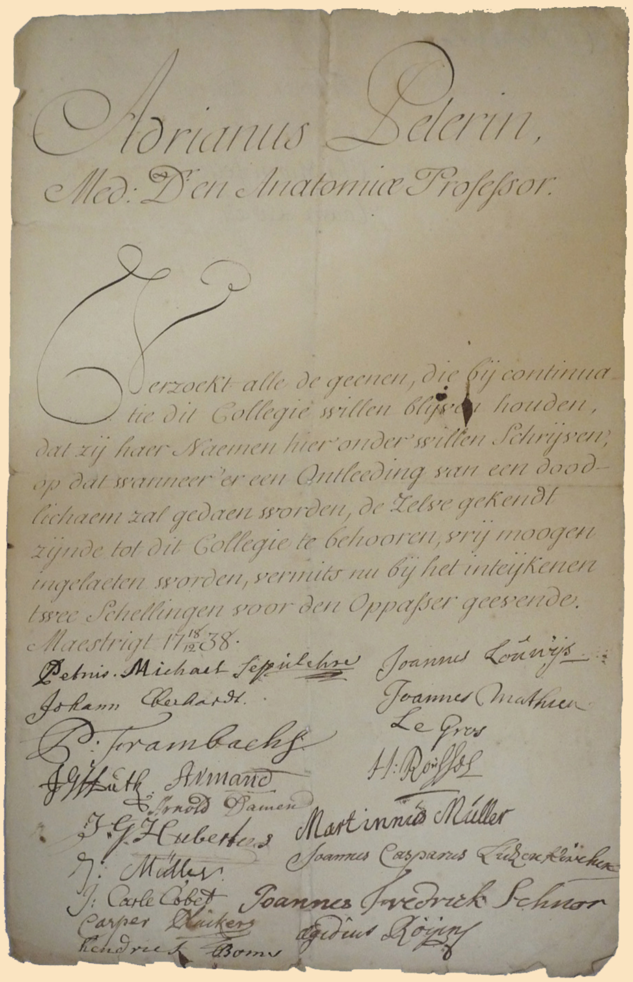
Pélerìn Symposium 2021

ABSTRACTBOEKJE

pélerìn
ARTS·ASSISTENTEN SYMPOSIUM

INHOUDS OPGAVE

Voorwoord


Adrianus Pélerin,
Med: D'en Anatomiæ Professor.

Verzoekt alle de geenen, die bij continua-
tie dit Collegie willen blijven houden,
dat zij haer Naemen hier onder willen Schrijven,
op dat wanneer'er een Ontleding van een dood-
lichaem zal gedaen worden, de Zelve gekendt
zijnde tot dit Collegie te behooren, vrij moogen
ingelaeten worden, vermits nu bij het inteijkenen
twee Schellingen voor den Oppasser geevende.
Maestrigt 17 18/12 38.

De Stichting Pélerìn

Sinds 1996 kent de Stichting Pélerin de Pélerin Wetenschapsprijs toe aan het beste onderzoek verricht door een arts-assistent of promovendus in het Maastricht Universitair Medisch Centrum. Het symposium heeft als doel jonge artsonderzoekers te stimuleren en schept de mogelijkheid voor het presenteren van wetenschappelijk onderzoek.

Dit jaar zal het symposium voor de 26e keer plaatsvinden. Echter het fundament voor dit symposium werd al ruim 250 jaar geleden gelegd.

In 1738 werd Adrianus Pélerin benoemd als eerste professor in de anatomie en chirurgie in Maastricht. Hij stond aan de wieg van het medisch onderwijs in Maastricht. Met zijn anatomische lessen verbeterde hij de medische zorg in het militair hospitaal van de garnizoenstad Maastricht. Tevens was Pélerin verbonden aan de illustere School van Maastricht, een instelling die studenten voorbereidde op een verdere universitaire studie. Ofwel een Maastrichtse bacheloropleiding avant la lettre. Tijdens zijn opleiding verrichte hij onderzoek naar het op dat moment endemische pokkenvirus. In 1719 promoveerde Pélerin in Leiden op het proefschrift “de Variolis”. Zijn proefschrift heeft hoogstwaarschijnlijk bijgedragen aan de vroegtijdige invoering van de pokkenvaccinatie in Maastricht.

In de geest van Pélerin zijn zowel wetenschap als opleiding gebundeld in het jaarlijkse Pélerin Wetenschapssymposium.

De Pélerìn Stichting wil de kwaliteit en de continuïteit van academische patiëntenzorg bevorderen

Het Pélerinsymposium 2021

KIEZEN OF DELEN?

Welkom bij de 26e editie van het Pélerin wetenschapssymposium! Het thema van dit jaar is "Kiezen of delen?". Durf jij te beweren dat al jouw keuzes zuiver en weloverwogen zijn? En hoe zit het met de keuzes die je maakt in de kliniek, of tijdens het onderzoek? Wellicht word je wel meer beïnvloed dan je denkt. De gastsprekers van dit jaar, Rob Urgert en Joep van Deudekom, nemen onze keuzes onder de loep en bieden tips om valkuilen te vermijden.

Helaas heeft ook dit jaar de COVID-19 pandemie invloed op ons symposium. Ondanks dat de cijfers in het land beter en beter lijken te worden, blijven er strikte maatregelen gelden voor evenementen zoals ons symposium. Gelukkig konden we hier dit jaar goed op inspelen en hebben we eruit gehaald wat we konden: een mooi hybride symposium. Zo kan onze top 5 een live presentatie geven en beoordeeld worden door de aanwezige vakjury, maar kunnen ook alle collega's, vrienden en familie vanuit thuis meekijken met onze livestream. Daarnaast hebben de genomineerden voor de Pitch Prijs en Semi-artsen Prijs ook dit jaar weer interessante pitches opgenomen over hun onderzoek.

Welke is uw favoriete pitch?
Kijk snel op onze website of YouTube!

Pélerìn Symposium 2021

6 oktober 2021
17:30 uur - 20:00 uur

Volg de livestream via
www.mumc.nl/pelerin

Kortom, wij zijn blij dat we dit jaar weer de mogelijkheid hebben om zoveel interessant onderzoek te kunnen presenteren aan u.
Wij wensen u een leerzame en vooral ook plezierige avond toe!

ORGANISATIE 2021

pélerìn
ARTS-ASSISTENTEN SYMPOSIUM

Al vroeg in het jaar beginnen wij achter de schermen met de voorbereidingen voor het symposium. De organisatie bestaat uit 7 gedreven, actieve maar vooral ook gezellige leden uit verschillende vakgebieden (zie hiernaast). Om de continuïteit van het symposium te waarborgen blijft elk lid voor 2 jaar in de organisatie, waarbij per jaar de helft wisselt. Zo kunnen we alle leerzame ervaringen van dit jaar weer meenemen in de organisatie van het Pélerìn symposium volgend jaar! Interesse? Kijk op onze website!

Van links naar rechts:
Ashkan Rezazadeh Ardabili - Maag- Darm- Leverziekten
Maud van Dinther - Neurologie
Roxanne Ploumen - Heelkunde
Sorina Simon - Radiologie
Kees de Mooij - Heelkunde
Kim Hintzen - Farmacologie & Toxicologie
Lotte Scheres - Oogheelkunde

WINNAARS VOORGAANDE EDITIES

Editie 2020

Pélerìn Wetenschapsprijs: Veronique Schiffer
AAV-prijs: Carine Leung
Publieksprijs: Remon Korenblik & Michiel Henkens
Semi-artsen prijs: Ashkan Rezazadeh

(Afbeeldingen op volgorde vanaf linksboven tegen de klok in)

