.

OBJECTIVE:

To introduce infarct probability maps to estimate the location and extent of tissue damage based on patient baseline characteristics and treatment type.

METHODS:

Cerebral infarct probability maps were created by combining automatically segmented infarct distributions using follow-up CT images of 281 patients from the MR CLEAN trial. Comparison of infarct probability maps allows visualization and quantification of probable treatment effects. Treatment impact was calculated for 10 Alberta Stroke Program Early CT Score (ASPECTS) and 27 anatomical regions.

RESULTS:

The insular cortex had the highest infarct probability in both control and IAT populations (47.2% and 42.6%, respectively). Comparison showed significant lower infarct probability in 4 ASPECTS and 17 anatomical regions in favor of IAT. Most salvaged tissue was found within the ASPECTS M2 region, which was 8.5% less likely to infarct.

CONCLUSIONS:

Probability maps intuitively visualize the topographic distribution of infarct probability due to treatment, which makes it a promising tool for estimating the effect of treatment.

Impactfactor: 3.551

Two-Year Outcome after Endovascular Treatment for Acute Ischemic Stroke

van den Berg LA, Dijkgraaf MG, Berkhemer OA, Fransen PS, Beumer D, Lingsma HF, Majoie CB, Dippel DW, van der Lugt A, van Oostenbrugge RJ van Zwam WH, Roos YB; MR CLEAN Investigators*: Keizer K, **Tielbeek AV**

N Engl J Med. 2017 Apr 6;376(14):1341-1349

BACKGROUND:

Several trials involving patients with acute ischemic stroke have shown better functional outcomes with endovascular treatment than with conventional treatment at 90 days after initiation of treatment. However, results on long-term clinical outcomes are lacking.

METHODS:

We assessed clinical outcomes 2 years after patients were randomly assigned to receive either endovascular treatment (intervention group) or conventional treatment (control group) for acute ischemic stroke. The primary outcome was the score on the modified Rankin scale at 2 years; this scale measures functional outcome, with scores ranging from 0 (no symptoms) to 6 (death). Secondary outcomes included all-cause mortality and the quality of life at 2 years, as measured by means of a health utility index that is based on the European Quality of Life-5 Dimensions questionnaire (scores range from -0.329 to 1, with higher scores indicating better health).

RESULTS:

Of the 500 patients who underwent randomization in the original trial, 2-year data for this extended follow-up trial were available for 391 patients (78.2%) and information on death was available for 459 patients (91.8%). The distribution of outcomes on the modified Rankin scale favored endovascular treatment over conventional treatment (adjusted common odds ratio, 1.68; 95% confidence interval [CI], 1.15 to 2.45; P=0.007). There was no significant difference between the treatment groups in the percentage of patients who had an excellent outcome (i.e., a modified Rankin scale score of 0 or 1). The

mean quality-of-life score was 0.48 among patients randomly assigned to endovascular treatment as compared with 0.38 among patients randomly assigned to conventional treatment (mean difference, 0.10; 95% CI, 0.03 to 0.16; P=0.006). The cumulative 2-year mortality rate was 26.0% in the intervention group and 31.0% in the control group (adjusted hazard ratio, 0.9; 95% CI, 0.6 to 1.2; P=0.46). CONCLUSIONS:

In this extended follow-up trial, the beneficial effect of endovascular treatment on functional outcome at 2 years in patients with acute ischemic stroke was similar to that reported at 90 days in the original trial.

Impactfactor: 72.406

Radiotherapie

ABVD or BEACOPPbaseline along with involved-field radiotherapy in early-stage Hodgkin Lymphoma with risk factors: Results of the European Organisation for Research and Treatment of Cancer (EORTC)-Groupe d'Étude des Lymphomes de l'Adulte (GELA) H9-U intergroup randomised trial

Fermé C, Thomas J, Brice P, Casasnovas O, Vranovsky A, Bologna S, Lugtenburg PJ, Bouabdallah R, Carde P, Sebban C, Eghbali H, Salles G, van Imhoff GW, Thyss A, Noordijk EM, Reman O, **Lybeert ML**, Janvier M, Spina M, Audhuy B, Raemaekers JM, Delarue R, Anglaret B, de Weerdt O, Marjanovic Z, Tersteeg RJ, de Jong D, Brière J, Henry-Amar M; European Organisation for Research and Treatment of Cancer Lymphoma Group, and; Groupe d'Étude des Lymphomes de l'Adulte

Eur J Cancer. 2017 Aug;81:45-55

PURPOSE:

For early-stage Hodgkin lymphoma (HL), optimal chemotherapy regimen and the number of cycles to be delivered remain to settle down. The H9-U trial compared three modalities of chemotherapy followed by involved-field radiotherapy (IFRT) in patients with stage I-II HL and risk factors (NCT00005584).

PATIENTS AND METHODS:

Patients aged 15-70 years with untreated supradiaphragmatic HL with at least one risk factor (age = 50, involvement of 4-5 nodal areas, mediastinum/thoracic ratio = 0.35, erythrocyte sedimentation rate (ESR) = 50 without B-symptoms or ESR = 30 and B-symptoms) were eligible for the randomised, open label, multicentre, non-inferiority H9-U trial. The limit of non-inferiority was set at 10% for the difference between 5-year event-free survival (EFS) estimates. From October 1998 to September 2002, 808 patients were randomised to receive either the control arm 6-ABVD-IFRT (n = 276), or one of the two experimental arms: 4-ABVD-IFRT (n = 277) or 4-BEACOPPbaseline-IFRT (n = 255).

RESULTS:

Results in the 4-ABVD-IFRT (5-year EFS, 85.9%) and the 4-BEACOPPbaseline-IFRT (5-year EFS, 88.8%) were not inferior to 6-ABVD-IFRT (5-year EFS, 89.9%): difference of 4.0% (90%CI, -0.7%-8.8%) and of 1.1% (90%CI,-3.5%-5.6%) respectively. The 5-year overall survival estimates were 94%, 93%, and 93%, respectively. Patients treated with combined modality treatment chemotherapeutic regimen comprising doxorubicin (Adriamycin), bleomycin, vincristine (Oncovin), cyclophosphamide, procarbazine, etoposide and prednisone (BEACOPP)baseline more often developed serious adverse events requiring supportive measures and hospitalisation compared with patients receiving the chemotherapeutic regimen comprising doxorubicin (Adriamycin), bleomycin, vinblastine and dacarbazine (ABVD).

CONCLUSIONS:

The trial demonstrates that 4-ABVD followed by IFRT yields high disease control in patients with early-stage HL and risk factors responding to chemotherapy. Although non-inferior in terms of efficacy, four cycles of BEACOPPbaseline were more toxic than four or six cycles of ABVD.

Impactfactor: 6.029

Breast Cancer Risk After Radiation Therapy for Hodgkin Lymphoma: Influence of Gonadal Hormone Exposure

Krul IM, Opstal-van Winden AW, Aleman BM, Janus CP, van Eggermond AM, De Bruin ML, Hauptmann M, Krol AD, Schaapveld M, Broeks A, Kooijman KR, Fase S, **Lybeert ML**, Zijlstra JM, van der Maazen RW, Kesminiene A, Diallo I, de Vathaire F, Russell NS, van Leeuwen FE

Int J Radiat Oncol Biol Phys. 2017 Nov 15;99(4):843-853

BACKGROUND: Young women treated with chest radiation therapy (RT) for Hodgkin lymphoma (HL) experience a strongly increased risk of breast cancer (BC). It is unknown whether endogenous and exogenous gonadal hormones affect RT-associated BC risk.

METHODS:

We conducted a nested case-control study among female 5-year HL survivors treated before age 41. Hormone exposure and HL treatment data were collected through medical records and questionnaires for 174 BC case patients and 466 control patients. Radiation dose to breast tumor location was estimated based on RT charts, simulation films, and mammography reports.

RESULTS: We observed a linear radiation dose-response curve with an adjusted excess odds ratio (EOR) of 6.1%/Gy (95% confidence interval [CI]: 2.1%-15.4%). Women with menopause <30 years (caused by high-dose procarbazine or pelvic RT) had a lower BC risk (OR, 0.13; 95% CI, 0.03-0.51) than did women with menopause =50 years. BC risk increased by 6.4% per additional year of post-RT intact ovarian function (P<.001). Among women with early menopause (<45 years), hormone replacement therapy (HRT) use for =2 years did not increase BC risk (OR, 0.86; 95% CI, 0.32-2.32), whereas this risk was nonsignificantly increased among women without early menopause (OR, 3.69; 95% CI, 0.97-14.0; P for

interaction: .06). Stratification by duration of post-RT intact ovarian function or HRT use did not statistically significantly modify the radiation dose-response curve.

CONCLUSIONS: BC risk in female HL survivors increases linearly with radiation dose. HRT does not appear to increase BC risk for HL survivors with therapy-induced early menopause. There are no indications that endogenous and exogenous gonadal hormones affect the radiation dose-response relationship.

Impactfactor: *5.133*

Cone-Beam CT-based position verification for oesophageal cancer: Evaluation of registration methods and anatomical changes during radiotherapy

van Nunen A, van der Sangen MJ, van Boxtel M, van Haaren PM

Technical Innovations & Patient Support in Radiation Oncology 2017;(3-4):30–36.

Purpose: To evaluate different registration methods, setup margins and number of corrections for CBCT-based position verification for oesophageal cancer and to evaluate anatomical changes during the course of radiotherapy treatment.

Methods: From 50 patients, 440 CBCT-scans were registered automatically using a soft tissue or bone registration algorithm and compared to the clinical match. Moreover, relevant anatomical changes were monitored. A sub-analysis was performed to evaluate if tumour location influenced setup variations. Margin calculation was performed and the number of setup corrections was estimated. Results were compared to a patient group previously treated with MV-EPID based position verification.

Results: CBCT-based setup variations were smaller than EPID-based setup variations, resulting in smaller setup margins of 5.9 mm (RL), 7.5 mm (CC) and 4.7 mm (AP) versus 6.0 mm, 7.8 mm and 5.5 mm, respectively.

A reduction in average number of setup corrections per patient was found from 0.75 to 0.36. From all automatically registered CBCT-scans, a clipbox around PTV and vertebras combined with soft tissue registration resulted in the smallest setup margins of 5.9 mm (RL), 7.7 mm (CC), 4.8 mm (AP) and smallest average number of corrections of 0.38. For distally located tumours, a setup margin of 7.7 mm (CC) was required compared to 5.6 mm for proximal tumours. Reduction of GTV volume, heart volume and change in diaphragm position were observed in 16, 10 and 15 patients, respectively.

Conclusions: CBCT-based set-up variations are smaller than EPID-based variations and vary according to tumour location. When using kV-CBCT a large variety of anatomical changes is revealed, which cannot be observed with MV-EPID.

Impactfactor: --

De rol van PET/CT bij oligometastatische ziekte

Roef MJ, **van der Sangen MJ**, Hurkmans CW

NTVO : Ned Tijdschr Oncol 2017;14(7):256-64

De diagnostiek en behandeling van oligometastatische ziekte staat de laatste jaren toenemend in de belangstelling. PET/CT is een ‘total body’ beeldvormende techniek met een relatief goede opbrengst in de detectie van zowel regionale lymfogene metastasen als van metastasen op afstand en heeft daarom vaak de voorkeur boven andere modaliteiten. Zo wordt PET/CT steeds vaker ingezet bij de (re)stadiëring, radiotherapieplanning en follow-up. Bij het gebruik van PET/CT dient men zich bewust te zijn van de beperkingen van het onderzoek. Zowel apparatuur-als patiëntgebonden factoren liggen hieraan ten grondslag.

Impactfactor: --

Elective breast radiotherapy including level I and II lymph nodes: A planning study with the humeral head as planning risk volume

Surmann K, van der Leer J, Branje T, van der Sangen M, van Lieshout M, Hurkmans CW

Radiat Oncol. 2017 Jan 18;12(1):22

BACKGROUND:

The aim of this study was to assess the dose to the humeral head planning risk volume with the currently used high tangential fields (HTF) and compare different planning techniques for breast radiotherapy including axillary level I and II lymph nodes (PTVn) while sparing the humeral head.

METHODS:

Ten patients with left-sided breast cancer were enrolled in a planning study with 16 fractions of 2.66 Gy. Four planning techniques were compared: HTF, HTF with sparing of the humeral head, 6-field IMRT with sparing of the humeral head and VMAT with sparing of the humeral head. The humeral head?+?10 mm was spared by restricting V40Gy?<?1 cc.

RESULTS:

The dose to the humeral head was too high with HTF (V40Gy on average 20.7 cc). When sparing the humeral head in HTF, PTVn V90% decreased significantly from 97.9% to 89.4%. 6-field IMRT and VMAT had a PTVn V90% of 98.2% and 99.5% respectively. However, dose to the lungs, heart and especially the contralateral breast increased with VMAT.

CONCLUSIONS:

The humeral head is rarely spared when using HTF. When sparing the humeral head, the 6-field IMRT technique leads to adequate PTV coverage while not increasing the dose to the OARs.

Impactfactor: 2.568

Extended adjuvant aromatase inhibition after sequential endocrine therapy (DATA): a randomised, phase 3 trial

Tjan-Heijnen VC, van Hellemond IE, Peer PG, Swinkels AC, Smorenburg CH, **van der Sangen MJ**, Kroep JR, De Graaf H, Honkoop AH, Erdkamp FL, van den Berkmortel FW, de Boer M, de Roos WK, Linn SC, Imholz AL, Seynaeve CM; Dutch Breast Cancer Research Group (BOOG) for the DATA Investigators.: Nieuwenhuijzen GA

Lancet Oncol. 2017 Nov;18(11):1502-1511

BACKGROUND:

The effect of extended adjuvant aromatase inhibition in hormone receptor-positive breast cancer after sequential endocrine therapy of tamoxifen followed by an aromatase inhibitor for a 5-year treatment period still needs clarification. To address this issue, we began the DATA study to assess different durations of anastrozole therapy after tamoxifen.