Pélerin Wetenschapsprijs voorgaande edities

1996 Drs. M.J. Bonten, afdeling interne geneeskunde
1997 Drs. H.W. van Straaten & drs. L. Koster-Kamphuis, afdeling kindergeneeskunde
1998 Drs. J.A. de Priester, afdeling radiologie
1999 Drs. R.J. van Oostenbrugge, afdeling neurologie
2000 Drs. L. Hofstra, afdeling cardiologie
2001 Drs. S.W.Olde Damink, afdeling algemene heelkunde
2002 Drs. E. Hoitsma, afdeling neurologie
2003 Drs. A.W. Nap, afdeling gynaecologie & obstetrie
2004 Drs. F.M. van Dielen, afdeling algemene heelkunde
2005 Drs. V.C. Cappendijk, afdeling radiologie
2006 Drs. M.A. Hoving, afdeling neurologie
2007 Drs. J. Trip, afdeling neurologie
2008 Drs. J.P. Derikx, afdeling algemene heelkunde
2009 Drs. M.G. Snoeijs, afdeling algemene heelkunde & Drs. J.V. Been, afdeling kindergeneeskunde
2010 Drs. J.G. Bloemen, afdeling algemene heelkunde
2011 Drs. E.J. Rondagh, afdeling maag-, darm- & leverziekten
2012 Drs. A.H. Arits, afdeling dermatologie
2013 Drs. R.M. Schols, afdeling algemene heelkunde
2014 Drs. T. Brinkhuizen, afdeling dermatologie
2015 Drs. M. Dickman, afdeling oogheelkunde
2016 Drs. J. Beugels, afdeling plastische chirurgie
2017 Drs. M.W. Smulders, afdeling cardiologie
2018 Drs. M.H.E Jansen, afdeling dermatologie
2019 Drs. B. Corten, afdeling heelkunde

Genomineerden 2021

PÉLERÌN WETENSCHAPSPRIJS

FIEKE ADAN – DERMATOLOGIE
JUDITH LUBRECHT – KINDERGENEESKUNDE
MARISSA MEEGDES – MEDISCHE ONCOLOGIE
BRAM OLIJ – HEELKUNDE
RIANNE WILLEMSEN – MEDISCHE ONCOLOGIE

PÉLERÌN PITCH PRIJS

MOHAMMED GHOSSEIN – CARDIOLOGIE
FLORIS HENDRIKS – INTERNE GENEESKUNDE
JOHANNA KREUTZ – KINDERGENEESKUNDE
MARJOLEIN LIGTHART - HEELKUNDE
ROB VAN GASSEL - INTENSIVE CARE
BABETTE VERKOUTEREN – DERMATOLOGIE

PÉLERÌN SEMI-ARTS PRIJS

ANOUK CAMMAN – KINDERGENEESKUNDE
GLENN DAMS – RADIOLOGIE
MAXIMILIAN KLOFT - PATHOLOGIE
BOB KNAPEN – RADIOLOGIE
SILKE VAN MEIJL – RADIOLOGIE

Genomineerd voor Pélerìn Wetenschapsprijs

Optical coherence tomography versus regular punch biopsy in the diagnosis and subtyping of basal cell carcinoma: a multi-center randomized non-inferiority trial

Fieke Adan, Patty J. Nelemans, Tjinta Brinkhuizen, Sharon R.P. Dodemont, Janneke P.H.M. Kessels, Patricia J.F. Quaedvlieg, Gert-Jan Dermont, Veronique J.L. Winnepenninckx, Myrurgia Abdul Hamid, Brigitte A.B. Essers, Nicole W.J. Kelleners-Smeets and Klara Mosterd.

Department of Dermatology

Introduction:
In the Netherlands, an estimated 110,000 biopsies are performed each year for basal cell carcinoma (BCC) diagnosis. With a steep increase in the incidence of BCC, there is an unmet need for a cost-effective diagnostic method. Currently, histopathological examination of a punch biopsy is the gold standard to discriminate BCC from alternative diagnoses and to determine the histopathologic subtype. Recently, imaging methods such as optical coherence tomography (OCT), have become available for non-invasive diagnosis of skin lesions. Use of OCT to diagnose BCC may obviate the need for biopsy, resulting in more efficient and potentially cost-saving patient care.

Methods:
We conducted a multi-center randomized non-inferiority trial in three Dutch hospitals. Patients with an indication for biopsy of a lesion clinically suspected for BCC were randomized to OCT-guided diagnosis and treatment or to regular care, in which diagnosis and treatment is always based on a biopsy. The main endpoint for the non-inferiority trial was the proportion of patients free from tumour recurrence 1 year after treatment. For the cost-effectiveness analysis, the main endpoint was the incremental cost-effectiveness ratio defined as extra cost per gained QALY. Secondary, diagnostic performance parameters were assessed.

Results:
In total, 598 patients were included from March 2019 through September 2020. To date, 453/598 (75.8%) patients have completed 1 year follow-up, of which 9 recurrences have been diagnosed in the OCT group versus 14 in the regular care group. The absolute difference (OCT versus regular care) was -2.05% (95% CI: -6.08 to 1.98), where the upper limit of the 95% CI does not exceed the predefined non-inferiority margin of 10%.
The area under the receiver operating curve (AUC) was 95.2% for OCT. In this clinical setting, 65.6% of biopsies could have been avoided. An OCT-guided diagnostic pathway would result in a mean cost reduction of €75 per patient compared to regular care. The final cost-effectiveness analysis will be conducted this July, when follow-up is complete.

Conclusion:
Based on preliminary results, OCT guided diagnosis and treatment is non-inferior to regular care. OCT is a valuable tool in diagnosis and subtyping of BCC, substantially reducing the need for biopsy, which is potentially cost-saving.

Genomineerd voor Pélerìn Wetenschapsprijs

Weight changes during the COVID-19 pandemic in children with and without overweight and obesity, and the effects of prior lifestyle intervention.

⁎Arayess, L., ⁎Lubrecht, J.W., Reijnders, D., Hesselink, M.L., Ten Velde, G.L., van Loo, C., Janse, A.J., Von Rosenstiel, I.A., Van Mil, E.G.A.H., Verweij, M., Vreugdenhil, A.C.E.
⁎These authors contributed equally to this work

Department of Paediatrics

Introduction:
The current COVID-19 pandemic and associated governmental measures profoundly impact the lifestyle of children. School closures potentially lead to loss of daily structure, affecting meal times, physical activity and sleeping habits. We hypothesize that these circumstances exacerbate weight gain in children, in particular in children with overweight and obesity. The aim of this study was to determine perceived and objectively measured body weight change in children in The Netherlands during the first months of the COVID-19 pandemic and the effect of a prior lifestyle intervention.

Methods:
Perceptions of weight change were reported by 150 children and parents of the Children, Obesity and Lifestyle during COVID-19 (COLC) study (cohort A). Objectively measured anthropometric data was obtained from 66 children with overweight/(severe) obesity from the expertise Centre for Overweight Adolescent and Children's Healthcare (COACH; cohort B).

Results:
In cohort A, 43% of children with overweight or obesity perceived weight gain during the pandemic, compared to 15% of lean children (p=0.02). Overall, the BMI z-score of children from the COACH expertise centre increased by 0.065 (0.198) during the first five months of the pandemic (p=0.01). Longer participation in the lifestyle intervention (>1 year vs. <1 year,) and having two parents with a Dutch nationality associated with less weight gain during the pandemic, specifically in children with obesity (p=0.02 and p=0.03, respectively).

Conclusion:
During the first phase of the COVID-19 pandemic, especially children with overweight and obesity were at risk for accelerated weight gain. The beneficial effects of a lifestyle intervention on weight change in children with obesity during the pandemic, underline the importance of strong support of vulnerable populations during crises like this and other unexpected situations, and pleads for the acceleration of wide implementation of lifestyle interventions for children.

Genomineerd voor Pélerìn Wetenschapsprijs

Subtype discordance rates and initial systemic treatment choices in patients with advanced breast cancer in 2007-2018: a study of the SONABRE Registry

Marissa Meegdes, Khava I.E. Ibragimova, Dorien J.A. Lobbezoo, Ingeborg J.H. Vriens, Frans L.G. Erdkamp, M. Wouter Dercksen, Birgit E.P.J. Vriens, Kirsten N.A. Aaldering, Manon J.A.E. Pepels, Linda M.H. van de Winkel, Ananda Hochstenbach-Waelen, Sandra M.E. Geurts, Vivianne C.G. Tjan-Heijnen

Department of Medical Oncology

Introduction:
The growing knowledge on the occurrence of conversion of the hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) during the disease course of breast cancer emphasises the importance to obtain a biopsy of a metastatic site before treatment decisions are made.

Methods:
All 2854 patients diagnosed with advanced breast cancer from 2007-2018 in seven hospitals were selected from the Southeast Netherlands Advanced Breast cancer (SONABRE) registry to assess the biopsy rate at initial diagnosis of metastatic disease. Subtype discordance rates were determined for patients with a known subtype of the primary tumour and an initial metastatic site. Next, multivariate logistic regression analyses were performed to identify factors influencing biopsy rate and discordance. Finally, initial systemic treatment choices per concordant and discordant subtypes were evaluated.