METHODS:

DATA was a prospective, randomised, open-label, multicentre, phase 3 study done in 79 hospitals in the Netherlands. We randomly assigned postmenopausal women with hormone receptor-positive early breast cancer with no signs of disease recurrence after 2-3 years of adjuvant tamoxifen to either 3 or 6 years of anastrozole treatment (1 mg orally once a day) in a 1:1 ratio. We used TENALEA (Trans European Network for Clinical Trials Services) for the randomisation procedure. Stratification factors were nodal status, hormone receptor status, HER2 status, and tamoxifen treatment duration. The primary study endpoint of this analysis was disease-free survival starting beyond 3 years after randomisation (adapted disease-free survival). Here we report the final analysis from the DATA trial, which is registered with ClinicalTrials.gov, number NCT00301457.

FINDINGS:

Between June 28, 2006, and Aug 10, 2009, we screened 1912 patients of whom 955 were assigned to the 3-year group and 957 to the 6-year anastrozole treatment group. 1860 patients were eligible (931 in the 6-year group and 929 in the 3-year group) and 1660 were disease free 3 years after randomisation. The 5-year adapted disease-free survival was 83·1% (95% CI 80·0-86·3) in the 6-year group and 79·4% (76·1-82·8) in the 3-year group (hazard ratio [HR] 0·79 [95% CI 0·62-1·02]; p=0·066). Patients in the 6-year treatment group had more adverse events than those in the 3-year treatment group, including all-grade arthralgia or myalgia (478 [58%] of 827 in the 6-year treatment group vs 438 [53%] of 833 in the 3-year treatment group) and osteopenia or osteoporosis (173 [21%] vs 137 [16%]).

INTERPRETATION:

We cannot recommend the use of extended adjuvant aromatase inhibition after 5 years of sequential endocrine therapy in all postmenopausal women with hormone receptor-positive breast cancer.

Erratum in: Correction to Lancet Oncol 2017; 18: 1502-11. [Lancet Oncol. 2017]

Impactfactor: 33.900

Heart position variability during voluntary moderate deep inspiration breath-hold radiotherapy for breast cancer determined by repeat CBCT scans

van Haaren P, Claassen-Janssen F, **van de Sande I**, Boersma L, **van der Sangen M**, Hurkmans C

Phys Med. 2017 Aug;40:88-94.

Voluntary moderate deep inspiration breath hold (vmDIBH) in left-sided breast cancer radiotherapy reduces cardiac dose. The aim of this study was to investigate heart position variability in vmDIBH using CBCT and to compare this variability with differences in heart position between vmDIBH and free

breathing (FB). For 50 patients initial heart position with respect to the field edge (HP-FE) was measured on a vmDIBH planning CT scan. Breath-hold was monitored using an in-house developed vertical plastic stick. On pre-treatment CBCT scans, heart position variability with respect to the field edge (?HP-FE) was measured, reflecting heart position variability when using an offline correction protocol. After registering the CBCT scan to the planning CT, heart position variability with respect to the chest wall (?HP-CW) was measured, reflecting heart position variability when using an online correction protocol. As a control group, vmDIBH and FB computed tomography (CT) scans were acquired for 30 patients and registering both scans on the chest wall. For 34 out of 50 patients, the average HP-FE and HP-CW increased over the treatment course in comparison to the planning CT. Averaged over all patients and all treatment fractions, the ?HP-FE and the ?HP-CW was 0.8±4.2mm (range -9.4-+10.6mm) and 1.0±4.4mm (range -8.3-+10.4mm) respectively. The average gain in heart to chest wall distance was 11.8±4.6mm when using vmDIBH instead of FB. In conclusion, substantial variability in heart position using vmDIBH was observed during the treatment course.

Impactfactor: 1.990

Individualized early death and long-term survival prediction after stereotactic radiosurgery for brain metastases of non-small cell lung cancer: Two externally validated nomograms

Zindler JD, Jochems A, Lagerwaard FJ, Beumer R, Troost EGC, Eekers DB, Compter I, **van der Toorn PP**, Essers M, Oei B, Hurkmans CW, Bruynzeel AM, Bosmans G, Swinnen A, Leijenaar RT, Lambin P

Radiother Oncol. 2017 May 123(2):189-194. Epub 2017 Feb 23

INTRODUCTION:

Commonly used clinical models for survival prediction after stereotactic radiosurgery (SRS) for brain metastases (BMs) are limited by the lack of individual risk scores and disproportionate prognostic groups. In this study, two nomograms were developed to overcome these limitations.

METHODS:

495 patients with BMs of NSCLC treated with SRS for a limited number of BMs in four Dutch radiation oncology centers were identified and divided in a training cohort (n=214, patients treated in one hospital) and an external validation cohort n=281, patients treated in three other hospitals). Using the training cohort, nomograms were developed for prediction of early death (<3months) and long-term survival (>12months) with prognostic factors for survival. Accuracy of prediction was defined as the area under the curve (AUC) by receiver operating characteristics analysis for prediction of early death and long term survival. The accuracy of the nomograms was also tested in the external validation cohort.

RESULTS:

Prognostic factors for survival were: WHO performance status, presence of extracranial metastases, age, GTV largest BM, and gender. Number of brain metastases and primary tumor control were not prognostic factors for survival. In the external validation cohort, the nomogram predicted early death statistically significantly better ($p<0.05$) than the unfavorable groups of the RPA, DS-GPA, GGS, SIR, and Rades 2015 (AUC=0.70 versus range AUCs=0.51-0.60 respectively). With an AUC of 0.67, the other nomogram predicted 1year survival statistically significantly better ($p<0.05$) than the favorable groups of four models (range AUCs=0.57-0.61), except for the SIR (AUC=0.64, $p=0.34$). The models are available on www.predictcancer.org.

CONCLUSION:

The nomograms predicted early death and long-term survival more accurately than commonly used prognostic scores after SRS for a limited number of BMs of NSCLC. Moreover these nomograms enable individualized probability assessment and are easy into use in routine clinical practice.

Impactfactor: 4.328

Influence of the Extent and Dose of Radiation on Complications After Neoadjuvant Chemoradiation and Subsequent Esophagectomy With Gastric Tube Reconstruction With a Cervical Anastomosis

Koëter M, Kathiravetpillai N, Gooszen JA, van Berge Henegouwen MI, Gisbertz SS, **van der Sangen MJ**, Luyer MD, Nieuwenhuijzen GA, Hulshof MC

Int J Radiat Oncol Biol Phys. 2017 Mar 15;97(4):813-821

PURPOSE: To detrmine, in a large series, the influence of the extent and dose of radiation to the fundus of the stomach and mediastinum on the development and severity of anastomotic complications in patients with esophageal cancer treated with neoadjuvant chemoradiation followed by esophagectomy with cervical anastomosis.

METHODS AND MATERIALS: Between 2005 and 2012, 364 consecutive patients with esophageal cancer treated with neoadjuvant chemoradiation (41.4 Gy combined with chemotherapy) followed by esophagectomy were included. The future anastomotic region in the fundus was determined, and the mean dose, V20-V40, and upper planning target volume border in relation to mediastinal length, expressed as the mediastinal ratio, were calculated.

RESULTS: Anastomotic leakage occurred in 22% and anastomotic stenosis in 41%. Logistic regression analysis revealed no influence of age, comorbidity, mean fundus dose, V20-V40, or the mediastinal ratio on the incidence of anastomotic leakage or anastomotic stenosis. In 28% of the patients severe complications (Clavien-Dindo score of =IIIB) occurred. The presence of multiple comorbidities (hazard ratio 2.4 [95% confidence interval 1.3-4.5], P=.006) and a mediastinal ratio of 0.5 to 1.0 (hazard ratio 1.9 [95% confidence interval 1.0-3.5], P=.036) were both independent predictors of severe complications.

CONCLUSION: With a mean radiation dose of 24.2 Gy to the future anastomotic region of the gastric fundus, the radiation dose was not associated with the incidence of anastomotic leakage or anastomotic stenosis. The incidence of severe complications was associated with a high superior mediastinal planning target volume border.

Impactfactor: 4.495

Ovarian Function Recovery During Anastrozole in Breast Cancer Patients With Chemotherapy-Induced Ovarian Function Failure

van Hellemond IE, Vriens IJ, Peer PG, Swinkels AC, Smorenburg CH, Seynaeve CM, **van der Sangen MJ**, Kroep JR, de Graaf H, Honkoop AH, Erdkamp FL, van den Berkmortel FW, Kitzen JJ, de Boer, de Roos WK, Linn SC, Imholz AL, Tjan-Heijnen VC; Dutch Breast Cancer Research Group (BOOG).

J Natl Cancer Inst. 2017 Dec 1;109(12).

Background:

Aromatase inhibitors (AIs) are given as adjuvant therapy for hormone receptor-positive breast cancer in postmenopausal women, also to those with chemotherapy-induced ovarian function failure. The current analysis reports on endocrine data of patients with chemotherapy-induced ovarian function failure who were included in the phase III DATA study assessing different durations of adjuvant anastrozole after tamoxifen.

Methods:

We identified all patients with chemotherapy-induced ovarian function failure. Women who underwent a bilateral ovariectomy or used luteinizing hormone-releasing hormone agonists before random assignment were excluded. Plasma estradiol and follicle-stimulating hormone levels were monitored until 30 months after random assignment at local laboratories. We aimed to determine the ovarian function recovery (OFR) rate during AI use by the cumulative incidence competing risk method and analyzed the trend of estradiol levels during AI use by a nested case-control approach in which a subset of control subjects were compared with the OFR patients excluding the value at OFR diagnosis.

Results:

The 329 eligible patients had a median age of 50.0 years (range = 45-57 years) at random assignment. Thirty-nine patients developed OFR, corresponding with a 30-month recovery rate of 12.4%. Of these, 11 (28.2%) were age 50 years or older at AI initiation. The estradiol level decreased statistically significantly by 37.8% (95% CI = 27.4% to 46.7%) over the initial 30 months of AI treatment in both groups. However, the estradiol levels in the women who experienced OFR remained statistically significantly higher (difference = 20.6%, 95% CI = 2.0% to 42.7%) prior to OFR diagnosis compared with those who did not experience OFR.

Conclusions:

The risk of OFR during AI treatment in breast cancer patients with chemotherapy-induced ovarian function failure is relevant, even beyond 45 years. Furthermore, women experiencing OFR had statistically significant higher estradiol levels during AI treatment (before OFR) than those without, with potential consequences regarding efficacy.

Impactfactor: 12.589

Timed Get Up and Go Test and Geriatric 8 Scores and the Association With (Chemo-)Radiation Therapy Noncompliance and Acute Toxicity inÂ Elderly Cancer Patients

Middelburg JG, Mast ME, de Kroon M, Jobsen JJ, Rozema T, Maas H, Baartman EA, Geijsen D, van der Leest AH, van den Bongard DJ, van Loon J, **Budiharto T**, Coebergh JW, Aarts MJ, Struikmans H, LPRO (Dutch National Organization for Radiotherapy in the Elderly)

Int J Radiat Oncol Biol Phys. 2017 Jul 15 98(4):843-849. Epub 2017 Jan 29

PURPOSE:

To investigate whether the Geriatric 8 (G8) and the Timed Get Up and Go Test (TGUGT) and clinical and demographic patient characteristics were associated with acute toxicity of radiation therapy and noncompliance in elderly cancer patients being irradiated with curative intent.

METHODS AND MATERIALS:

Patients were eligible if aged =65 years and diagnosed with breast, non-small cell lung, prostate, head and neck, rectal, or esophageal cancer, and were referred for curative radiation therapy. We recorded acute toxicity and noncompliance and identified potential predictors, including the G8 and TGUGT.

RESULTS:

We investigated 402 patients with a median age of 72 years (range, 65-96 years). According to the G8, 44.4% of the patients were frail. Toxicity grade =3 was observed in 22% of patients who were frail according to the G8 and 9.1% of patients who were not frail. The difference was 13% (confidence interval 5.2%-20%; P=.0006). According to the TGUGT 18.8% of the patients were frail; 21% of the frail according to the TGUGT developed toxicity grade =3, compared with 13% who were not frail. The difference was 7.3% (confidence interval -2.7% to 17%; P=.11). Overall compliance was 95%. Toxicity was most strongly associated with type of primary tumor, chemotherapy, age, and World Health Organization performance status. Compliance was associated with type of primary tumor and age.

CONCLUSIONS:

The usefulness of the TGUGT and G8 score in daily practice seems to be limited. Type of primary tumor, chemoradiotherapy, age, and World Health Organization performance status were more strongly associated with acute toxicity. Only chemoradiotherapy and age were associated with noncompliance. Overall the compliance was very high. To allow better-informed treatment decisions, a more accurate prediction of toxicity is desirable.

Impactfactor: 5.133

Spoedeisende Hulp

Comments on: Effect of warming bupivacaine 0.5% on ultrasound-guided axillary plexus block. Randomized prospective double-blind study by W. Trabelsi, A.B. Gabsia, A. Lebbi, W. Sammoud, I. Labbène, S. Kchelfi, M. Ferjani, published in Orthop Traumatol Surg Res 2017;103:71-75
Smits GJP
Orthop Traumatol Surg Res. 2017 Jun 103(4):627. Epub 2017 Apr 4
Geen abstract beschikbaar
Impactfactor: 1.468

Procedural sedation and analgesia practices by emergency physicians in the Netherlands: a nationwide survey
Kuypers MI, **Smits GJP**, Valkenet SC, **Thijssen WAMH**, Plötz FB
Int J Emerg Med. 2017 Dec 15;10(1):33

BACKGROUND: Several efforts have been made to assure and to improve the quality of procedural sedation and analgesia (PSA) performed by emergency physicians (EPs) in The Netherlands. This study investigated the current PSA practice and competences of EPs in both adult and paediatric patients. In particular, if residency and current training, awareness of guidelines is sufficient for registered EPs to adequately perform PSA and if the availability of both adult and paediatric PSA in the ED is adequate.

METHODS: A cross-sectional nationwide survey was performed amongst Dutch EPs (n?=?463) in June 2016. We collected data on background, training, practice, and competencies of both adult and paediatric PSA. We investigated guideline adherence, reasons for not performing PSA, and desired improvements.

RESULTS: The respondents (n?=?191) represented 84.6% hospitals with EPs and 41.3% of all EPs in The Netherlands. Nearly all EPs (97.8%) performed PSA in adult patients compared to only 59.1% who performed PSA in paediatric patients (p?<?0.001). The major reason for not performing paediatric PSA was caused by a lack of exposure during the training-program (74.1%). PSA-guideline knowledge (98.3%) and PSA related adverse event registration (98.3%) were excellent. Lack of 24/7-availability of both adult and paediatric emergency department PSA was mainly caused by a shortage of EPs. Self-reflection indicated that EPs feel less competent in performing paediatric PSA when compared to adult PSA.

CONCLUSION: This nationwide survey demonstrates that there is still a significant gap between the performance of adult and paediatric PSA even though guideline adherence and registration of PSA-related adverse events appear to be adequate. Enhancement of paediatric PSA training in combination with an increase of EP-staffing can help improve the availability of adult and paediatric PSA in the emergency department.

Impactfactor: --

Procedural sedation in the emergency department by Dutch emergency physicians: a prospective multicentre observational study of 1711 adults
Smits GJ, Kuypers MI, Mignot LA, Reijners EP, Oskam E, Van Doorn K, **Thijssen WA**, Korsten EH
Emerg Med J. 2017 Apr;34(4):237-242. Epub 2016 Oct 21

OBJECTIVE: To describe our experience performing ED procedural sedation in a country where emergency medicine (EM) is a relatively new specialty.

METHODS: This is a prospective observational study of adult patients undergoing procedural sedation by emergency physicians (EPs) or EM residents in eight hospitals in the Netherlands. Data were collected on a standardised form, including patient characteristics, sedative and analgesic used, procedural success, adverse events (classified according to World SIVA) and rescue interventions.

RESULTS: 1711 adult cases were included from 2006 to 2013. Propofol, midazolam and esketamine (S+ enantiomer of ketamine) were the most used sedatives (63%, 29% and 8%). We had adverse event data on all patients. The overall adverse event rate was 11%, mostly hypoxia or apnoea. There was no difference in adverse event rate between EPs and EM residents. However, there was a significantly higher success rate of the procedure when EPs did the procedural sedation (92% vs 84%). No moderate (unplanned hospital admission or escalation of care) or sentinel SIVA outcomes occurred (pulmonary aspiration syndrome, death or permanent neurological deficit).

CONCLUSION: Adverse events during procedural sedation occurred in 11% of patients. There were no moderate or sentinel outcomes. All events could be managed by the sedating physician. In a country where EM is a relatively new specialty, procedural sedation appears to be safe when performed by EPs or trained EM residents and has comparable adverse event rates to international studies.

Impactfactor: 1.861

Urologie

Cancer survivors' preference for follow-up care providers: a cross-sectional study from the population-based PROFILES-registry

Huibertse LJ, van Eenbergen M, de Rooij BH, Bastiaens MT, Fossion LM, de la Fuente RB, Kil PJ, **Koldewijn EL**, Meier AH, Mommers RJ, Niemer AQ, Oddens JR, Oomens EH, Prins M, de Roos KP, Thissen MR, Timmermans MW, Wijsman BP, van de Poll-Franse LV, Ezendam NP

Acta Oncol. 2017 Feb;56(2):278-287

BACKGROUND:

The best practice for the organization of follow-up care in oncology is under debate, due to growing numbers of cancer survivors. Understanding survivors' preferences for follow-up care is elementary for designing patient-centred care. Based on data from prostate cancer and melanoma survivors, this study aims to identify: 1) preferences for follow-up care providers, for instance the medical specialist, the oncology nurse or the general practitioner; 2) characteristics associated with these preferences and 3) the preferred care provider to discuss cancer-related problems.

MATERIAL AND METHODS:

Survivors diagnosed with prostate cancer (N?=?535) and melanoma (N?=?232) between 2007 and 2013 as registered in The Netherlands Cancer Registry returned a questionnaire (response rate was 71% and 69%, respectively). A latent class cluster model analysis was used to define preferences and a multinomial logistic regression analysis was used to identify survivor-related characteristics associated with these preferences.

RESULTS:

Of all survivors, 29% reported no preference, 40% reported a preference for the medical specialist, 20% reported a preference for both the medical specialist and the general practitioner and 11% reported a preference for both the medical specialist and the oncology nurse. Survivors who were older, lower/intermediate educated and women were more likely to have a preference for the medical specialist. Lower educated survivors were less likely to have a preference for both the medical specialist and the general practitioner. Overall, survivors prefer to discuss diet, physical fitness and fatigue with the general practitioner, and hereditary and recurrence with the medical specialist. Only a small minority favored to discuss cancer-related problems with the oncology nurse.

CONCLUSION:

Survivors reported different preferences for follow-up care providers based on age, education level, gender and satisfaction with the general practitioner, showing a need for tailored follow-up care in oncology. The results indicate an urgency to educate patients about transitions in follow-up care.

Impactfactor: 3.730

Case report. Infarction of a testis in a patient suffering from sickle cell anaemia / Case report. Infarcering van een testis bij een patiënt met sikkelcelanemi

Beulens AJ, **Kuenen MB**, Yo LS, **Koldewijn EL**

Tijdschr Urol (2017) 7: 188-90

Of all patients who visit the Emergency Room (ER) with scrotal pain, only a small number is diagnosed with testicular torsion. After physical examination and ultrasound with colour doppler of the scrotum the majority of these patients are diagnosed with another condition, in most cases an epididymo-orchitis. However, in some cases there a less common cause for the pain is found. We present the case of a 20-year-old Haitian male in our ER, suffering from an acute painful left testicle, caused by testicular infarction based on sickle cell anaemia.

Impactfactor: --

Current training on the basics of robotic surgery in the Netherlands: Time for a multidisciplinary approach?

Brinkman W, de Angst I, Schreuder H, Schout B, Draaisma W, Verweij L, **Hendrikx A**, van der Poel H

Surg Endosc. 2017 Jan;31(1):281-287

INTRODUCTION:

The following research questions were answered: (1) What are the training pathways followed by the current robot professionals? (2) Are there any differences between the surgical specialties in robot training and robot use? (3) What is their opinion about multidisciplinary basic skills training?

METHODS:

An online questionnaire was sent to 91 robot professionals in The Netherlands. The questionnaire contained 21 multiple-choice questions focusing on demographics, received robot training, and their opinion on basic skills training in robotic surgery.

RESULTS:

The response rate was 62 % (n = 56): 13 general surgeons, 16 gynecologists, and 27 urologists. The urologists performed significantly more robotic procedures than surgeons and gynecologists. The kind of training of all professionals varied from a training program by Intuitive Surgical, master-apprenticeship with or without duo console, fellowship, and self-designed training programs. The training did neither differ significantly among the different specialties nor the year of starting robotic surgery. Majority of respondents favor an obliged training program including an examination for the basics of robot skills training.

CONCLUSION:

Training of the current robot professionals is mostly dependent on local circumstances and the manufacturer of the robot system. Training is independent of the year of start with robotic surgery and speciality. To guarantee the quality of future training of residents and fellows in robot-assisted surgery, clear training goals should be formulated and implemented. Since this study shows that current training of different specialities does not differ, training in robotic surgery could be started by a multidisciplinary basic skills training and assessment.

Impactfactor: 3.540

High educational impact of a national simulation-based urological curriculum including technical and non-technical skills

de Vries AH, Schout BM, van Merriënboer JJ, Pelger RC, **Koldewijn EL**, Muijtjens AM, Wagner C

Surg Endosc. 2017 Feb;31(2):928-936. Epub 2016 Jul 7

BACKGROUND:

Although simulation training is increasingly used to meet modern technology and patient safety demands, its successful integration within surgical curricula is still rare. The Dutch Urological Practical Skills (D-UPS) curriculum provides modular simulation-based training of technical and non-technical basic urological skills in the local hospital setting. This study aims to assess the educational impact of implementing the D-UPS curriculum in the Netherlands and to provide focus points for improvement of the D-UPS curriculum according to the participants.

METHODS:

Educational impact was assessed by means of qualitative individual module-specific feedback and a quantitative cross-sectional survey among residents and supervisors. Twenty out of 26 Dutch teaching hospitals participated. The survey focussed on practical aspects, the D-UPS curriculum in general, and the impact of the D-UPS curriculum on the development of technical and non-technical skills.

RESULTS:

A considerable survey response of 95 % for residents and 76 % for supervisors was obtained. Modules were attended by junior and senior residents, supervised by a urologist, and peer teaching was used. Ninety percent of supervisors versus 67 % of residents judged the D-UPS curriculum as an important addition to current residency training (p = 0.007). Participants' aggregated general judgement of the modules showed a substantial percentage favorable score (M ± SE: 57 ± 4 %). The impact of training on, e.g., knowledge of materials/equipment and ability to anticipate on complications was high, especially for junior residents (77 ± 5 and 71 ± 7 %, respectively). Focus points for improvement of the D-UPS curriculum according to the participants include adaptation of the training level to residents' level of experience and focus on logistics.

CONCLUSION:

The simulation-based D-UPS curriculum has a high educational impact. Residents and supervisors consider the curriculum to be an important addition to current residency training. Focus points for improvement of the D-UPS curriculum according to the participants include increased attention to logistics and integration of a spiral learning approach.

Impactfactor: 3.540

Initiative Comprehensive Prostate Cancer Network in South-East Netherlands / Initiatief Comprehensive Prostate Cancer Network (CPCN) in Zuidoost Nederland

Jean-Paul A. van Basten, Rik M. Somford, Joost de Baaij, Michiel Sedelaar**, Eric Vrijhof**

Tijdschrift voor urologie, October 2017, Volume 7, Issue 6–7, pp 134–144

The current diagnostics and therapies of prostate cancer is complex. Complex interventions such as robot-assisted radical prostatectomies require concentration in order to achieve a measurable optimal quality level. Volume is necessary to implement and evaluate short-cyclical quality improvements. In

addition, volume is needed to provide continuous insight to all involved medical and nursing care professionals and to create an optimal logistic and quality structure. In regional Comprehensive Prostate Cancer Networks (CPCNs) care is concentrated where necessary and close to home if possible. In addition, there is an emphatic role for each hospital member, in collaboration with the first line. The starting point of a CPCN is to provide the same level of care at all locations within this network, through information uniformity, diagnostics, care paths, participation in quality indicators, including Patient Reported Outcome Measures (PROMs), continuous monitoring, quality improvement and science. Collaboration on the medical care lines offers not only benefits for the patient, but also for the participating agencies. Such cooperation is cost-effective and will reduce overdiagnostics and unnecessary treatment. Improvement of outcomes and processes, and cost control, are realized according to Santeon's value based health care methodology. This article describes the initiatives in our region, which together form a first step towards such a CPCN.

Impactfactor: --

Minimal Device Encrustation on Vesair Intravesical Balloons in the Treatment of Stress Urinary Incontinence: Analysis of Balloons Removed from Women in the SOLECT Trial

van Koeveringe GA, De Wachter S, Zuckerman JM, Tommaselli G, **de Wildt MJ**, Everaert KC, Michielsen DP, Wyndaele JJ

Adv Ther. 2017 Jul;34(7):1686-1694

INTRODUCTION:

Encrustation of urinary biomaterials is common; however, the incidence of surface deposition on the Vesair® intravesical pressure-attenuation balloon has not been previously reported. The purpose of this analysis is to determine the incidence and potential risk factors for encrustation of the Vesair intravesical balloon.

METHODS:

The SOLECT trial is a prospective randomized controlled trial conducted at several European centers to evaluate the safety and efficacy of the Vesair balloon for the treatment of female stress urinary incontinence (SUI). Women included in the study demonstrated SUI symptoms for more than 12 months without complicating factors, such as history of recurrent urinary tract infections or nephrolithiasis. All balloons removed from women enrolled in the SOLECT trial were analyzed for surface characteristics and encrustation. Surface deposition severity was quantified and composition analyzed with infrared spectroscopy and scanning electron microscopy. Incidence of surface deposition was tabulated and risk factors analyzed.

RESULTS:

One hundred and five balloons removed from 75 women were included in this analysis. Measurable stone deposition of less than 1.5 mm was found on four balloons (3.8%), surface granules were noted on 42 (40.0%), surface film on 11 (10.5%), and both granules and film on two (1.9%). Analysis identified calcium oxalate both in measurable encrustation deposits as well as those with surface granulation. Pooled analysis found that dwell time was a risk factor for calcium deposition.

CONCLUSION:

The rate of encrustation on the Vesair intravesical balloon is low and does not appear to increase the rate of adverse outcomes or reduce clinical efficacy.

Impactfactor: *2.709*

Psoas hitch ureteral reimplantation after surgery for locally advanced and locally recurrent colorectal cancer: Complications and oncological outcome

van den Heijkant F, Vermeer TA, **Vrijhof EJ**, Nieuwenhuijzen GA, **Koldewijn EL**, Rutten HJ

Eur J Surg Oncol. 2017 Oct;43(10):1869-1875.

INTRODUCTION:

The most important prognostic factor for oncological outcome of rectal cancer is radical surgical resection. In patients with locally advanced T4 rectal cancer (LARC) or locally recurrent rectal cancer (LRRC) (partial) resection of the urinary tract is frequently required to achieve radical resection. The psoas bladder hitch (PBH) technique is the first choice for reconstruction of the ureter after partial resection and this bladder-preserving technique should not influence the oncological outcome.