Results:
The overall biopsy rate is 60%. Factors associated with obtaining a biopsy are the period of diagnosis since 2010, an unknown subtype of primary tumour, a metastatic site of soft or visceral tissue, and a metastatic-free interval (MFI) beyond three months. The overall discordance rate is 18%. Receptor subtype discordance is found to be associated with the HR+/HER2+ subtype of primary tumour (vs. HR+/HER2- subtype, OR=8.47; 95% CI:5.10-14.09), and a MFI of 3-24 months (vs. MFI <3 months, OR=2.52; 95% CI:1.15-5.52). None of the given adjuvant therapies were associated with a higher risk for subtype discordance. Following loss or gain of a receptor status a different pattern for the use of endocrine and HER2-targeted therapies are seen.

Conclusion:
The findings of this study highlight the importance of obtaining biopsy of metastatic disease, especially in the HR+/HER2+ subtype and in patients with a MFI of 3-24 months, as the possibility of subtype discordance has implications for treatment options.

Genomineerd voor Pélerìn Wetenschapsprijs

Laparoscopic versus open hemihepatectomy: The ORANGE II PLUS multicenter randomized controlled trial.

Robert S. Fichtinger, Luca A. Aldrighetti, Roberto I. Troisi, Mohammed Abu Hilal, Robert P. Suttcliffe, Marc G.H. Besselink, Somaiah Aroori, Krishna V. Menon, Bjørn E. Edwin, Mathieu D'Hondt, Valerio Lucidi, Tom F. Ulmer, Rafael Diaz-Nieto, Zahir Soonawalla, Steven White, Gregory Sergeant, Francesca Ratti, Bram Olij, Christoph Kümmerli, Lloyd Brandts, Siân A. Pugh, Zina Eminton, John N. Primrose, Ronald M. Van Dam, ORANGE II PLUS Collaborative

Department of Surgery

Introduction:
Surgical resection forms the mainstay of curative treatment for liver cancers. The laparoscopic approach in major liver resections is increasingly being performed. Randomized evidence to show superiority of laparoscopic (LH) compared to open hemihepatectomy (OH) for perioperative and oncological outcomes is lacking.

Methods:
Patients undergoing hemihepatectomy for accepted indications were randomized 1:1 to either LH or OH in 16 European centers. Patients and ward personnel were blinded until postoperative day 4. The primary endpoint was time to functional recovery (TFR). Defined as being independently mobile with adequate oral intake and normalizing liver function. Secondary outcomes included length of hospital stay (LOS), postoperative 90-day morbidity, 90-day mortality and and 3-year survival. Recruitment of 350 patients was needed to detect a 2-day reduction in TFR with 2-sided $\alpha = 0.04$ and 80% power. Groups were compared using unadjusted linear, logistic and Cox regression analyses and Mann-Whitney-U-test. All analyses were by intention-to-treat (ITT).

Results:
179 eligible patients were randomly assigned to LH and 173 to OH between October 2013 and January 2019. 135/179 (75%) patients in the LH group and 142/173 (82%) patients in the OH group had cancer: 162 CRLM, 47 HCC, 47 cholangiocarcinoma, 21 other metastases. Primary ITT-analysis included 327 patients (LH 164 vs OH 163) and demonstrated a significant reduction in TFR: LH 4 days (IQR 2-6) vs OH 5 days (IQR 3-7), P< 0.001. LOS was similarly different: LH 5 days (IQR 2-8) vs OH 6 days (IQR 4-8), P= 0.002. In the LH group 15% (24/164) of patients experienced complications > Clavien-Dindo IIIa within 90 days of surgery vs 18% (30/163) in the OH group, P= 0.36. There were 5 deaths (3.0%) within 90 days of surgery in the LH group vs 5 (3.1%) in the OH group, P= 0.99. At a median follow-up of 37 months (IQR 24-50 months) 3-year survival rate was 58% for LH vs 65% for OH (HR 1.16, 99% CI0.68-1.98, P= 0.49).

Conclusion:
LH is superior to OH in terms of TFR and LOS. No significant differences in oncological outcomes were observed but follow-up continues to permit a mature survivalanalysis.

Genomineerd voor Pélerìn Wetenschapsprijs

Development and external validation of a prediction model for tube feeding dependency for at least four weeks during chemoradiotherapy for head and neck cancer

Anna C.H. Willemsen, Annemieke Kok, Laura W.J. Baijens, Jan Paul de Boer, Remco de Bree, Lot A. Devriese, Chantal M.L. Driessen, Carla M.L. van Herpen, Frank J.P. Hoebers, Johannes H.A.M. Kaanders, Rebecca T. Karsten, Sander M.J. van Kuijk, Roy I. Lalisang, Arash Navran, Susanne R. Pereboom, Annemie M.W.J. Schols, Chris H.J. Terhaard, Ann Hoeben

Department of Medical Oncology

Introduction:
Patients who receive chemoradiotherapy or bioradiotherapy (CRT/BRT) for locally advanced head and neck squamous cell carcinoma (LAHNSCC) often experience high toxicity rates, interfering with oral intake, leading to (temporary) tube feeding (TF) dependency. International guidelines recommend gastrostomy insertion when the expected use of TF exceeds four weeks. We aimed to develop and externally validate a prediction model to identify patients who require TF for at least four weeks and would benefit from prophylactic gastrostomy insertion.

Methods:
A retrospective cohort study was performed in four tertiary head and neck cancer centers in the Netherlands. The prediction model was developed using data from University Medical Center Utrecht and the Netherlands Cancer Institute. Externally validation was performed using data from Maastricht University Medical Center and Radboud University Medical Center, with the latter being more reserved with gastrostomy insertions. The primary endpoint was TF dependency for at least four weeks initiated during CRT/BRT or within 30 days after CRT/BRT completion. Potential predictors were extracted from electronic health records and radiotherapy dose-volume parameters were calculated. Backward stepwise regression was performed to generate the model.

Results:
The developmental and validation cohort included 409 and 334 patients respectively. Multivariable regression analysis showed predictive value for pretreatment weight change, texture modified diet, Eastern Cooperative Oncology Group performance status (ECOG PS), tumor site, nodal classification, mean radiation dose to the contralateral parotid gland, and to the oral cavity. The risk for TF for at least four weeks = 1/(1 + e-LP), in which LP = −1.419 − 0.038∗pretreatment weight change + 0.448∗diet texture + 0.674∗ECOG PS − 0.793∗tumor site + 0.646∗nodal classification + 0.027∗contralateral parotid gland dose + 0.022∗oral cavity dose. The area under the receiver operating characteristics curve for this model was 0.73 and after external validation 0.62. Positive and negative predictive values for a risk of 90% or higher for TF dependency for at least four weeks were 81.8% and 42.3% respectively.

Conclusion:
We developed and externally validated a prediction model to estimate TF-dependency for at least four weeks in LAHNSCC patients treated with CRT/BRT. This model can be used to guide personalized decision-making on prophylactic gastrostomy insertion in clinical practice.

Genomineerd voor Pélerìn Pitch prijs

Physical disability and respiratory outcomes in mechanically ventilated COVID-19 survivors after hospital discharge

Rob J.J. van Gassel, Julia Bels, Bas C.T. van Bussel, Rein Posthuma, Hester A. Gietema, Jeanine Verbunt, Iwan C.C. van der Horst, Steven W.M. Olde Damink, Susanne van Santen, Marcel C.G. van de Poll

Department of Intensive Care

Introduction:
Long-term outcomes of patients following respiratory failure due to severe COVID-19 has not been well documented. We performed a comprehensive health assessment in mechanically ventilated COVID-19 survivors to assess the impact of respiratory and skeletal muscle injury sustained during ICU stay on physical performance at three months following hospital discharge.

Methods:
All mechanically ventilated COVID-19 patients admitted to our ICU during the first European pandemic wave (March - June 2021) were included into the pre-registered, prospective MaastrICCht Intensive Care COVID cohort. At three months follow-up, participants underwent a full pulmonary function test (PFT), a high-resolution computed tomography (HRCT) scan of the chest, a detailed physical assessment and completed a bundle of questionnaires assessing health-related quality of life, fatigue and mental health.