METHODS:

Demographic and clinical data were collected prospectively for all patients operated on for LARC or LRRC between 1996 and 2014 who also underwent a psoas hitch ureter reconstruction. Urological complications and oncological outcome were assessed.
RESULTS:
The sample comprised 70 patients, 30 with LARC and 40 with LRRC. The mean age was 62 years (range: 39-86). Postoperative complications occurred in 38.6% of patients, the most frequent were urinary leakage (22.9%), ureteral stricture with hydronephrosis (8.6%) and urosepsis (4.3%). Surgical re-intervention was required in 4 cases (5.7%), resulting in permanent loss of bladder function and construction of a ureter-ileo-cutaneostomy in 3 cases (4.3%). Oncological outcome was not influenced by postoperative complications.
CONCLUSION:
The rate of complications associated with the PBH procedure was higher in our sample than in previous samples with benign conditions, but most complications were temporary and did not require surgical intervention. We conclude that the bladder-sparing PBH technique of ureter reconstruction is feasible in locally advanced and recurrent rectal cancer with invasion of the urinary tract after pelvic radiotherapy.
Impactfactor: 3.522

Boeken

Algemeen Klinisch Laboratorium

R.J. Almeida, **S.L.M. van Loon**, U. Kaymak, A.M. Wilbik, **V. Scharnhorst**, **A. Boer**
Modeling patients' methylmalonic acid levels using probabilistic fuzzy systems – p. 1-6
In: 2017 IEEE International Conference on Fuzzy Systems (FUZZ-IEEE), 9-12 July 2017, Naples, Italy
Piscataway : Institute of Electrical and Electronics Engineers Inc., 2017
ISBN: 978-1-5090-6035-1

Anesthesiologie

H. Yan, P.M.E. Van Gorp, U. Kaymak, Lei Ji, X. Lu, Choo Chiap Chiau, **H. Korsten**, Huilong Duan
Variance analysis in task-time matrix clinical pathways – p. 253-6
In: 2017 IEEE EMBS International Conference on Biomedical & Health Informatics (BHI)
[sl] : IEEE, 2017

Cardiologie

Zimmermann FM, Pijls NH, Nunen LX, Tonino WA
Chapter 6: The Coronary Circulation – p. 105-120
In: Interventional Cardiology, 2nd edition
Authors: Habib Samady, William Fearon, Alan C. Yeung, Spencer B. King
[sl] : McGraw-Hill Education, 2017
ISBN: 9780071820363

Chirurgie

Jakimowicz JJ, **Smulders JF**
Cholecystectomy - p. 139-43
In: Surgical Principles of Minimally Invasive Procedures
Editor: Bonjer J
[s.l.] : Springer International Publishing, 2017
ISBN: 978-3-319-43194-9

Maag-darm-leverziekten

Swager AF, Sharma P, Bergman JJ, **Curvers WL**
Chapter 6: Applications of NBI HRE and preliminary data: Barrett's esophagus and adenocarcinoma – p. 60-71
In: Comprehensive atlas of high-resolution endoscopy and narrowband imaging, 2nd ed.
Edited by: Jonathan Cohen
Oxford : Wiley Blackwell; 2017.
ISBN: 9781118705933

Orthopedie

Hendriks JG, van Kempen RW, van Dommelen L
6.3 Treatment of prosthetic joint infection – p. 150-156
In: Management of Periprosthetic Joint Infection
Editor: Kühn, Klaus-Dieter
[s.l.] : Springer, 2017
ISBN print: 9783662544686
ISBN ebook: 9783662544693

Promoties

Promovendi

Chirurgie

Pouwels JH
Perioperative physiology and optimalisation in bariatric and metabolic surgery
Maastricht : Maastricht University, 2017
ISBN: 9789462996045
Promotiedatum: 31-05-2017

Simkens GA
Refining Selection Criteria for Cytoreductive Surgery and HIPEC : in patients with peritoneal metastases of colorectal origin
[s.l.] : [s.n.], 2017
ISBN: 9789463321150
Promotiedatum: 13-01-2017

Gynaecologie

Putten LJ van der
Prognostic markers and the individualized management of endometrial carcinomas
Nijmegen : Radboud Universiteit, 2017
ISBN: 9789462956254
Promotiedatum: 06-04-2017

Inwendige Geneeskunde

Bernards N
Treatment and survival of patients with metastatic upper gastrointestinal cancer : hard to digest?
Rotterdam : Erasmus University, 2017
ISBN: 9789492303127
Promotiedatum: 13-04-2017

Razenberg LG
Systemic treatment for advanced colorectal cancer : bridging the gap between clinical studies and daily practice
Erasmus Universiteit Rotterdam, 2017
ISBN: 9789462995284
Promotiedatum: 21-04-2017

Salden BN
Nutritional interventions focusing on gastrointestinal and metabolic health
Maastricht: Universiteit Maastricht, 2017
ISBN: 9789463331296
Promotiedatum: 17-03-17

Vriens BE
Neoadjuvant chemotherapy in breast cancer: efficacy, response assessment and axillary strategy
Maastricht : Universiteit Maastricht, 2017
Promotiedatum: 13-12-2017

Plastische Chirurgie

Kerver AL
Computer assisted surgical anatomy mapping : applications in surgical anatomy research, tailor-made surgery and presonalized teaching
Rotterdam : Erasmus Universiteit Rotterdam, 2017
ISBN: 9789491462399
Promotiedatum: 12-09-2017

Urologie

Vries AH de
Training in Urology. Time to Test!: Development of skills training and assessment tools
Amsterdam : Vrije Universiteit Amsterdam, 2017
ISBN: 9789402804584
Promotiedatum: 31-05-2017

(Co)-Promotoren:

Chirurgie

Buise MP

Co-promotor bij:

- Pouwels JH - Perioperative physiology and optimalisation in bariatric and metabolic surgery
  Promotiedatum: 31-05-2017

Hingh IH de

Co-promotor bij:

- Simkens GA- Refining Selection Criteria for Cytoreductive Surgery and HIPEC : in patients with peritoneal metastases of colorectal origin
  Promotiedatum: 13-01-2017

Kusters M

Co-promotor bij:

- Holman F A - Challenges in Treating Patients with Locally Advanced and Locally Recurrent Rectal Carcinoma
  Promotiedatum: 30-11-2017
- Jorritsma-Bosman SJ - Optimization of treatment for locally recurrent rectal cancer
  Promotiedatum: 19-12-2017

Nienhuijs SW

Co-promotor bij:

- Pouwels JH - Perioperative physiology and optimalisation in bariatric and metabolic surgery
  Promotiedatum: 31-05-2017
- Simkens GA - Refining Selection Criteria for Cytoreductive Surgery and HIPEC : in patients with peritoneal metastases of colorectal origin
  Promotiedatum: 13-01-2017

Nieuwenhuijzen GA

Co-promotor bij:

- Holman FA - Challenges in Treating Patients with Locally Advanced and Locally Recurrent Rectal Carcinoma
  Promotiedatum: 30-11-2017
- Jorritsma-Bosman SJ - Optimization of treatment for locally recurrent rectal cancer
  Promotiedatum: 19-12-2017

Rutten HJ

Promotor bij:

- Holman FA - Challenges in Treating Patients with Locally Advanced and Locally Recurrent Rectal Carcinoma
  Promotiedatum: 30-11-2017
- Jorritsma-Bosman SJ - Optimization of treatment for locally recurrent rectal cancer
  Promotiedatum: 19-12-2017
- Simkens GA - Refining Selection Criteria for Cytoreductive Surgery and HIPEC : in patients with peritoneal metastases of colorectal origin
  Promotiedatum: 13-01-2017

Teijink JA
Promotor bij:

- Pouwels JH - Perioperative physiology and optimalisation in bariatric and metabolic surgery
  Promotiedatum: 31-05-2017
- Winkes MB - Chronic Exertional Compartment Syndrome of the Deep Posterior Lower Leg and Forearm
  Promotiedatum: 05-04-2017

Dermatologie

Steijlen P
Promotor bij:

- Nellen RGL – Studies on mendelian disorders of cornification
  Promotiedatum: 19-01-2017

Inwendige Geneeskunde

Creemers GJ
Co-promotor bij:

- Bernards N - Treatment and survival of patients with metastatic upper gastrointestinal cancer : hard to digest?
  Promotiedatum: 13-04-2017
- Razenberg LG - Systemic treatment for advanced colorectal cancer : bridging the gap between clinical studies and daily practice
  Promotiedatum: 21-04-2017

Hingh I.H.J.T. de
Co-promotor bij:

- Razenberg LG - Systemic treatment for advanced colorectal cancer : bridging the gap between clinical studies and daily practice
  Promotiedatum: 21-04-2017

Maag-darm-leverziekten

Curvers WL
Co-promotor bij:

- Swager A - Volumetric laser endomicroscopy for the detection of early Barrett's neoplasia
  Promotiedatum: 02-06-2017

Schoon EJ
Co-promotor bij:

- Sommen F vd. - Computer-aided detection of early Barrett's cancer
  Promotiedatum: 15-11-2017

Urologie

Koldewijn EL
Co-promotor bij:

- Vries AH de - Training in Urology. Time to Test!: Development of skills training and assessment tools
  Promotiedatum: 31-05-2017

Wetenschapsavond
Catharina Ziekenhuis
2018

Presentaties

Cardiologie

Comparison of features from electrocardiography and photoplethysmography for atrial fibrillation detection in 24-hour measurements

Linda M. Eerikäinen, Lukas Dekker, Alberto G. Bonomi, Fons Schipper, Rik Vullings, Helma M. de Morree, Ronald M. Aarts

Background: Atrial fibrillation (AF) is the most common sustained arrhythmia. The challenges in diagnosing AF are the occasional episodes which can be also without symptoms. Therefore, long-term monitoring solutions are required. Photoplethymosgraphy (PPG) is an unobtrusive, easy-to-use, low-cost measuring modality for long-term use that is suitable for measuring cardiovascular parameters, such as heart rate.

Aims: In this study, our aim is to analyze how well the features computed for AF detection from PPG perform compared when calculated from to the gold standard (electrocardiography (ECG)) in 24-hour monitoring.

Methods: The dataset consisted of recordings of ECG, PPG, and accelerometer (ACC) from 26 patients (8 with 100% AF, 18 no AF) assigned to a 24-hour Holter measurement. Seven features from inter-beat intervals for AF detection (Shannon entropy, Root Mean Square of Successive Differences (RMSSD), normalized RMSSD, pNN40, pNN70, sample entropy, and coefficient of sample entropy (cosEn)) were calculated both from ECG and PPG in 120s windows shifting every 30s. Movement intensity computed from accelerometer was used to exclude segments during high motion. The performance for PPG was calculated with (PPG+ACC) and without using the movement information.

Results: Overall, the best feature from both measurement modalities was cosEn (kappa: ECG: 0.973; PPG: 0.916; PPG+ACC: 0.955). The coverage for ECG was 91%, whereas for PPG and PPG+ACC 55% and 31%, respectively.

Conclusion: Detection of AF with PPG in 24-hour measurements can reach comparable results to ECG when segments with high motion are excluded. However, there is a cost in coverage. Innovative aspects: This is the first study showing a comparison in performance of PPG and ECG (gold standard) when the same features are computed and used for AF detection in 24-hour measurements in a daily life setting.

Chirurgie

Eye-tracking to differentiate viewing behavior of surgeons and trainees during laparoscopic pancreatoduodenectomy

Brinkman DJ, van der Vliet WJ, Besselink MG, Bosscha K, Busch OR, van Dam RM, Festen S, van Hilst J, de Hingh IH, Karsten TM, Lips DJ, de Rooij T, Song Y, Luyer MD for the Dutch Pancreatic Cancer Group

Introduction: Training is important to reduce learning curve associated morbidity and mortality after laparoscopic pancreatoduodectomy (LPD). However, it remains unclear how surgical performance differs between experts and trainees. Eye-tracking could objectively measure surgical performance through viewing patterns.

Aim: To investigate if eye-tracking can differentiate surgeons and trainees with different grades of experience in performing LPD.

Methods: Participants consisted of experts on laparoscopic pancreatic surgery, experts on open pancreatic surgery and surgical residents. Eye movement was captured using a Tobii® X-60 eye-tracker as subjects were presented with three videos of critical steps of LPD. Main outcome measures included number of fixations, fixation time and length of saccades.

Results: Eighteen participants were included. There was a high Pearson correlation coefficient (>0.6; p<0.05) between the three videos regarding each physician, which indicates consistent performance. The mean fixation time was longer for laparoscopic experts (475 ms, n=8) compared to open experts (142 ms, n=3) and residents (285 ms, n=7; p=0.01), whereas the number of fixations were lower (631 vs. 796 vs. 735 respectively, p=0.042), indicating that laparoscopic experts were quicker in finding regions of interest. Surgical residents had the longest length of saccades (336 pixels), although not statically significant compared to laparoscopic and open experts (327 and 134 pixels respectively; P=0.42).

Conclusion: This pilot study shows that eye-tracking can demonstrate differences in fixation between

surgeons and residents with different grades of experience in performing LPD. Eye-tracking could be a tool to monitor surgical expertise and discover which elements of LPD are critical to lay emphasis on during training.

Novel features of this study: It remains unclear how surgical performance differs between experts and trainees. Eye tracking is a novel tool that can measure what surgeons visually focus on during surgery. We show for the first time that eye-tracking can demonstrate differences between physicians with different grades of experience in performing laparoscopic pancreatic surgery.

Gynaecologie

Hedgehog signalling pathway is activated in high-grade serous ovarian carcinoma

P van der Ploeg, LAM van Lieshoutb, A van de Stolped, W Verhaegh, RLM Bekkers, JMJ Piek

Introduction High-grade serous ovarian carcinoma (HGSOC) is the most lethal gynaecological cancer. This is caused by the fact that most tumours are detected at late stage of disease and limited therapeutic options. Therefore, there is an urgent need for development of targeted therapies. Signalling transduction pathways (STP) are chains of biochemical events controlling gene expression. One such STP is the Hedgehog (Hh) pathway. Previous research yielded contradictory results of Hh activity in ovarian cancer, possibly due to erroneous use of separate components of the pathway as a marker for activity (1-5). In addition, it highlighted the need for identification tools in the patient population (6, 7).

The current study used a novel computational diagnostic approach, enabling quantitative measurements of the functional activity of oncogenic pathways based on inferring pathway activity from its specific target gene mRNA levels, which has been biologically validated (8).

As Fallopian tube epithelium is the tissue of tumour origin, we aimed to determine Hh activity in HGSOC and normal oviduct and thereby providing new insights for patient selection and targeted therapy. Methods Target gene levels were measured using publicly available Affymetrix microarrays of HGSOC (n=10) and normal oviduct (n=10), resulting in pathway activity scores, which were statistically analysed. Results We demonstrated upregulated Hh activity (p=0.001) in HGSOC compared to normal oviduct and confirmed the need for patient selection in case of targeted therapy.

Conclusion Our model showed significantly upregulated Hh activity in HGSOC compared to normal oviduct, suggesting selected Hh-active HGSOC as an interesting therapeutic target. Innovative elements of the study (50 words)

Complex keyprotein interactions and their influence on pathway activity lead to tremendous amounts of data, making clinical implementation difficult. This approach combines keyprotein activity of the STP into output on the functional phenotype of the tumour in its affected microenvironment, which can eventually indicate pathways used to tailor individual therapy.

Posters

Anesthesiologie

Pain upon inserting a peripheral intravenous catheter: does the size matter?