Results:
We included a total of 94 patients between March and June 2021. Fifty-two (55%) patients were alive three months after hospital discharge and 48 survivors (92%) participated in the follow-up study. The median age of the participants was 63 [55-68], 69% was male and the median duration of ventilation was 19 [9 - 29] days.
At three months, survivors still had significant respiratory impairment, with both fibrosis and ground glass present on chest CT in 90% of survivors and a median diffusion capacity on pulmonary function testing of 61% [50-69]% of predicted. Physical performance measured by 6-minute walking distance was below 80% of predicted in 48% of patients. Patients with impaired physical performance had more muscle weakness (MRC-sum score 53 [51 - 56] vs 59 [56 - 60], P<0.001), lower lung diffusion capacity (54% [44 - 66%] vs 68% [61 - 72%], P=0.002) and experienced more fatigue and worse health-related quality of life. Impaired diffusion capacity and increased intermuscular adipose tissue on HR-CT were both independently associated with physical performance of survivors.

Conclusion:
Both physical and respiratory sequelae are common in mechanically ventilated COVID19 survivors at 3 months after hospital discharge and negatively impact health-related quality of life. These early data provide valuable insight into the impact of severe COVID19 on funcitonal outcomes and can help aid rehabilitative efforts in these patients.

Genomineerd voor Pélerìn Pitch prijs

Serial assessment of myocardial injury markers in mechanically ventilated COVID-19 patients: `the prospective longitudinal Maastricht Intensive Care COVID (MaastrICCht) cohort`

Mohammed A. Ghossein*, Rob G.H. Driessen*, Frank van Rosmalen, Jan-Willem E.M. Sels, Thijs Delnoij, Alma Mingels, Antonius M.W. van Stipdonk, Frits W. Prinzen, Sander M.J. van Kuijk, Iwan J.C.C. van der Horst, Kevin Vernooy, Bas van Bussel, Chahinda Ghossein-Doha
*both authors contributed equally

Department of Cardiology

Introduction:
Myocardial injury during Coronavirus Disease 19 (COVID-19) is associated with intensive care unit (ICU) admission and in-hospital mortality. However, it is unknown how myocardial injury develops over the disease course during COVID-19 and whether the reported relation between myocardial injury and prognosis in a non-ICU ward can be translated to the ICU setting. Therefore, we performed a prospective study with serial measurements over the full course of ICU admission in mechanically ventilated COVID-19 patients until death or discharge.

Methods:
As part of the prospective MaastrICCht cohort, all first-wave COVID-19 patients admitted to the ICU in the Maastricht UMC+ were subject to a predefined repeated set of ECG characteristics and myocardial injury markers, including high sensitivity troponin T (hsTnT) and N-terminal pro-B-type Natriuretic Peptide (NT-proBNP). The study population was categorized in survivors and non-survivors. With linear mixed-effects regression, differences in ECG characteristics and myocardial injury markers over time between both groups were adjusted for sex, age, APACHE-II score, daily creatinine levels, hypertension, diabetes mellitus, and obesity.

Results:
We included 91 patients of which 58 (64%) survived and 33 patients (36%) died. A total of 628 serial ECG's, 1565 hsTnT, and 1559 NT-proBNP values were assessed. ECG abnormalities occurred in two third of the whole population, with the most prevalent being signs of right-ventricular strain (72%), ST-segment deviation (61%), P-wave split (76%), and QRS fragmentations (96%), without significant differences between non-survivors and survivors. Hs-TnT was significantly lower for survivors compared to non-survivors at day 1 (ß -0.55 (-1.04; -0.07, p = 0.028). The change over time in Hs-TnT did not differ significantly between the two groups. NT-proBNP at day 1 did not differ significantly between the groups, but over time it decreased significantly more in the survivor group (ß -0.08 (-0.12; -0.05, p<0.001), also after adjustments.

Conclusion:
Two third of COVID-19 patients showed ECG abnormalities in the ICU setting, without relevant differences between survivors and non-survivors. In contrast, both baseline HsTnT and change in NT-proBNP were strongly associated with mortality. Our findings underscore the importance of both baseline as well as serial assessment of cardiac biomarkers in the ICU setting.

Genomineerd voor Pélerìn Pitch prijs

Amino acid removal during hemodialysis can be compensated for by protein ingestion and is not compromised by intradialytic exercise: a randomized controlled cross-over trial

Floris K. Hendriks, Joey S.J. Smeets, Janneau M.X. van Kranenburg, Natascha J.H. Broers, Frank M. van der Sande, Lex B. Verdijk, Jeroen P. Kooman, and Luc J.C. van Loon

Department of Human Biology and Department of Internal Medicine

Introduction:
Patients with end-stage renal disease (ESRD) undergoing hemodialysis experience a rapid decline in skeletal muscle mass and strength. Hemodialysis removes amino acids (AAs) from the circulation, thereby lowering plasma AA concentrations and stimulating muscle catabolism. To support muscle maintenance in hemodialysis patients, intradialytic protein ingestion and exercise are increasingly implemented in clinical practice. However, it is not known whether these interventions modulate AA removal during hemodialysis.

Methods:
Ten patients (age: 65±16 y, male/female: 8/2, BMI: 24.2±4.8 kg/m2) with ESRD undergoing hemodialysis participated in this cross-over trial. During four 4-h hemodialysis sessions each patient ingested, in a randomized order, 40 g protein (PRO) or a non-protein placebo (PLA) both at rest, as well as following 30 min of intradialytic exercise (PRO+EX and PLA+EX, respectively). Blood and spent dialysate samples were collected every 30 min throughout hemodialysis to assess AA concentrations. Plasma AA concentrations, plasma AA availability (iAUC of plasma AA concentrations throughout hemodialysis), and AA removal were analyzed by repeated-measures ANOVA's.

Results:
Pre-hemodialysis plasma AA concentrations averaged 2.93±0.40 mmol/L, with no differences between treatments (P=0.66). During PLA and PLA+EX treatments, subsequent plasma AA concentrations decreased over time to 1.84±0.18 and 1.83±0.16 mmol/L, respectively (time effect P<0.001), with no differences between treatments (P=0.94). Plasma AA concentrations increased following protein ingestion up to peak values of 4.40±0.45 and 4.37±0.73 mmol/L during PRO and PRO+EX treatments, respectively (time effect P<0.001), with no differences between treatments (P=0.18). Accordingly, plasma AA availability was greater during PRO and PRO+EX treatments (49±87 and 70±34 mmol/L/240 min, respectively) when compared to PLA and PLA+EX treatments (-227±54 and -208±68 mmol/L/240 min, respectively; protein effect P<0.001; exercise effect P=0.21). AA removal was greater during PRO and PRO+EX treatments (16.6±2.2 and 17.3±2.3 g, respectively) when compared to PLA and PLA+EX treatments (9.8±2.0 and 10.2±1.6 g, respectively; protein effect P<0.001; exercise effect P=0.32).

Conclusion:
Protein ingestion during hemodialysis compensates for AA removal and increases plasma AA availability both at rest and during recovery from intradialytic exercise. Intradialytic exercise does not compromise AA removal or reduce plasma AA availability during hemodialysis in a post-absorptive or post-prandial state.

Genomineerd voor Pélerìn Pitch prijs

Children with celiac disease develop nutrient deficiencies while following a gluten-free diet

Johanna M. Kreutz, Laura Heynen and Anita C.E. Vreugdenhil

Department of Paediatrics

Introduction:
Celiac disease (CD) is a chronic auto-immune disease, triggered by gluten, associated with malabsorption and consequential nutritional deficiencies. Following a gluten-free diet (GFD) is currently the only effective treatment of CD. Unfortunately, the GFD itself is hypothesized to be a risk factor for nutrient deficiencies as well. Despite their clinical significance, consensus is lacking on the pattern and frequency of nutrient deficiencies in CD and the usefulness of their assessment during follow-up.

Methods:
This single center retrospective chart review aimed to map the occurrence of detected nutrient deficiencies in serological follow-up in a pediatric CD expertise center. Serological micronutrient levels that were determined during routine clinical visits were investigated, at moment of diagnosis and during follow up of children with CD visiting the MUMC+ department of pediatrics. Additional information was reviewed, among others anthropometrics, clinical symptoms, medication, gender and age at diagnosis. Nutrient deficiencies were defined using laboratory reference ranges.