Fredericus H.J. van Loon, MSc; Lisette A.P.M. Puijn, RN; Wesly H. van Aarle; Angelique T.M. Dierick-van Daele PhD; Arthur R.A. Bouwman MD

Introduction: Approximately 1,2 billion peripheral intravenous catheters are inserted across the world annually. Each intravenous catheter insertion is a painful and invasive procedure, which affects cognitive abilities by increasing anxiety and discomfort in patients.

Aim: We hypothesized that inserting a smaller sized peripheral intravenous catheter has a lower level of pain sensation when compared to a larger sized catheter.

Methods: This observational, cross-sectional study was conducted between May and October 2016 and performed in the operating theatre complex of the Catharina Hospital (Eindhoven, The Netherlands). Any patient, aged 18 years or older, was eligible to participate. Experienced anesthesiologists and nurse anesthetists routinely obtained peripheral intravenous access according to standards of care.

Results: The main outcome was the relation between the experienced pain upon inserting the peripheral intravenous catheter with the size of the cannula. A total of 1,063 patients were included, with a mean pain score of 3.3 ± 2.2. No correlation could be detected between pain and the size of the inserted peripheral intravenous catheter (Spearman's ? = 0.03, p = 0.311). Placement of an 18 gauge catheter on the dorsum of the hand in the dominant site resulted in the lowest pain score when compared to other sized catheters inserted on different sites (NRS = 2.6 ± 1.8, p < 0.001).

Conclusion: In conclusion, inserting a smaller sized peripheral intravenous catheter did not result in lower pain sensation. To prevent pain upon inserting a PIVC, an unsuccessful attempt must be avoided, especially in patients with a predicted high-risk profile on the A-DIVA scale.

Vernieuwende elementen: Met de resultaten van dit observationeel onderzoek is bepaald dat de maat van de PIVC niet van invloed is op de pijnbeleving. Daarentegen moet ingezet worden op een succesvolle eerste punctie tot het inbrengen van een PIVC.

Apotheek

CDSS assisted pharmacist's intervention improves outcome in hospitalized patients with severe hypokalemia: a time series analysis

Arthur TM Wasylewicz, Rene JE Grouls, Toine CG Egberts, and Erik HM Korsten

Introduction: Hypokalemia is one of the most frequent electrolyte disturbances in hospitalized patients. Severe hypokalemia requires immediate treatment because of the increased risk on cardiac arrhythmia and sudden death. Adequate response to such hypokalemias has been shown to be suboptimal. Clinical decision support systems (CDSSs) are seen as a solution to improve response. Therefore, a clinical rule (CR) was implemented into the CDSS of the Catharina Hospital Eindhoven (CHE).

Aim: The aim of this study was to evaluate patient outcomes after implementation of the CR combined with hospital pharmacist consultation of the physician compared to showing only passive alerts.

Methods: A before- after study with an interrupted time-series design was performed comparing four endpoints representing patient outcomes. Adult patients were included admitted in the CHE between 2007 till 2017, hospitalized at least 24 hours, with a serum potassium below 2.9 mmol/L measured at least 24 hours after hospitalization, and no prescription for potassium supplementation during severe hypokalemia. Patients were included only once. Hemodialysis patients were excluded.

Results: 638 patients in the control period and 874 in the intervention were included. In the intervention period a significant decrease was seen in time to reach normokalemia, 63h versus 44h (p<0.001), as well as an increase in the percentage of patients reaching normokalemia 82 versus 90% (p<0.001). Furthermore, duration of hospitalization significantly decreased after the intervention (p<0.001) 541 and 497 hours respectively. Only a trend toward lower in-hospital mortality was found (p=0.14).

Conclusion: Implementation of a CDSS assisted pharmacist's intervention improved outcomes for patients with severe hypokalemia.

New elements: This is the first study to examine the difference in patient outcomes between 'normal' passive alerting and advanced CDSS assisted active alerting of extreme laboratory results. Also, this is the first study to do a time-series analysis to compensate for improvement due to other factors.

Cardiologie

Regional Collaboration for Improving Care for Atrial Fibrillation Patients: Data from the Netherlands Heart Network

H.P. Cremers (Netherlands Heart Network, Veldhoven, the Netherlands); C. Hoorn (Catharina Hospital, Eindhoven, the Netherlands); H.P.A. van Veghel (Netherlands Heart Network, Veldhoven, the Netherlands); L.J.H.J. Theunissen (Maxima Medical Center, Veldhoven, the Netherlands); S. de Jong (Elkerliek Hospital, Helmond, the Netherlands); P. Polak (St. Anna Hospital, Geldrop, the Netherlands); P. van der Voort (Catharina Hospital, Eindhoven, the Netherlands); L.R.C. Dekker (Catharina Hospital, Eindhoven, the Netherlands)

PURPOSE: Guideline non-adherence often results in suboptimal atrial fibrillation (AF) treatments. Large academic and referral hospitals demonstrated positive effects of protocolled, nurse-led outpatient AF clinics. Although, similar results have not been indicated in small peripheral hospitals yet, ample opportunities are present when collaboration is initiated on a regional level. Therefore, this study assesses the effectiveness of outpatient AF clinics, including AF guideline adherence, in the South East Brabant region.

METHODS: In this prospective cohort study newly diagnosed AF-patients of 4 hospitals involved in the Netherlands Heart Network are used. Data regarding patient relevant outcome measures (i.e. EHRA score, stroke, major bleedings, readmissions, and adverse effects of medication) and quality indicators (i.e. outcome-, process-, and structural measures) are gathered at baseline and 6 months of follow-up. To assess effectiveness of outpatient AF clinics descriptive, logistic, and linear regression analyses are performed using SPSS 21.0.

RESULTS: In the analyses 448 AF-patients were included. After 6 months significant improvements regarding EHRA-score, hypertension, and type of AF were indicated. Furthermore, results on patient relevant outcomes indicated 23 hospitalizations, no major bleedings, 2 strokes, no adverse effects of medication and no AF-patient deceased. Regarding guideline adherence, all hospitals met the required norms (=90%), which is superior to previously published results.

CONCLUSION : Collaboration between cardiologists in a regional setting permits further improvement of AF care. In this ongoing project reference populations as well as quality of life and healthcare costs will be measured in addition to more extensive follow-up to provide further conclusions on the patient value for AF-patients.

INNOVATIVE ELEMENTS FOR THIS STUDY

- Netherlands Heart Network is the first successful implementation of an integrated care delivery system that targets cardiac patients' outcome measures in the full cycle of care;
- Intensive collaboration between all healthcare providers in the South East Brabant region results in improved guideline adherence and increased patient relevant outcomes.

Chirurgie

Should the Extended Lateral Approach Remain Part of Standard Treatment in Displaced Intra-articular Calcaneal Fractures?

SCP Jansen, J Bransen, G van Montfort, AT Besselaar, AH van der Veen

Background: The position of the extended lateral approach (ELA) as standard surgical technique for calcaneal fractures is being criticized.

Aim: To evaluate the results of the ELA in our hospital and to determine whether this approach should remain standard therapy.

Methods: This retrospective cohort study included patients with displaced intra-articular calcaneal fractures treated with the ELA between January 2010 and September 2015. Exclusion criteria were open fractures, simultaneously existing unilateral relevant foot or ankle trauma, and unobtainability of information on the postoperative course. Outcome measures were the VAS-FA score, AOFAS, surgical site infections (SSIs) and reoperations.

Results: 60 patients with 64 fractures were included. The AOFAS was determined for 42 fractures, with a median score of 83 (range 33-100) and 55% good to excellent scores. The VAS-FA was completed for 44 fractures, with a mean score of 61.0 (SD 23.4). We found 10.9% superficial SSIs successfully treated with antibiotics. In 4.7% of patients a deep SSI was diagnosed, wherefore premature implant removal was necessary. Patients with a SSI did not have significant lower VAS-FA or AOFAS scores than patients

without a SSI (p=0.318 respectively p=0.766). Implant removal in absence of SSIs was necessary in 17 patients because of pain, and 3 patients needed secondary arthrodesis because of persistent pain.
Conclusion: The ELA proved to be a safe procedure and moreover the most common complications did not influence the long-term outcomes of patients. However, recent literature demonstrates that less invasive techniques seem to exceed the ELA with respect to wound complications.
Vernieuwende elementen: Deze studie toont aan dat de resultaten van de ELA in het CZE vergelijkbaar zijn met de resultaten uit gespecialiseerde level-1-traumacentra. Echter, recente literatuur toont aan dat de sinus tarsi benadering goede functionele en anatomische resultaten geeft met significant minder wondcomplicaties. Daarom zal het Catharina overgaan op deze 'nieuwere' techniek.

Uitkomst van de repeat sentinel node procedure heeft geen invloed op prognose bij patiënten met een recidief mammacarcinoom

Ingrid G.M. Poodt, MD, Guusje Vugts, MD, PhD, Adriana J.G. Maaskant-Braat, MD, PhD , Adri C. Voogd, MD, PhD, Robert-Jan Schipper, MD, PhD , Rudi M.H. Roumen, MD, PhD, Grard A.P. Nieuwenhuijzen, MD, PhD. On behalf of the Sentinel Node And Recurrent Breast Cancer (SNARB) research group.

Achtergrond en doelstelling: Kennis van de regionale lymfeklierstatus bij patiënten met een recidief mammacarcinoom kan belangrijk zijn voor een betere locoregionale controle. De SNARB studie heeft de uitvoerbaarheid van de repeat sentinel node procedure(re-SNP)aangetoond. Echter is het tot nu toe onbekend wat de prognostische waarde is van de uitslag van de re-SNP.
Methode: De SNARB studie is een nationale registratiestudie waarin patiënten met een lokaal recidief mammacarcinoom werden geïncludeerd. Deze patiënten ondergingen lymfoscintigrafie en een re-SNP. Met behulp van survival analyses werd de prognostische waarde van de uitslag van de re-SNP op het ontwikkelen van afstandsmetastasen bepaald.
Resultaten: Van de 515 geïncludeerde patiënten, had 44.7% een negatieve re-SNP, 8.9% een positieve re-SNP en bij 46.4% was de re-SNP niet succesvol. Na een mediane follow-up duur van 5.1 jaar, ontwikkelde 22.3% een re-recidief. Dit betrof in 3.9% een lokaal re-recidief (N=20), 3.5% een regionaal re-recidief (N=18) en 15% werd gediagnosticeerd met afstandsmetastasen (N=77). Het 5-jaars metastasevrije interval was 84% (95% BI, 81-88%). Onafhankelijke prognostische factoren voor het krijgen van afstandsmetastasen zijn o.a. een triple negatieve recidief tumor, en het niet krijgen van adjuvante chemotherapie. De uitkomst van de re-SNP had geen significante invloed op het ontwikkelen van afstandsmetastasen, met een HR van 1.66(BI, 0.80-3.46) van positieve re-SNP versus negatieve re-SNP(P=0.174).
Conclusie: De uitslag van een re-SNP heeft geen invloed op de prognose van patiënten met een recidief mammacarcinoom. De waarde van chirurgische lymfeklierstadiering bij een recidief mammacarcinoom staat hiermee ter discussie. Adjuvante behandeling met chemotherapie lijkt daarentegen wel van prognostisch belang.
Vernieuwende elementen: Grootste studie van patiënten met een recidief ipsilateraal mammacarcinoom, waarbij een re-SNP is uitgevoerd. Tot nu toe was de prognostische waarde van de re-SNP onbekend. Deze studie heeft een grote klinische impact, aangezien we de waarde van chirurgische lymfeklierstadieringen d.m.v. re-SNP, na de gevonden resultaten, erg ter discussie stellen.

Dialyse

Nieuwe inzichten artsenvisite aan de stoel

Jennifer van Moll

Achtergrond: Signalen omtrent onduidelijkheid taak- rolverdeling tussen de nefroloog, verpleegkundig specialist en dialyseverpleegkundige, de vaak beperkte rol en inbreng van de dialyseverpleegkundige en de patiënt, dat de visite vaak gericht is op medische aspecten en dat het holisme te beperkt aan bod komt. Ook blijkt uit VIM-meldingen dat er incidenten ontstaan tijdens of na de artsenvisite door miscommunicatie en/of het ontbreken van communicatie, onvoldoende en/of geen verpleegkundige inbreng en het onzorgvuldig uitwerken van de visite.
Doelstelling: Medio 2018 is de tevredenheid van de patiënt, nefroloog, verpleegkundig specialist en dialyseverpleegkundige omtrent de artsenvisite (aan de stoel), beoordeeld met een score van minimaal een 8.
Methode: Middels verscheidende literatuurstudies is data verzameld over welke belemmerende en bevorderende factoren van invloed zijn op het verloop van een artsenvisite, wat volgens ontwikkelde expertisegebieden de taakverdeling tussen nefroloog, verpleegkundig specialist en

dialyseverpleegkundige is en wat de rechten van patiënten zijn omtrent participatie in het zorgproces. Bij nefrologen en een verpleegkundig specialist werden semigestructureerde interviews afgenomen en onder de dialyseverpleegkundigen is een enquête gehouden. Ook werden enquêtes van het al uitgevoerde patiënttevredenheidsonderzoek geraadpleegd.
Resultaten: De nefrologen en de verpleegkundig specialist zijn over het algemeen tevreden met het verloop van de artsenvisite aan de stoel echter is er onder de dialyseverpleegkundigen verdeeldheid betreffende de tevredenheid. De meerderheid van de patiënten geven aan tevreden te zijn betreffende de bejegeningen van de nefrologen en dialyseverpleegkundigen.
Conclusie: De tevredenheid onder de dialyseverpleegkundigen is erg wisselend. Belemmerende factoren als onduidelijkheid rondom hun taken worden gegeven.
Aanbevelingen: Duidelijkheid creëren rondom taak- rolverdeling, duidelijke onderlinge communicatie, patiëntparticipatie stimuleren.
Implementatievoorstel: Het samenstellen van een projectgroep met een vakinhoudelijke leider. De projectgroep bestaat uit minimaal één nefroloog, één verpleegkundig specialist en één dialyseverpleegkundige. In het begin zal de projectgroep gemiddeld éénmaal per maand samenkomen.

Geriatrie

Effect van implementatie van allergieën en bijwerkingen module op informatieoverdracht tussen het ziekenhuis en de eerste lijn bij ouderen

P.A. Schoonakker (arts-assistent geriatrie Helmond); dr. S. Houterman; M. C. H. Kerskes; dr. C. M. J. van der Linden (allen Catharina ziekenhuis)

Achtergrond: De informatieoverdracht tussen ziekenhuizen en de eerste lijn na ziekenhuisopname verloopt suboptimaal. Sinds 28 september 2016 is een allergieën en bijwerkingen module in gebruik genomen in het elektronisch patiëntendossier van het Catharina Ziekenhuis Eindhoven om deze informatieoverdracht te verbeteren.
Doelstelling: Het evalueren van het effect van de implementatie van een allergieën en bijwerkingen module op de informatieoverdracht van allergieën en bijwerkingen tussen het ziekenhuis en de eerste lijn, middels een retrospectief, observationeel onderzoek binnen de geriatrische populatie.
Materialen en methode: De informatieoverdracht van allergieën en bijwerkingen vóór de implementatie van de module (pre-groep) is vergeleken met de informatieoverdracht na de implementatie (post-groep). De primaire uitkomstmaat is het percentage van de allergieën en bijwerkingen die tijdens de opname in het ziekenhuis bekend zijn, waarbij adequate medicatiebewaking in de eerste lijn plaatsvindt binnen vier weken na ontslag, uitgesplitst in medicatiebewaking bij de openbare apotheek en medicatiebewaking bij de huisarts of specialist ouderengeneeskunde.
Resultaten: In totaal werden 103 opname episodes bestudeerd, waarvan 49 in de pre-groep en 54 in de post-groep. Bij de openbare apotheek vond adequate medicatiebewaking plaats voor resp. 17% en 48% van deze allergieën of bijwerkingen (p=0,054). Bij de huisarts of specialist ouderengeneeskunde was in resp. 22% en 44% sprake van adequate medicatiebewaking (p=0,16).
Conclusie: Het implementeren van een allergieën en bijwerkingen module in het elektronisch patiëntendossier heeft geleid tot een statistisch niet significante, maar onzes inziens wel klinisch relevante verbetering van de medicatiebewaking voor allergieën en bijwerkingen in de eerste lijn na ontslag uit het ziekenhuis.
Vernieuwende element: het invoeren van de allergieën en bijwerkingen module en het verzenden van een AMOR bij ontslag is een relatief eenvoudige aanpassing die niet alleen ziekenhuis breed, maar in principe ook in andere ziekenhuizen kan worden toegepast.

Gynaecologie

Ultrasound-based strain mapping for quantitative characterization of uterine activity outside pregnancy

Celine Blank, Y. Huang, Federica Sammali, Nienke Petronella Maria Kuijsters, Massimo Mischi, Benedictus Christiaan Schoot

Introduction and objective: Successful In-Vitro Fertilization (IVF) is achieved in 30% of the procedures only. Implantation failure can possibly be caused by dysfunction of the uterine peristalsis (UP). The IVF

success rate can therefore be improved by novel methods enabling objective and non-invasive characterization of UP. In this study, strain mapping based on optical flow is applied on two-dimensional (2D) transvaginal ultrasound (TVUS) videos to quantify UP outside pregnancy.
Methods: Eight healthy women, with a natural regular cycle, underwent 4-minute TVUS during active (before ovulation) and inactive (late luteal) phases of the menstrual cycle. Regions of interest (ROIs) were chosen to include the junctional zone close to the fundus. Strain mapping based on optical flow was applied to calculate and visualize strain variations in the ROIs. We considered contraction as negative strain and relaxation as positive strain. The obtained strain maps were rendered with suitable color maps; red color for relaxation and blue color for contraction.
Results: In each recording, 2D strain maps were created in longitudinal and transversal directions of the uterus. The figure shows an example of strain map in transversal direction for both active and inactive phases. We can clearly visualize the variations in strain around the junctional zone, revealing the propagation of the peristatic movement.
Conclusion: The obtained results suggest the feasibility of accurate strain mapping in the uterus outside pregnancy and the possibility to classify the UP for different phases of the menstrual cycle. In the future, extension to three-dimensional strain analysis will be considered to provide more accurate results that are robust to out of plane motion.
Innovative elements: For the first time, the proposed research seeks to measure and characterize UP through quantitative analysis of uterine motion and strain by ultrasound imaging. Successful implementation of the analysis will represent a breakthrough for understanding the activity of a non-pregnant uterus and will open up a new era for IVF.
Active phase
Inactive

Texture analysis as new diagnostic tool for adenomyosis: preliminary results

Jenny Soomers, Celine Blank, Rob Vogels, Alette Giesen-Daniels, Cristina Caresio and Benedictus Christiaan Schoot.

Introduction: Nowadays, no consensus has been reached on a golden standard for the diagnosis of adenomyosis. This may lead to inconsistent preoperative diagnostics, obscureness for both specialists and patients, and difficultly comparing research outcomes.
Objective: The aim of this study was to ascertain if texture analysis is an objective reproducible method to differentiate between healthy tissue and adenomyosis tissue.
Methods: Data of 20 women who underwent a hysterectomy and a MRI prior were retrospectively collected. These women were divided into two groups: 10 healthy subjects and 10 women diagnosed with adenomyosis based on histopathology examination. Exclusion criteria were pregnancy, postmenopausal women, (suspected) malignancy, Asherman syndrome, MRI imports or MRI with strong artifacts. Three sagittal plane magnetic resonance T2-Weighted uterus images were selected per MRI from each woman. Using MATLAB, manual segmentation of a Region of Interest (ROI) within the uterus (excluding the cervix and the endometrium) was performed. From this, 80 texture features (1° Order, 2° Order, High order, LBP) were extracted, and an average value of 3 images was taken.
Results: All 80-texture features separately, except one, do not evince a significant difference between the two groups. Thought after removing correlated features, a subset of 20 texture features remains, and the summation of these 20 texture features appears to be significant (Figure 1).
Conclusion: Our study suggest that texture analysis has a highly distinctiveness, and consequently helping to diagnose adenomyosis. Further validation studies and prospective studies will eventually reduce specificity and sensitivity to accurate values.
Unique elements: To our knowledge, no previous study has extracted pattern features of the uterus. By improving the diagnosis of adenomyosis, we expect the disease will be detected earlier, recognized more frequently and treated better.

Inwendige geneeskunde

From intention to STI prevention: An online questionnaire on barriers and facilitators for discussing sexual risk behaviour among HIV nurses

Suzanne de Munnik | Sigrid C.J.M. Vervoort PhD| Heidi S.M. Ammerlaan dr, PhD |Gerjo Kok, prof | Chantal den Daas PhD

Aims: We aimed to elucidate facilitators and barriers that HIV nurses experience in discussing sexual risk behaviour with HIV-positive men who have sex with men, using variables from a previous qualitative study and the theory of planned behaviour.
Background: HIV-positive men who have sex with men are frequently diagnosed with sexually transmitted infections, which can be reduced if HIV nurses discuss sexual risk behaviour.
Design: An online questionnaire was disseminated in April 2015 among all HIV nurses in the Netherlands.
Methods: We assessed variables, such as attitudes, shame, ability, knowledge and time concerns. A regression analysis was conducted with "intention to discuss sexual risk behaviour" as an outcome variable.
Results: The questionnaire was completed by 60 of 79 HIV nurses. Overall, participants reported high intentions to discuss sexual risk behaviour, and 38% of the variance was explained by attitude, sexual preference, knowing ways to introduce the topic and experiencing enough time or viewing it as a priority. In addition, high intenders significantly differed from low intenders in "experienced shame," "relation with patients," "non-verbal communication," "subjective norm" and "knowledge."
Conclusion: Improving sexual health in HIV care translates into improving opportunities and the facilitating factors in initiating the discussion of sexual risk behaviour rather than removing barriers HIV nurses experience. Interventions should mainly focus on improving the HIV nurses' perceived ability to initiate the topic of sexual risk behaviour and to utilize the jargon and terminology that is commonly used among men who have sex with men.
New elements
Omitting sexuality is not due to the lack of motivation or belief that it is important, but the discomfort of bringing it up, being perceived as preaching or giving priority to other important topics. By discussing sexuality during HIV visits, healthcare providers can contribute to preventing both STIs and secondary transmission of HIV.

Maag-darm-leverziekten

Barrett's patients overestimating their esophageal cancer risk have more reflux symptoms and a decreased quality of life

MCM van der Ende-van Loon, MCs1, WD Rosmolen, MCs3, S Houterman PhD2 , EJ Schoon MD PhD1 WL Curvers MD PhD1.

Background and aims: Barrett Esophagus (BE) is a premalignant condition that affects patients' quality of life (QoL) and it may be psychological burden due to the threat of developing an esophageal adenocarcinoma (EAC). The aim of this study was to assess the EAC risk perceived by non- dysplastic BE patients and associate the perceived EAC risk with illness perceptions and QoL.
Methods : This cross-sectional questionnaire study included 233 BE patients aged 18-75, from a database in a tertiary referral center for BE. Based on their annual- and lifetime EAC risk estimations measured with the Magnifying Glass scale patients were divided into an overestimate- and an underestimate group. Differences between these groups were assessed on demographics, reflux symptoms, the medical Outcomes Study Short Form-36 (SF-36) and the Brief Illness Perception Questionnaire (B-IPQ).
Results: The questionnaires were completed by 68% patients of which 41% patients overestimated their annual risk and 25% overestimated their lifetime risk of developing EAC. Overestimating an EAC risk is associated with significant lower means in QoL on the domains: bodily pain, general health, vitality and physical functioning, significant worse illness perceptions and significant more reflux and dyspeptic symptoms.

Conclusions: Overestimating the EAC risk by BE patients is associated with decreased QoL and worse illness perceptions, which is most likely caused by reflux symptoms as well as dyspeptic symptoms. These should be adequately treated and patients may be in need of extra support and specific information about their EAC risk.

Innovatie: In tegenstelling tot onderzoek naar nieuwe behandel- en detectiemethoden is er weinig onderzoek gedaan naar de ervaringen van Barrett patiënten. Met dit onderzoek is een start gemaakt met het vergroten van de kwaliteit van zorg voor de niet dysplastische Barrett patiënten welke verder gaat dan de deuren van ons ziekenhuis.

The Dutch national ERCP quality registration with RAF-E does not correlate with clinical ERCP outcome.

Meijer SC, Lennard LP, MD, PhD

Background and study aim: Since January 1. 2016 endoscopists in the Netherlands are obligated to register their Endoscopic Retrograde Cholangiopancreatography (ERCP) in a national ERCP quality registration (NEQR). This evaluates ERCP quality and volume per centre and endoscopist. NEQR a self-assessment is based on the Rotterdam Assessment Form for ERCP (RAF-E), which does not score complications. This study examines whether NEQR correlates with objective post-ERCP clinical outcomes such as complications and mortality in a tertiary referral centre.

Patients and methods: A retrospective cohort study of all ERCPs performed at the Gastroenterology Department of a tertiary referral centre, between January 1. 2016 and January 1. 2017, examining the registered data in the NEQR and individual patient data including ERCP outcomes in the local electronic medical records. The Spearman's rank correlation coefficient was performed to measure correlations between NEQR self-assessments and post-ERCP complications and mortality.

Results: 333 procedures were performed, of which 254 were registered in the NEQR (76.3%). Registered and non-registered patients showed equal characteristics and results. No significant correlations were found between the subjective self-assessment and objective post-ERCP outcomes, except a weak negative correlation between stent placement self-assessment and post-ERCP total complications (r=-0.315; p=0.018) and post-ERCP cholangitis (r=-0.308; p=0.021).

Conclusion: The currently used national quality registration for ERCP (NEQR) does not correlate with post-procedural clinical outcomes. We believe that objective and harder clinical outcome measures will enhance representativeness of the mostly subjective NEQR results. Therefore NEQR should be combined with the already existing national complication database.

Innovative element of this study: Quality measurement of procedures performed in gastroenterology is of broad and current interests. This study proposes to improve objectiveness and representativeness of the quality measurement of ERCPs performed in the Netherlands by combining the national ERCP quality registration with the already existing national complication database

Orthopedie

Mandr-in of Mandr-uit?

Linda van den Broek, Ilse-Marita Smeulders, Ynette van Orsouw, Robin van Kempen, Saskia Houterman

Inleiding: Uit de wetenschappelijke literatuur blijkt dat een Mandrin vaak wordt geplaatst zonder een duidelijke indicatie en dat het een verhoogd risico op infectie geeft.. Op de afdeling Orthopedie wordt volgens het protocol als er geen indicatie meer is voor een infuus, deze standaard vervangen door een Mandrin. In deze studie is onderzocht in hoeverre het niet standaard plaatsen van een Mandrin tot een verminderde kans op een infectie leidt en of het tot minder klachten leidt bij de patiënt en de werklast verminderd.

Methode: In juni t/m juli 2017 werden patiënten van de verpleegafdeling Orthopedie prospectief vervolgd. Alle patiënten op Unit A (11 bedden) kregen standaard geen Mandrin en de patiënten op Unit B (13 bedden) kregen standaard wel een Mandrin als het infuus verwijderd werd. Gegevens werden door de verpleegkundigen verzameld tijdens opname aan de hand van een enquêteformulier gericht op tekenen van infectie en klachten van de patiënt.

Resultaten: In totaal werd er van 40 patiënten (n=16 wel Mandrin/ n=24 geen Mandrin) complete data verzameld. 100% van de geplaatste Mandrins werd niet gebruikt, bij 50% van deze patiënten was sprake van Mandrin-gerelateerde klachten en 6% had tekenen van infectieverschijnselen. Bij geen van de patiënten zonder Mandrin moestopnieuw een infuus geplaatst worden.

Conclusie: Uit dit onderzoek blijkt dat het standaard plaatsen van een Mandrin niet nodig is. Door het weglaten van een Mandrin kunnen infecties worden voorkomen en hebben patiënten minder klachten

gerelateerd aan de Mandrin. Ook vermindert het de werklast voor de verpleegkundigen, omdat er een standaard handeling verdwijnt.
Vernieuwde elementen: Er heeft een aanpassing plaatsgevonden in het protocol en in het verpleegplan waarbij het standaard plaatsen van de Mandrin is vervallen. Het onderzoek is opgepakt voor 'SlimFit', omdat er op jaarbasis een besparing van 600 euro mogelijk is, uitgaande van 85% minder Mandrin-plaatsingen alleen al op de verpleegafdeling Orthopedie.

Bracefase tijdens Ponseti behandeling beïnvloed de kwaliteit van leven van klompvoetpatiënten.