Results:
The data of 130 children were reviewed at moment of diagnosis and follow-up after initiation of a GFD. During follow-up, a deficiency in iron, ferritin, vitamin D, vitamin B12, folate and zinc occurred in 18/52, 11/52, 17/44, 3/65, 8/60, 4/43 patients, respectively. No hypocalcemia or vitamin B6 deficiency was found at any moment during follow-up, regardless of nutrient status at diagnosis.

Conclusion:
This investigation of routinely assessed serological micronutrient values show varying prevalence of nutrient deficiencies in children with CD following a GFD. The findings suggest that risk to develop calcium or vitamin B6 deficiencies while following a GFD is negligible, while iron status, folate and vitamin D levels and their dietary intake should receive particular attention in the management of pediatric CD. This study highlights the necessity to structurally investigate the risk of developing nutrient deficiencies on a GFD and the potential risk factors herein. This could consequentially enable a more evidence based approach to the management of pediatric CD, regarding routine serological investigation.

Genomineerd voor Pélerìn Pitch prijs

Sarcopenia and myosteatosis predict adverse outcomes after emergency laparotomy: a multi-centre observational cohort study

Samantha Body⁎, Marjolein AP Ligthart⁎, Saqib Rahman, James Ward, Peter May-Miller, Philip H Pucher⁎, Nathan J Curtis⁎, Malcolm A West⁎ for the Wessex Research Collaborative.
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Department of Surgery

Introduction:
Emergency laparotomy has one of the highest morbidity and mortality rates of all surgical interventions. Body composition (BC) objectively identifies patients at risk of adverse outcomes in elective cancer cohorts, however evidence is lacking in emergency surgery. Therefore, the aim of this study is to determine the relationship between body composition (BC), specifically low skeletal muscle mass (sarcopenia) and poor muscle quality (myosteatosis) and outcomes in emergency laparotomy patients.

Methods:
An observational cohort study of patients undergoing emergency laparotomy at ten English hospitals was performed. BC analyses were performed at the third lumbar vertebrae level using preoperative CT images to quantify skeletal muscle index (SMI) and skeletal muscle radiation attenuation (SM-RA). Sex-specific SMI and SM-RA were determined, with the lower tertile splits defining sarcopenia (low SMI) and myosteatosis (low SM-RA). Accuracy of mortality risk prediction, incorporating SMI and SM-RA variables into risk models was assessed with regression modelling.

Results:
Six hundred and ten patients were included. Sarcopenia and myosteatosis were both associated with increased risk of morbidity (52.1% vs. 45.1%, p=0.028; 57.5% vs. 42.6%, p=0.014), 30-day mortality (9.5% vs. 3.6%, p=0.010; 14.9% vs. 3.4%, p<0.001), and 1-year mortality (27.4% vs. 11.5%, p<0.001; 29.7% vs.12.5%, p<0.001). Risk-adjusted 30-day mortality was significantly increased by sarcopenia (OR 2.56 (95%CI 1.12-5.84), p=0.026) and myosteatosis (OR 4.26 (2.01-9.06), p<0.001), similarly at 1-year (OR 2.66 (95%CI 1.57-4.52), p<0.001; OR 2.08 (95%CI 1.26-3.41), p=0.004). BC data increased discrimination of the existing National Emergency Laparotomy Audit (NELA) mortality risk-prediction model for 30-day mortality (AUC 0.838, 95%CI 0.835-0.84).

Conclusion:
Sarcopenia and myosteatosis are associated with increased adverse outcomes in emergency laparotomy patients.

Genomineerd voor Pélerìn Pitch prijs

Prognostic factors for treatment failure after imiquimod treatment in basal cell carcinoma.

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Department of Dermatology

Introduction:
Imiquimod 5% cream is the most effective, non-invasive treatment for superficial and nodular basal cell carcinoma (sBCC and nBCC). However, approximately 20% of patients experience treatment failure for unknown reasons. The objective of this study was to identify clinical and histological prognostic factors for treatment failure to imiquimod.

Methods:
Data were derived from 189 sBCC and 73 nBCC patients who participated in two randomized-controlled trials on the efficacy of imiquimod. In both trials, imiquimod was applied once daily, five times a week for 6 weeks. Treatment failure was evaluated by an investigator at 12 month post treatment and had to be histologically confirmed. Candidate prognostic factors were categorized into three groups: 1) patient and tumor characteristics available at baseline (sex, age, tumor size and location), 2) factors related to treatment (treatment compliance and severity of skin reaction, based on patient diaries) and 3) histological characteristics (tumor thickness, invasion depth, thickness of epidermis, and the amount/presence of: infiltrate, plasma cells, parakeratosis, ulceration, erosion, blood vessels and solar elastosis). To evaluate the association between potential prognostic factors and 1-year treatment failure, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated with the use of mixed-effects multivariable logistic regression analyses.

Results:
Treatment failure occured in 41 of 262 BCCs (15.6%). Male sex (21.4% failure), BCCs on the lower extremities (35.9% failure) and less than severe skin reaction (20% and 33.3% failure in mild/moderate and absent skin reaction respectively) were associated with a significantly increased risk of treatment failure. After mutual adjustment for these factors, the OR for male sex, and mild/moderate and absent skin reaction (compared to severe skin reaction) remained statistically significant: OR 2.51 (95% CI 1.17-5.39), and OR 3.30 (95% CI 1.25-8.72) and 4.91 (95% CI 1.34-17.90), respectively. None of the histologic characteristics, including tumor thickness and invasion depth, were associated with risk of treatment failure.

Conclusion:
No histologic characteristics were associatied with risk of treatment failure. Risk of treatment failure after imiquimod treatment was higher in both men and patients with a less severe skin reaction. This information is particularly relevant for the shared-decision making process and follow-up policy after treatment.

Genomineerd voor Pélerìn semi-arts prijs

I-FABP as a marker for minimally invasive evaluation of disease activity in adults with coeliac disease in a multi-centre international cohort

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Department of Pediatrics

Introduction:
Coeliac disease (CD) is a common enteropathy characterized by villous atrophy due to a gluten-induced immune response. A sensitive, minimally invasive marker for evaluation of intestinal healing after initiating a gluten free diet (GFD) in patients with CD is missing. Although the autoantibody anti-tTG-IgA is a well-established marker for screening, it does not reflect the degree of disease activity accurately. Additionally, a marker for seronegative patients is lacking. Intestinal-fatty acid binding protein (I-FABP), a circulatory marker for enterocyte damage, is a promising additional follow-up marker. This study examines the added value of I-FABP in minimally invasive evaluation of disease activity of CD after initiating a GFD in adults.

Methods:
Adults with established CD and available blood samples from a medical centre in Sweden, Italy and the United States of America were included in this multi-centre international cohort study. Blood draw and biopsies were performed when clinically relevant at moment of diagnosis and during follow-up. I-FABP serum levels were measured using an ELISA. Results were analysed using Mann-Whitney U tests and Kruskall Wallis tests with Dunnetts post-hoc test

Results:
Two hundred seventy-one samples of adults with CD were included. An increasing trend of I-FABP levels with increasing Marsh grade was shown at time of diagnosis (N=128). The I-FABP levels differ significantly ($p<0.05$) between Marsh grade 3C (3104.69 ±2233 U/mL) and Marsh 0 (1192 ±927 U/mL). A decrease of mean I-FABP levels was observed in the first two weeks after initiating a GFD (3172 vs 1301.4 U/mL) while anti-tTG-IgA levels remained above the cut-off value. During long-term follow-up, I-FABP levels in patients with Marsh grade 3A-3C were elevated compared to Marsh 0 and 2.

Conclusion:
In this multi-centre cohort study, I-FABP serum levels seem to correlate to the degree of intestinal damage at diagnosis and during follow-up in CD. This confirms results of previous studies suggesting that I-FABP is a promising minimally invasive marker for follow-up after initiating a GFD. This study is the first to show this corelation in an international cohort and to indicate that I-FABP could be a promising marker for long-term follow-up of disease activity as well.

Genomineerd voor Pélerìn semi-arts prijs

Retrospective analysis of 2 different types of percutaneous radiologic gastrostomy (PRG), evaluation of outcomes and complications.