L. Melis1 A.T. Besselaar1,2, M.C. van der Steen1

Achtergrond In Nederland worden ongeveer 200 kinderen per jaar geboren met 1 of 2 klompvoet(en). Dit is een aangeboren afwijking bestaande uit een sterk afwijkende, niet te corrigeren voetstand. De goudenstandaard behandeling, de Ponseti methode, bestaat uit een gips- en een bracefase. Tijdens deze bracefase dragen de patiënten een abductiebrace tot de leeftijd van 4 jaar.
Doelstelling Het doel van het onderzoek is om zicht te krijgen op de impact van de brace op het leven van de patiënten. Hiervoor wordt de kwaliteit van leven bij klompvoetkinderen tijdens de bracefase in de Ponseti methode vergeleken met gezonde leeftijdsgenoten.
Methode In deze retrospectieve analyse van het prospective klompvoetcohort, hebben we de TAPQOL van klompvoetpatiënten in de bracefase vergeleken met referentiedata van gezonde leeftijdsgenoten. De TAPQOL is een gevalideerde vragenlijst voor ouders van kinderen tot 6 jaar. Dit algemene meetinstrument bestaat uit 12 subschalen die verdeeld zijn over de domeinen fysiek, sociaal, cognitief en emotioneel functioneren en zo een beeld geeft van gezondheid gerelateerde kwaliteit van leven van het kind.
Resultaten
Data van 97 klompvoetpatiënten werden vergeleken met de gegevens van 241 gezonde kinderen. Klompvoetpatiënten scoorden significant lager op de subschalen eetlust, longproblemen, slaap, levendigheid, motorisch functioneren en communicatie, terwijl qua gedrag minder problemen gerapporteerd werden. Oudere klompvoetpatiënten scoorden weliswaar lager op deze subschaal.
Conclusie Gedurende de braceperiode vertonen klompvoetpatiënten op verschillende subschalen afwijkende waarden ten aanzien van kwaliteit van leven in vergelijking met gezonde leeftijdsgenootjes. Het onderzoek zal zich verder richten op de oorzaken hiervan en of deze factoren van belang zijn in de ogen van ouders en behandelaars.
Vernieuwend Er is geen literatuur beschikbaar over de kwaliteit van leven tijdens de brace-periode van de Ponseti behandeling bij klompvoet kinderen terwijl de bracefase een intensief onderdeel van de behandeling is. Verminderde brace-compliance is de belangrijkste risicofactor voor een terugval van de klompvoet. Naar verwachting levert dit onderzoek aanknopingspunten op die van belang zijn bij brace-compliance.

Antibiotica profylaxe bij acute prothese infecties na heup- of knieprothesiologie

AC Heineken1, JM Fonville2, M Wegdam-Blans2, JGE Hendriks3, RJA van Wensen1, **MC van der Steen**

Achtergrond: Met het groeiend aantal geplaatste heup- en knieprotheses, neemt helaas ook het aantal patiënten met een (verdenking op) prothese-infecties (prosthetic joint infection, PJI) toe. De behandeling voor acute infecties bestaat uit debridement, antibiotica, irrigatie en implantaat-behoud (DAIR). De antibiotica worden blind gestart in afwachting van microbiologische kweekresultaten. Over deze antibioticumkeuze is geen consensus in derdelijns infectie-centra.
Doelstelling
Optimalisatie van de empirische antibioticumtherapie voor effectieve behandeling van de meeste patiënten in de "blinde" fase binnen DAIR, door retrospectieve analyse van PJI verwekkers en hun resistentiepatroon.
Methode
Patiënten met een verdenking op acute PJI tussen 2012 en 2016 werden retrospectief onderzocht. Van de 82 casussen analyseerden we de kweekuitslagen en antibiotica resistentiepatronen op patiënt-niveau voor flucloxacilline (huidige behandeling), cefazoline, vancomycine en amoxicilline/clavulaanzuur.
Resultaten
Peroperatief genomen kweken van orthopedisch materiaal, leidde bij 53 van de 82 casussen tot positieve kweekuitslagen. In totaal werden 37 verschillende micro-organismen geïdentificeerd. Bij 15 patiënten werd meer dan één micro-organisme gekweekt. Het meest voorkomende micro-organisme, Staphylococcus aureus, was aanwezig bij 31 patiënten. Vervolgens evalueerden we voor elke patiënt in

de PJI groep het totaal aan micro-organismen en hun resistentiepatronen. Flucloxacilline was een adequate therapie in 72% van de patiënten, tegenover 77% bij amoxicilline/clavulaanzuur, 79% bij cefazoline en 87% bij vancomycine.
Conclusie
De huidige behandeling met flucloxacilline heeft duidelijk een suboptimale dekkingsgraad binnen de patiëntpopulatie die met DAIR behandeld worden bij een verdenking op een acute PJI. Alhoewel vancomycine de hoogste dekkingsgraad heeft kan dit middel bij langdurig gebruik leiden tot ernstige complicaties. Cefazoline lijkt daarom het beste alternatief.
Vernieuwende elementen
Op basis van deze resultaten wordt in overleg met de orthopedisch chirurgen, medisch microbiologen en apotheek het protocol voor de empirische antibiotische behandeling van PJI gewijzigd in zowel het Catharina Ziekenhuis als het Máxima Medisch Centrum.

Betrouwbaarheid en precisie van talus volumemetingen op MRI beelden bij de klompvoet gedurende de gipsperiode binnen de Ponseti-behandeling

AM Voermans a,b, S Siegler c, AT Besselaar b,d, MC van der Steen b

ACHTERGROND: De Ponseti-methode is de standaard behandeling bij klompvoeten, een aangeboren afwijking van de stand van de voet. Een specifiek fenomeen bij behandelde patiënten is het ontstaan van een afgeplatte talus. Het is echter onbekend wanneer dit ontstaat. Uit eerder uitgevoerd Amerikaanse onderzoek zijn MRI beelden gedurende de gipsperiode, de eerste fase in de Ponseti-behandeling, beschikbaar. Het is echter de vraag of deze MRI data geschikt is om eventuele afplatting van de talus op te sporen.
DOEL: De betrouwbaarheid en precisie van de segmentatie van de talus op deze MRI beelden bepalen.
METHODE: Van twee patiënten zijn gedurende de gipsperiode binnen de Ponseti-behandeling, bij iedere contole, MRI scans in drie posities beschikbaar. De verkregen beelden zijn eenmaal gesegmenteerd door operator 1 en driemaal door operator 2. Volumemetingen van de talus gebaseerd op de segmentaties zijn gemaakt. De inter- en intra-observer ICC en CVRMS zijn bepaald voor deze volumes. Een goede betrouwbaarheid wordt geïndiceerd door ICC>0.75 en een goede precisie door CVRMS<10%.
RESULTATEN: Voor de inter-observer vergelijking was de ICC 0.662 (95% BI [0.283;0.862]) en CVRMS was 11.8%. Voor de intra-observer vergelijking was de ICC 0.747 (95% BI [0.501;0.893]) en CVRMS was 12.8%. Zowel de inter- als intra-observer vergelijkingen vallen buiten de referentiewaarden.
CONCLUSIE: Het is niet mogelijk om de voorhanden zijnde MRI beelden voldoende betrouwbaar en precies te segmenteren. Wanneer het volume niet overeenkomt, zal de vorm van de talus ook niet overeenstemmen. De beschikbare MRI beelden zijn ongeschikt om de eventuele vormverandering van de talus gedurende de gipsperiode van de Ponseti-methode op te sporen.
VERNIEUWENDE ELEMENTEN: Een afgeplatte talus benadeelt de bewegingsvrijheid van de enkel en kan tot beperkingen op latere leeftijd leiden. Dit onderzoek is een eerste stap in een project gericht op het verkrijgen van meer inzicht in het ontstaan van de afgeplatte talus in klompvoeten bij behandelde patiënten middels de Ponseti-methode.

Plastische Chirurgie

Hoe komt een nieuw patient-reported outcome measure (PROM) tot stand in een multi-center study? De ontwikkeling van de WOUND-Q.

Emiel L.W.G. van Haren; **Tert C. van Alphen**; Lotte Poulsen; Anne Klassen: Chris Gibbons, **Maarten M. Hoogbergen**, Andrea L. Pusic

Achtergrond: Wereldwijd hebben miljoenen mensen last van chronische wonden met verschillende oorzaken zoals: druk ulcera, diabetische voet, radiatieschade en chirurgische wonden. Hoewel veel wonden spontaangenezen vergt een deel intensieve en tijdrovende behandelingen, wat een grote (economische) impactheeft op de zorg. Tot op heden is er geen goed meetinstrument beschikbaar voor het meten vankwaliteit van leven en kwaliteit van zorg bij chronische wond patiënten.
Doelstelling: Een nieuw patient-reported outcome measure (PROM) ontwikkelen welke wereldwijd gebruikt kan worden voor chronische wond patiënten.
Methode: Patiënten met diverse soorten chronische wonden zijn benaderd vanuit Canada(n=21), Verenigde Staten(n=12), Denemarken(n=12) en Nederland(n=15). Interviews hebben de impact verkend van
wonden op health-related quality of care(HR-QoL) en patiënten ervaringen ten aanzien van de geleverde

zorg. Hierbij is een conceptueel raamwerk ontwikkeld en een databank met items voor de ontwikkeling van de vragenlijst: de WOUND-Q.
Resultaten: Patiënten waren tussen de 23-93 jaar en hadden 1-20 wonden. De meeste type wonden bij patiënten waren: veneuze ulcera(n=15), decubitus(n=15), chirurgische wonden(n=9) en diabetische voet ulcera(n=8). De gevonden thema's hebben geleid tot het verkrijgen van een conceptueel framework. Middels cognitieve interviews en expert-input van diverse internationale wondexperts is feedback gekregen waaruit de definitieve vragenlijst is opgesteld (16 schalen met 226 items).
Conclusie: De WOUND-Q is gevormd uit een sterke kwalitatieve basis van chronische wond patiënten waarbij,volgens de hoogste wetenschappelijke standaarden, een nieuw state-of-the art PRO instrument isontwikkeld. Dit zal de standaard worden binnen het meten van HR-QoL en kwaliteit van zorg binnen de chronische wondzorg.
Vernieuwende elementen: Evidence based medicine heeft in toenemende maten de standaard gezet, hierin worden de patiëntperspectieven gemeten middels PRO's in clinical outcome research. De WOUND-Q is de eerste PRO voor chronische wond patiënten. Deze heeft een brede kwalitatieve basis, hoge responsiviteit en content validiteit welke ontwikkeld is door een internationaal consortium.

Spoedeisende Hulp

Hematoma block for distal radius fractures: ouch!

Drs. G Smits, dr. W Thijssen, dr. A van der Veen, dr. A Bouwman, Prof. E Korsten

Background: Hematoma block is a quick and easy local anesthetic method for reducing pain during reduction of distal radius fractures. It involves injection of a local anesthetic into the fracture cavity. In the Netherlands, is almost the sole technique used for anesthetizing these fractures. However, analgesic effect varies according to the literature. The objective of this study was to measure how many patients experience severe pain with fracture reduction after a standardized hematoma block.
Methods: This is a prospective observational study of patients aged 18 and older requiring closed reduction for dislocated distal radius fractures in the emergency department. Lidocaine 1% (20ml) was injected into the fracture site. The fracture was reduced in vertical fingertrap traction. Pain on reduction was measured with a verbal numerical rating scale (VNRS 0-10).
Results: 280 patients with a mean age of 65 years were included. 37% of patients experienced severe pain (VNRS 7-10) during reduction. Severe pain was not associated with years of experience in emergency medicine of the doctor, or being able to aspirate blood (form the fracture hematoma) just before injection.
Conclusions: A hematoma block provided insufficient analgesia for reduction of distal radius fractures in 37% of patients. We need to find more effective analgesic techniques like nerve blocks or modified local anesthetic techniques.
What this study adds: All published studies on hematoma block so far report only median pain scores. Besides being the largest study to date, this is the first (and largest) study reporting the proportion of severe pain.

TUE_Biomedical Engineering

Computer models as decision support tools in perioperative fluid administration

Tilaï T. Rosalina*, R. Arthur Bouwman†, Marc R. van Sambeek†, H. Erik Korsten†*, Kevin Lau‡ Rick Bezemer‡, Frans N. van de Vosse*, Peter H.M. Bovendeerd*

Inevitably, computer models will enter the clinical workflow as a decision support tool. In these models, patient-specific measurements are combined with physical and physiological knowledge to predict data that cannot be measured directly. This can be particularly useful, in cases where clinical data are very limited. This will enable us to make the step from evidence-based decision making (valid for the average patient), to patient-specific decision support
A typical clinical procedure where information is limited, is fluid administration in critically ill patients. This intervention remains difficult due to the lack of direct measurements, and large interpatient variability. Fluid administration is necessary to maintain blood pressure and perfusion, however, fluid overload can lead to edema related complications. The key to fluid administration with the least complications possible, is to find

the fluid balance. The benefit of using a physiology based mathematical model is this balance can be calculated.

In this project we aim to develop a decision support model that can assist in determining patient specific fluid administration protocols. To show the potential of such a model, we simulated the infusion of crystalloids in a normo- and hypovolemic volunteer study [1,5]. The mathematical model combines fluid exchange in the body [4] with the regulated cardiovascular [3] and renal system [2].

In agreement with the experimental data, infusion of saline resulted in an immediate increase in plasma volume. On a longer time scale the fluid was redistributed to the interstitium and partly excreted as urine. Additionally, cardiovascular responses were similar to the experimental data. This shows that a generic fluid exchange model is able to capture physiological changes in healthy volunteers during infusion and hemorrhage. Future work includes extending the model to reproduce clinical measurements such as pulse pressure variations. Subsequently the model will be tested on different patient datasets.