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Department of Radiology

Introduction:
Patients at risk of malnutrition often receive enteral feeding by PRG placement, e.g. pre-operative placement in patients suffering from head and neck cancer. Different sizes and locking mechanisms of these PRG tubes exist. Around 2018 interventional radiologists of the MUMC+ switched from using 12Fr to 14Fr catheters. Patients receiving the latter tend to have less complications however this hypothesis has not been objectified so far. The aim of this study is to retrospectively compare a 12Fr pigtail and a 14Fr balloon tube with respect to technical success, 30-day mortality and (tube-related) complications within 180 days.

Methods:
261 consecutive patients with PRG placement between January 2016 and June 2020 (150 pigtail and 111 balloon) were included. Primary outcomes were placement success, 30-day mortality, number of (tube-related) complications and days to first complication within 180 days. Data was retrospectively obtained from PACS-system and electronic health records. Approval to conduct this study was obtained (METC 2020-2246) and data was pseudonymized using CastorEDC. IBM SPSS Statistics 27 was used to analyze the data.

Results:
Baseline characteristics were not significantly different between the two groups besides BMI which was significantly higher in the balloon-group compared to the pigtail-group (22.72 vs. 24.76, P=0.018). The technical success rate was very high in both groups and did not significantly differ (97% vs. 99% , p=0.125). Mortality after PRG placement was very low and never related to the placement (N = 1 vs. N=3). The average number of complications within 180 days after initial PRG placement was lower in the balloon-group compared to the pigtail-group (0.90 vs. 0.62, p=0.032). Moreover, the number of days between initial placement and first complication was higher in the balloon group compared to the pigtail group (P=0.008, HR=1.611; 95% CI 1.132 – 2.292).

Conclusion:
Results demonstrate that the 14Fr balloon tube performs superior to the 12Fr pigtail tube with respect to tube-related complications, while technical success remains high and (procedure-related) 30 day mortality low. This was in line with our hypothesis. Thus, we strongly suggest to use 14Fr-balloon PRG catheters over the use of 12Fr-pigtail PRG catheters.

Genomineerd voor Pélerìn semi-arts prijs

The relationship between size and microarchitecture of negative regional lymph nodes in the resection specimen and survival in oesophageal cancer patients treated with either surgery alone or chemotherapy followed by surgery - results from the UK MRC OE02 trial

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Department of Pathology

Introduction:
Patients with resectable oesophageal cancer (OeC) have a 5-year overall survival (OS) of 25-47%. One of the strongest prognostic factors is the lymph node (LN) status. The regional tumour draining LNs play an important role in the host anti-tumour immune response. However, it is currently not known whether there are specific morphological changes in regional LNs after neoadjuvant cytotoxic chemotherapy. We hypothesized that the microarchitecture of tumour negative LNs (LNneg) differs between OeC patients treated by surgery alone (S patients) compared to those treated by chemotherapy followed by surgery (CS patients) and that the microarchitecture of LNnegs is related to OS.

Methods:
Digitized haematoxylin&eosin-stained sections of 305 OE02 trial OeC patients were analysed (146 S patients, 159 CS patients). The percentage of area of the different immune components (lymphocytes, germinal centre, histiocytes, vessels, other tissue (fat, connective tissue)) within the largest LNneg per patient was morphometrically quantified. The relationship between individual LN microarchitecture components, largest LNneg diameter and OS was analysed.

Results:
In CS patients, LNneg size was correlated to higher percentage of histiocytes ($p<0.0001$) and a lower percentage of germinal centres (GC) and lymphocytes ($p=0.03$ and $p<0.0001$, respectively). The LN area with GC was significantly reduced in LNnegs from CS patients compared to S patients (1% vs 2%, $p<0.01$). In multivariate analysis, patients with a higher histiocytes/lymphocytes ratio had significantly worse OS (HR: 1.15, 95% CI: 1.03-1.28, $p=0.02$).

Conclusion:
This is the first study to quantify and compare the microarchitecture components in LNnegs of OeC patients treated with surgery alone or chemotherapy followed by surgery. The results seem to suggest that the LNneg based host anti-tumour response changes after chemotherapy. Importantly, a shift from antibody-based to cell-based immune reaction appears to be indicative of worse survival. Further studies investigating LN microarchitecture in tumour positive LN are warranted in order to unravel the underlying biologic mechanisms and to translate results into post-surgery patient treatment decisions in the future.

Genomineerd voor Pélerìn semi-arts prijs

The effect of Microwave/Radiofrequency Ablation (MWA/RFA) on liver volume in patients with primary and secondary liver tumours; a single centre retrospective analysis.

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Department of Radiology

Introduction:
In order to reduce the chance of post-hepatectomy liver failure (PHLF), interventional techniques as Portal Vein Embolization (PVE) are often performed preoperatively to stimulate future liver remnant (FLR) hypertrophy. Thermal ablation can induce liver hypertrophy as well, which might further add to growth of the FLR when combined with PVE. Exact influence of radiofrequency or microwave ablation (RFA/MWA) on liver hypertrophy however remains unclear. We therefore retrospectively analysed volume changes after ablation of primary and secondary liver lesions in Maastricht University Medical Centre.

Methods:
46 patients, with primary or secondary (metastatic) liver tumours, treated by RFA/MWA between January 2015 - August 2020 without earlier liver treatment and no tumour in segment II/III, were included. Total Liver Volume (TLV) and segment II+III volume were calculated using OsiriX DICOM viewer (MRI) and Syngo.via (CT-scans). Absolute and percentages of total liver volume and segment II/III (distant segments) after 1-8, and >9 weeks in livers with primary/secondary liver tumour were used as primary outcomes. Secondary outcomes were absolute and percentages of ablation volume and netto volume (TLV - ablation volume).

Results:
46 patients (26 primary and 20 secondary liver tumours) were analysed. TLV in patients with secondary liver tumours increased after >9 weeks with a median of 2.74% (86.77mL). In contrast, TLV in patients with primary liver tumours decreased with a median of 0.45% (-20.99mL). The median difference of segment II/III at >9 weeks compared to baseline was 3.84% (7.14mL) and -0.76% (-13.90mL) for patients with secondary and primary liver tumours, respectively. The ablation volume decreased after >9 weeks with 55.42% (15.52mL) and 43.56% (-13.82mL), respectively in patients with secondary and primary liver tumours. Netto volume after >9 weeks increased in patients with secondary liver tumours with a median 4.53% (145.73mL), but decreased in patients with primary liver tumours with -0.08% (32.89mL).

Conclusion:
In patients with secondary tumours TLV, segments II/III and netto volume increased after MWA/RFA, while primary tumours showed a slight decrease. Suggesting a potential additional benefit of liver ablation to PVE in growth of the FLR in patients with secondary liver tumours, while no additional benefit is expected in patients with primary liver tumours.

Genomineerd voor Pélerìn semi-arts prijs

18F-FDG PET/MRI in breast cancer: response prediction in axillary lymph nodes

S. van Meijl, T.J.A. van Nijnatten

Department of Radiology

Introduction:
There is currently no imaging modality that can accurately predict response to neo-adjuvant chemo- with/without immunotherapy (NAC) in the axillary lymph nodes (ALNs) in breast cancer patients. Consequently, all patients will be treated with axillary surgery, irrespective of potential response. 18F-FDG PET/MRI is a new imaging modality; its accuracy in response prediction of the ALNs has not yet been determined. The purpose of this study was to investigate the diagnostic accuracy of 18F-FDG PET/MRI for response prediction in ALNs on NAC in breast cancer.

Methods:
A total of 31 breast cancer patients, treated with NAC, who underwent a 18F-FDG PET/MRI exam of the breast, (including complete axillary field of view) between 2014 and 2019 in Maastricht University Medical Centre were retrospectively included. The PET parameter maximum standardized uptake value (SUVmax) of ALNs was assessed. Furthermore, the axillary radiological- and pathological complete response (axillary rCR and axillary pCR, respectively) have been noted by, respectively, the radiologist and pathologist. The sensitivity is the percentage of patients correctly identified with residual disease; the specificity, on the other hand, is the percentage of patients correctly identified with axillary pCR. Bivariate logistic regression was performed in order to obtain the parameters that could predict axillary pCR post-NAC.

Results:
The median age was 50 years. 12 out of the 31 (39%) patients were considered clinically node-negative, while 19 (61%) were considered clinically node-positive. 20 patients achieved axillary pCR (64.5%). All 31 patients underwent a 18F-FDG PET/MRI exam pre-NAC, 30 patients mid-NAC (after 3-4 cycles) and 27 post-NAC (after 8-9 cycles). With regard to the clinically node-positive patients, mean percentage decrease of the axillary SUVmax between the pre- and mid-NAC PET/MRI is 79,5% for the axillary pCR and 56,6% for the axillary non-pCR subgroup (P-value = 0.034). The overall diagnostic performance parameters for prediction of nodal status were sensitivity, specificity, PPV and NPV of 50%, 90%, 71,4% and 78,3%, respectively. For clinically-node positive patients the diagnostic performance was 55,6%, 83,3%, 71,4% and 71,4%, respectively.

Conclusion:
18F-FDG PET/MRI has potential to serve as non-invasive imaging method regarding nodal (re)staging in breast cancer patients treated with neoadjuvant chemo- with/without immunotherapy.

Deep learning automated segmentation for muscle and adipose tissue from abdominal computed tomography in polytrauma patients

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*contributed equally to this work **joint senior author

Department of Surgery

Introduction:
Manual segmentation of muscle and adipose compartments from computed tomography (CT) axial images is a potential bottleneck in early rapid detection and quantification of sarcopenia.

Methods:
A prototype deep learning neural network was trained on a multi-centre collection of 3413 abdominal cancer surgery subjects to automatically segment truncal muscle, subcutaneous adipose tissue and visceral adipose tissue at the L3 lumbar vertebral level. Segmentations were externally tested on 233 polytrauma subjects.

Results:
Although after severe trauma abdominal CT scans are quickly and robustly delivered, with often motion or scatter artefacts, incomplete vertebral bodies or arms that influence image quality, the concordance was generally very good for the body composition indices of Skeletal Muscle Radiation Attenuation (SMRA) (CCC = 0.92), Visceral Adipose Tissue index (VATI) (CCC = 0.99) and Subcutaneous Adipose Tissue Index (SATI) (CCC = 0.99).

Conclusion:
In conclusion this article showed an automated and accurate segmentation system to segment the cross-sectional muscle and adipose area L3 lumbar spine level on abdominal CT. Future perspectives will include fine-tuning the algorithm and minimizing the outliers.

Long-term risk of cutaneous squamous cell carcinoma after four different treatments for actinic keratosis

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Department of Dermatology

Introduction:
An important aim of treatment of actinic keratosis (AK) is preventing cutaneous squamous cell carcinoma (cSCC). However, whether AK can really progress into cSCC is matter of debate and little is known about the effect of treatment on preventing cSCC.

Methods:
We evaluated the risk of cSCC and factors that may contribute to increased risk in a broad spectrum of patients with AK who participated in a randomized trial comparing four field-directed treatments of AK.
The primary outcome was the proportion of patients with cSCC in the target area during follow-up. Secondary outcomes were the associations between risk of cSCC and a priori defined potential prognostic factors; type of treatment, severity of AK, history of nonmelanoma skin cancer, and retreatment.

Results:
Of 624 patients, 26 patients were diagnosed with a histologically proven cSCC in the target area. The 4-year risk of developing cSCC in a previously treated area of AK was 3.7% and varied between 2.2% in patients treated with fluorouracil and 5.8% in patients treated with imiquimod. In patients with severe AK (Olsen grade III) the risk was 20.9% (95% CI: 10.8%–38.1%) and the risk was especially high (33.5%, 95% CI: 18.2%–56.3%) in patients with severe AK who needed retreatment.

Conclusion:
Risk of cSCC was highest in patients with Olsen grade III AK and was also substantially increased in patients who received retreatment. Fluorouracil is the most effective treatment in terms of AK lesion reduction, and seems to be more effective in preventing cSCC than the other three treatments.

The effect of low sodium intake on aldosterone and renin in essential hypertensives

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Department of Internal medicine

Introduction:
Dietary sodium intake plays an important role in blood pressure and sodium homeostasis through the activation or suppression of the renin-angiotensin-aldosterone system (RAAS). The purpose of this article is to identify the effect low sodium intake has on renin, aldosterone and the aldosterone-to-renin ratio.

Methods:
88 nonmedicated essential hypertensive patients who were previously on an ad libitum diet adhered to a low sodium diet (55mmol/d) for a week. All measurements were taken in the morning while patients were in a supine position. Changes in aldosterone, renin and the ratio thereof were assessed on the first three days (early response) and the seventh day (late response) after sodium restriction

Results:
Repeated measures ANOVA showed that both renin and aldosterone increased significantly in the early as well as the late response (aldosterone 307.26, 407.76 and 373.42 [p=0.001 and p=0.001], renin 17.542, 22.41 and 23.021 [p=0.001] on the first, third, and seventh day, respectively). Notably, repeated measures ANOVA revealed a normalisation trend of late-response aldosterone, and a persistent rise in renin (aldosterone 407.76 and 373.42, renin 22.41 and 23.021 for the third and seventh day, respectively). The ARR neither changed in the early nor in the late response. In the older age group (age >40), changes in renin and aldosterone were less volatile and the early renin response was more blunted, when compared with the younger age group (age ≤40).

Conclusion:
To conclude, an acute change in dietary sodium intake resulted in a significant rise of both aldosterone and renin as well as a possible disturbance of the RAAS which is seen as a slight dissociation between aldosterone and renin. The long-term effect of low sodium diet was not assessed in this study and therefore warrants further investigation.

Preoperative aerobic fitness and body composition variables play a critical role in the development and impact of postoperative complications in colorectal cancer surgery

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Department of Surgery

Introduction:
Preoperative aerobic fitness and body composition variables are promising physical fitness parameters to predict the risk for postoperative complications, as well as the impact of complications on postoperative recovery in patients with colorectal cancer (CRC) undergoing elective tumour resection. This study aimed to assess the associations and predictive potential of these preoperative physical fitness parameters regarding the occurrence and the impact of postoperative complications after elective CRC surgery.

Methods:
Preoperative aerobic fitness was assessed by the attained peak work rate at the Steep Ramp Test (10 W/10 s). Body composition was assessed as muscle mass and muscle density and measured using preoperative computed tomography scan analysis at the L3-level. Complications were graded by the Clavien-Dindo classification (CD). The impact of complications was determined by postoperative time to recovery of functioning. Multivariable logistic regression analyses were used to assess associations and to develop preliminary prediction models for postoperative complications and impact of complications on postoperative recovery.

Results:
Of 238 included patients, 96 (40.3%) developed postoperative complications (CD ≥I). Multivariable analysis including age, sex, comorbidities, tumour location, aerobic fitness, and body composition showed that better preoperative aerobic fitness significantly decreased the likelihood to develop postoperative complications (OR 0.57, 95% CI 0.36-0.89), and significantly predicted the occurrence of postoperative complications (area under the curve (AUC) 0.692, $p<0.001$). A prolonged time to postoperative recovery was strongly associated with lower muscle density (OR 4.14, 95% CI 1.28-13.41), regardless of confounders including preoperative aerobic fitness, and significantly predicted a higher impact of complications (AUC 0.674, $p=0.004$).

Conclusion:
Preoperative aerobic fitness was independently associated with the risk for developing postoperative complications, whereas preoperative muscle density was independently associated with time to postoperative recovery of functioning in case of complications following CRC surgery. Patients with lower aerobic fitness have a higher risk for complications. In case of complications, patients with a lower muscle density have an increased time to postoperative recovery of functioning, regardless of preoperative aerobic fitness levels. Both parameters could be valuable additives to preoperative risk assessment in patients undergoing CRC surgery to improve preoperative risk prediction and offer patient-tailored preoperative preventive interventions.

Adjuvant gemcitabine plus capecitabine versus gemcitabine monotherapy in a Dutch nationwide cohort of patients with pancreatic ductal adenocarcinoma.

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* share first authorship; ** share senior-authorship

Department of Medical Oncology

Introduction:
Evidence of the added value of capecitabine to adjuvant gemcitabine monotherapy in pancreatic ductal adenocarcinoma (PDAC) is limited to the ESPAC-4 trial. The aim of this study was to assess whether adjuvant gemcitabine plus capecitabine (GEMCAP) is superior to adjuvant gemcitabine monotherapy (GEM) in a Dutch nationwide cohort.

Methods:
Patients diagnosed with PDAC from 2015 to 2019 and treated with adjuvant GEM or GEMCAP without preoperative treatment were identified from the Netherlands Cancer Registry. The primary endpoint was overall survival (OS), measured from start of chemotherapy. OS for GEMCAP vs GEM was adjusted for prognostic factors (tumor size, lymph node involvement, resection margin, tumor differentiation, and treatment) in a multivariable Cox regression analysis. Secondary endpoint was completion of six chemotherapy cycles.