TUE_Electrical Engineering

On the Invariance of Remote SpO2 Measurements to the Pulsating Profile of the Skin in the red-infrared diagnostic window

Andreia Moço

Background— In remote mode, pulse oximetry (SpO2) measurements are based on photons remitted from the skin. As the photon path-lengths are influenced by wavelength and by the depth-dependent skin composition, the possible susceptibility of measurements to the confounding influence of skin properties cannot be readily pruned. The pulsating profile of the skin can be one of such properties; i.e., the relative magnitude of arteriolar pulsations within the upper-to-lower dermal layers. We hypothesize that the preference for SpO2 measurements in the red-infrared wavelength range ensures similarity in penetration depths and enables the desired invariance to the pulsating profile of the skin microvasculature and to blood content. We show diffuse reflectance measurements and Monte Carlo simulations of the normal and compressed skin, which support that the PPG-signal in red-infrared originates mostly from the deep vasculature. Complementarily, we use a skin model and assess, numerically, the accuracy of the ratio-of-ratios (RRs) method for estimating SpO2 under pulsatile profiles within estimated realistic ranges. We consider the RRs between red (R; 660 nm) and infrared (IR; 840 nm) and the 80-100% SpO2 range. Our results indicate that pulsating profile effects in remote SpO2 are negligible in red and infrared.

I. NOVELTY OF THIS INVESTIGATION: Translating knowledge from skin experiments and numerical methods into a meaningful recommendation for researchers and practitioners considering to work with next-generation contactless/camera-based SpO2 instruments.

II. AIM: We aim to show that, if red-infrared wavelengths are used in camera-based SpO2 systems, the ratio-of-ratios (RRs) method for estimating SpO2 will not be impaired by non-homogeneities in the pulsating profile of the skin.

III. METHODS: We assess the suitability of the 660 nm:840 nm selection for SpO2 by providing multispectral-PPG measurements which support that the red-IR PPG signals have depth-origin at the lower dermis. Then, as pulsatile effects cannot be directly measured in the skin, we use a skin model and a numerical approach to investigate the accuracy of the RRs method under two blood concentration configurations.

We model the skin as a multilayered structure comprising two pulsating layers. Tab. 1 lists the major Monte Carlo [3] settings used in our baseline model for determining skin reflectance and the layers' contributions to PPG signals. Complementarity, we assess pulsating profile effects under venous pooling. Pulsations are varied within estimated realistic ranges by configuring the relative percentage of arterial blood volume variations in the upper dermis. Other implementation details are found elsewhere [1, 2].

TABLE I. SETTINGS FOR THE FOUR-LAYERED BASELINE SKIN MODEL

Layers	Cb,b	rav,b	Cb,p	rav,p	P (%)	z (cm)
EPI	0	--	0	--	0	0.007
UD	1	1:1	2	1:3	0.1 vs. 1	0.025
LD	2	2:1	3	1:3	0.5	0.17
SC	3	2:1	4	1:3	0	0.3

Abbreviations and acronyms: EPI, epidermis; UD, upper dermis; LD, lower dermis; SC, subcutis; Cb [b/p], blood content [baseline/pooling]; rav [b/p], arterio-venous blood concentration ratio; P, percentage of pulsatile arterial blood volume variations, from diastole to systole; z, layer thickness.

IV. RESULTS: We verified that, when the upper dermis is occluded, the red-infrared part of the PPG spectrum remains unchanged, showing that this spectral range is mostly due to pulsations in the lower dermis. From out simulated diffuse reflectance (DR) and SpO2 versus RRs curves, it was seen that, in baseline and venous pooling conditions, P did not influence SpO2. We link this outcome with the relative flatness of the DR curve in the 660-900 nm range, and also with the similarity of penetration depths for the 660:840 nm selection, which supports our hypothesized invariance of the SpO2-RRs methodology to variations in the pulsating profile if the same vessels-depth are probed.

V. CONCLUSION: In conclusion, remote SpO2 systems in red-IR accommodate variations of the pulsating profile of the skin. This enforces our trust into algorithms combining multiple camera channels within red-infrared, while raising concerns about the robustness and reproducibility of algorithms aiming at SpO2 measurements in visible light [1].

Tabellen

Tabel 1: Overzicht aantal publicaties

Specialisme	Tijdschrift artikelen	Promoties	(Co)Promotor	Boek hoofdstuk	Totaal
Algemeen Klinisch Laboratorium	11			1	12
Anesthesiologie	17			1	18
Apotheek	12				12
Cardiologie	54			1	55
Cardiothoracale chirurgie	7				7
Chirurgie	73	3	5	1	82
Dermatologie	9				9
Dietetiek	3				3
Geriatrie	2				2
Gynaecologie	31	1			33
Intensive Care	4				4
Inwendige geneeskunde	26	3	1		30
Kindergeneeskunde	5				5
Klinische Fysica	8				8
Longgeneeskunde	9				9
Maag, darm, leverziekten	11		1	1	13
Neurologie	8				8
Nucleaire geneeskunde	1				1
Onderwijs en Onderzoek	1				1
Operatie kamers	1				1
Orthopedie	5			1	6
Pamm	2				2
Plastische chirurgie	4	1			5
Psychiatrie	1				1
Psychologie	1				1
Radiologie	3				3
Radiotherapie	8				7
Spoedeisende hulp	3				3
Urologie	7	1			8
Totaal	**327**	**9**	**7**	**6**	**349**

Tabel 2 Wetenschapsavond 2018

Specialisme	Presentaties	Posters	Totaal
Algemeen Klinisch Laboratorium		1	1
Anesthesiologie		1	1
Apotheek		2	2
Cardiologie	1	1	2
Chirurgie	2	3	5
Dialyse		1	1
Geriatrie		1	1
Gynaecologie	1	2	3
Inwendige geneeskunde		2	3
Maag-Darm-Leverziekten	1	2	3
Orthopedie		4	4
Plastische Chirurgie		1	1
Spoedeisende hulp		1	1
TUE – Biomedical Engineering		1	1
TUE- Electrical Engineering		1	1
Totaal	5	24	29

Tabel 3: Overzicht aantal artikelen en gemiddelde impactfactor per specialisme

Specialisme	Wi-1*	WI-2**	WN***	Totaal aantal artikelen	Gemiddelde impactfactor	Standaard deviatie
Algemeen Klinisch Laboratorium	11	0	0	11	9.781	12.656
Anesthesiologie	14	3	0	17	4.547	5.009
Apotheek	10	0	2	12	3.494	3.115
Cardiologie	50	3	1	54	8.407	12.800
Cardiothoracale chirurgie	7	0	0	7	2.250	1.500
Chirurgie	68	4	1	73	5.141	9.586
Dermatologie	6	1	2	9	1.082	15.240
Dietetiek	3	0	0	3	3.947	0
Geriatrie	0	0	2	2	0	0
Gynaecologie	31	0	0	31	4.356	4.036
Intensive Care	4	0	0	4	12.102	21.536
Inwendige geneeskunde	24	2	0	26	4.589	3.120
Kindergeneeskunde	5	0	0	5	3.674	1.561
Klinische Fysica	8	0	0	8	3.762	1.742
Longgeneeskunde	7	2	0	9	3.589	3.331
Maag, darm, leverziekten	10	1	0	11	4.695	2.666
Neurologie	8	0	0	8	22.170	31.075
nucleaire geneeskunde	0	0	1	1	0	0
Onderwijs en Onderzoek	1	0	0	1	3.747	0
Operatie kamers	1	0	0	1	1.677	0
Orthopedie	3	1	1	5	1.710	1.723
Pamm	2	0	0	2	3.973	0.503
Plastische chirurgie	2	1	1	4	0.738	0.972
Psychiatrie	1	0	0	1	9.478	0
Psychologie	0	1	0	1	1,270	0.9
Radiologie	3	0	0	3	3.591	0.345
Radiotherapie	7	1	0	8	8.710	10.791
SEH	2	1	0	3	1.110	0.981
Urologie	5	0	2	7	2.412	1.687
Totaal	293	21	13	327	3.498	7.538

WI-1* = Wetenschappelijk artikel in peer reviewed internationaal tijdschrift met Impact Factor
WI-2**= Wetenschappelijk artikel in peer reviewed internationaal tijdschrift zonder Impact Factor
WN***= Wetenschappelijk artikel in peer reviewed nationaal tijdschrift zonder Impact Factor

Tabel 4: Impactfactor per tijdschrift

Titel	Impact factor	Titel	Impact factor
Acta Cardiol	0.808	Cancer Manag Res	3.851
Acta Obstet Gynecol Scand	2.480	Cardiovasc Diabetol	4.752
Acta Oncol	3.156	Catheter Cardiovasc Interv	2.602
Acta Orthop	3.446	Chron Respir Dis	1.818
Adv Ther	2.709	Circ Cardiovasc Interv	6.598
Aging Cell	6.714	Circ Res	13.965
Aliment Pharmacol Ther	7.286	Circulation	19.309
Alzheimers Dement	9.478	Clin Biochem	2.434
Am Heart J	4.436	Clin Cancer Res	9.619
Am J Cardiol	3.398	Clin Chem Lab Med	3.432
Am J Clin Nutr	6.926	Clin Chim Acta	2.873
Am J Kidney Dis	7.623	Clin Colon Rectal Surg	0.839
Am J Perinatol	1.455	Clin Gastroenterol Hepatol	7.398
Am J Physiol Renal Physiol	3.611	Clin Oral Investig	2.308
Am J Transplant	6.165	Clin Rheumatol	2.365
Anaesthesia	4.741	Colorectal Dis	2.689
Ann Intern Med	17.202	Crit Care	5.358
Ann Noninvasive Electrocardiol	1.852	Crit Care Med	7.050
Ann Oncol	11.855		
Ann Surg	8.980	Dis colon rectum	3.519
Ann Surg Oncol	4.041	Dis Esophagus	2.571
Ann Thorac Surg	3.700		
		Echocardiography	1.314
BJOG	5.051	Emerg Med J	1.861
BMC Cancer	3.288	Endoscopy	6.107
BMC Health Serv Res	1.827	Eur Heart j	20.212
BMC Med Inform Decis Mak	1.643	Eur Heart J - Cardiovasc Img	5.990
BMC Med Res Methodol	3.295	Eur J Cancer	6.029
BMC Pregnancy Childbirth	2.263	Eur J Clin Microbiol Infect Dis	2.727
BMC Womens Health	1.572	Eur J Clin Nutr	3.057
BMJ Open	2.369	Eur J Gastroenterol Hepatol	1.968
Br J Anaesth	6.238	Eur J Nucl Med Mol Imaging	7.277
Br J Cancer	6.176	Eur J Obstet Gyn R B	1.666
Br J Clin Pharmacol	3.493	Eur J Prev Cardiol	3.606
Br J Dermatol	4.706	Eur J Surg Oncol	3.522
Br J Surg	5.899	Eur J Vasc Endovasc Surg	4.061
Brain	10.292	Eur Radiol	3.967
Breast Cancer Res Treat5.051	3.626	Eurointervention	5.193
		Fertil Steril	4.447

Gastrointest Endosc	6.501	J Knee Surg	1.657
Gynecol Oncol	4.959	J Low Genit Tract Dis	1.205
Haematologica	7.702	J Minim Invasive gynecol	3.061
Hand Clin	0.904	J Nat Cancer Inst JNCI	12.589
Health Psychol	3.458	J Neurointerv Surg	3.551
Heart Fail Rev	3.481	J Plast Reconstr Aesthet Surg	2.048
Heart Rhythm	4.825	J Ren Nutr	2.318
Hernia	1.932	J Steroid Biochem Mol Biol	4.561
HPB	3.290	J Surg Res	2.187
Hum Reprod	5.020	J Thorac Dis	2.365
		J Thromb Haemost	5.287
IEEE T med Imaging	3.942	J Vasc Surg	3.536
Int Arch Allergy immunol	2.720	JACC Cardiovasc Imaging	10.189
Int J Cancer	1.846	JACC Cardiovasc Interv	8.841
Int J Cardiol	6.189	JAMA	44.405
Int J Colorectal Dis	2.426	JAMA Dermatol	5.817
Int J Gynecol Cancer	2.369	Jama Surg	7.956
Int J Hyperthermia	3.262	JMIR Res Protoc	5.175
Int J Nurs Stud	3.755		
Int J Radiat Oncol Biol phys	5.133	Kidney Int	8.395
Int Urogynecol J	1.937		
Intensive Care Med	12.015	Lancet	47.831
Interact Cardiovasc Thorac Surg	1.857	Lancet Oncol	33.900
		Lancet Respir Med	19.287
J Adv Nurs	1.998	Langenbecks Arch Surg	2.203
J Am Acad Dermatol	7.002	Laryngoscope	2.471
J Am Coll Cardiol	19.896		
J Biomed Opt	2.530	Midwifery	1.948
J Cancer Surviv	3.051	Mod Pathol	5.728
J Cardiac Surg	0.518	Mult Scler	4.840
J Cardiol	2.732		
J Cardiothorac Surg	1.101	N Engl J Med	72.406
J Cardiothorac Vasc Anesth	1.699	Nephron	1.939
J Cardiovasc Surg	2.179	Neth Heart J	1.894
J Clin Anesth	1.677	Neth J Med	1.244
J Clin Endocrinol Metab	5.455	Neuro Oncol	7.786
J Clin Hypertens (Greenwich)	3.242	Neurogastroenterol Motil	3.617
J Clin Oncol	24.008	Neurology	8.320
J Diabetes Res	2.717	NPJ Prim Care Respir Med	2.793
J Electrocardiol	1.514		
J Endovasc Ther	2.838	Obes Surg	3.947
J Geriatr Oncol	2.852	OncoImmunology	7.719
J Hosp Infect	3.126	Oncology	2.262

Oncotarget	5.168	Radiat Oncol	2.568
Orthop J Sports Med	0.105	Radiother Oncol	4.328
Orthop Traumatol Surg Res	1.468	Reprod Biomed Online	3.249
		Respir Res	3.841
Pacing Clin Electrophysiol	1.486		
Pediatr Blood Cancer	2.513	Stroke	6.032
Pediatr Infect Dis J	2.486	Surg Endosc	3.747
Pediatr Neurol	2.018		
Pharmacogenet Genomics	2.184	Telemed J E Health	2.031
Phys Med	1.990	Ther Hypothermia Temp Manag	1.787
Phys Med Biol	2.742	Thorax	8.272
Physiol Meas	2.058	Trials	1.969
PLoS One	2.806	Tumour Biol	3.650
Prev Med	3.434		
		Vaccine	3.235
		Vasc Med	1.866

Auteursindex

een santeon ziekenhuis

Het Catharina Ziekenhuis maakt deel uit van Santeon

stz ziekenhuizen

Het Catharina Ziekenhuis is lid van de vereniging
Samenwerkende Topklinische Ziekenhuizen