Results:
We identified 778 patients, of whom 21.1% received GEMCAP and 78.9% received GEM. The median OS was 31.4 months (95% CI 26.8-40.7) for GEMCAP and 22.1 months (95% confidence interval (CI) 20.6-25.0) for GEM (HR 0.71, 95% CI 0.56-0.90; logrank p=0.004). After adjustment for prognostic factors, survival remained superior for patients treated with GEMCAP (HR:0.73, 95% CI 0.57-0.92, logrank p=0.009). Survival with adjuvant GEMCAP was superior to GEM in most subgroups of prognostic factors. Adjuvant chemotherapy was completed in 69.5% and 62.7% of the patients treated with GEMCAP and GEM, respectively (p=0.11).

Conclusion:
The addition of capecitabine to gemcitabine was superior to gemcitabine monotherapy and showed comparable cycle intensity in an unselected nationwide cohort of patients who underwent resection for PDAC.

Blood-brain barrier leakage at baseline and cognitive decline in cerebral small vessel disease: a 2-year follow-up study

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Department of Neurology

Introduction:
Blood-brain barrier (BBB) dysfunction is one of the pathophysiological mechanisms in cerebral small vessel disease (SVD). Previously, it was shown that BBB leakage volume is larger in patients with SVD compared with controls. In this study, we investigated the link between BBB leakage and cognitive decline over two years in patients with cSVD.

Methods:
At baseline, 51 patients with clinically overt cSVD (lacunar stroke or mild vascular cognitive impairment) received a dynamic contrast enhanced MRI scan to quantify BBB permeability in the normal appearing white matter (NAWM), white matter hyperintensities (WMH), cortical grey matter (CGM) and deep grey matter (DGM). Cognitive function in the domains executive function, information processing speed and memory was measured in all patients at baseline and after 2 years. The association between baseline BBB leakage and cognitive decline over two years was determined with multivariable linear regression analysis, corrected for age, sex, educational level, baseline WMH volume and baseline brain volume.

Results:
Regression analyses showed that higher baseline leakage volume and rate in the NAWM and CGM was significantly associated with increased overall cognitive decline. Furthermore, higher baseline leakage volume in the NAWM and CGM, and higher baseline leakage rate in the CGM was significantly associated with increased decline in executive function

Conclusion:
This longitudinal study showed that higher BBB leakage at baseline is associated with stronger cognitive decline, specifically in executive function, over 2 years of follow-up in patients with cSVD. These results emphasize the key role of BBB disruption in the pathophysiology and clinical progression of cSVD.

No influence of cholestasis on Portal Vein Embolization (PVE) -induced hypertrophy of the Future Liver Remnant.

Xinwei Chang*, Remon Korenblik*, Bram Olij, Bob Knapen, Christiaan van der Leij, Lloyd Brandts, Daniel Heise, Marcel den Dulk, Ulf Neumann, Frank G. Schaap, Ronald van Dam, Steven Olde Damink
*First authors contributed equally.

Department of Surgery

Introduction:
Experimentally induced hepatocellular bile salt accumulation impairs liver function and regeneration following partial hepatectomy. Portal vein embolization (PVE) is the current standard to induce future liver remnant (FLR) hypertrophy. The impact of cholestasis on PVE-induced FLR hypertrophy however remains unclear. We hypothesize that cholestasis impairs FLR hypertrophy in patients undergoing PVE.

Methods:
Patients with perihilar cholangiocarcinoma (pCCA) or colorectal liver metastases (CRLM), who underwent PVE before a (extended) right hemihepatectomy in Maastricht University Medical Center or Uniklinik RWTH Aachen between 2016 and 2019, were enrolled. Clinical and laboratory variables were recorded, and volume of segments II and III were considered as FLR and assessed on pre- and post-embolization CT scans. Diameters of left and right hepatic bile ducts were measured on pre-embolization scans. Serum bilirubin was used as a clinical marker of cholestasis. The degree of hypertrophy (DH) as percentual increase and kinetic growth rate (KGR) as percentage/week, were used to assess PVE-induced hypertrophy.

Results:
A total of 50 patients (31 CRLM, 19 pCCA) were included. FLR volumes increased significantly after PVE in both patients with CRLM and pCCA. DH and KGR did not differ between patients with CRLM and pCCA ($p = 0.880$ and $p = 0.822$, respectively). For patients with pCCA, unilateral drainage in FLR induced higher DH than bilateral drainage (6.7 [-0.1 to 10.9] versus 2.7 [0.4 to 5.7] %, $p = 0.012$). For the entire cohort of 50 patients, neither bilirubin levels before biliary drainage nor before PVE were correlated with DH or KGR. CRP levels before PVE were negatively correlated with DH ($\rho=-0.401$, $p=0.009$), and tended to be negatively correlated with KGR ($\rho=-0.300$, $p=0.054$).

Conclusion:
PVE induced similar hypertrophy of FLR in patients with and without cholestasis. inflammation response appears to be associated with impaired liver growth. Without taking the limitations of this retrospective analysis into account, these findings question the indication of draingage of the liver in cholestatic patients without any inflamation.

Patient-Reported Outcome Measurement-Haemorrhoidal Impact and Satisfaction Score (PROM-HISS): Development, Reliability and Construct Validity

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Introduction:
Haemorrhoidal disease (HD) is a frequently occurring disorder with a negative impact on a patient's quality of life. The Core Outcome Set (COS) for HD trials states that symptoms and satisfaction are the core outcomes to be evaluated using a Patient Reported Outcome Measure (PROM). We describe the development and validation of the PROM-Haemorrhoidal Disease and Satisfaction Score (PROM-HISS).

Methods:
The development of the PROM-HISS followed recommended guidelines for the development and validity of health status questionnaires. The items of the PROM-HISS were based on patient interviews, literature review and expert input. Face and content validity of the concept version were evaluated by conducting individual think-aloud interviews. Structural properties, reliability and construct validity were measured in a cross-sectional population. Reliability was tested by assessing the test-retest reliability, defined by the Intraclass Correlation Coefficient (ICC), and internal consistency measured with Cronbach's alpha. Construct validity was evaluated using confirmatory factor analysis (CFA) and hypotheses testing.

Results:
The PROM-HISS consisted of the following three domains: (1) HD symptoms, (2) impact of HD on daily life, and (3) satisfaction with treatment. The first domain comprised of five items focused on the experienced burden of blood loss, pain, prolapse, soiling and itching. The face and content validity check among 10 patients led to minor adjustments to the wording of some items. The PROM-HISS was completed by 102 patients (65% male), with a mean age of 58 years (23-81 years) and primarily diagnosed with HD grade III (39%). The ICCs of the different items in the domain 'Symptoms' ranged between 0.56 and 0.79 and were interpreted as good and the Cronbach's alpha value was 0.80 and considered satisfactory. The CFA provided further evidence for construct validity with a good model fit. In line with our hypotheses, a correlation was found between a high score on the symptoms of HD, a high impact of HD on daily life (Pearson's $r = 0.632$, $p<0.01$), and a low degree of satisfaction (Pearson's $r = 0.378$, $p<0.01$).

Conclusion:
The PROM-HISS is a reliable and valid instrument to evaluate symptoms of HD, impact on daily life and satisfaction with treatment.

Robotic thymectomy for thymomas: a retrospective follow-up study in the Netherlands

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Introduction:
The Maastricht University Medical Center+ (MUMC+) is a Dutch center of expertise for the treatment of patients with thymomas. Thymomas are thymic epthilial tumors and the neurological auto-immune disorder myasthenia gravis (MG) is often found as a paraneoplastic syndrome. The aim of this study was to investigate the long-term oncological-, surgical-, and neurological outcomes of all patients who underwent a robotic thymectomy for a thymoma in the MUMC+.

Methods:
We retrospectively analyzed the clinic-pathological data of all consecutive patients with a thymoma who underwent robotic thymectomy, using the DaVinci Robotic System at the MUMC+ between April 2004 and December 2018. Because most of the patients were referred to the MUMC+ only for thymectomy, the follow-up data was requested in 60 referring Dutch hospitals. This study was approved by the ethical committee of the MUMC+ (METC number: 2018-0491 and amendment 2018-0491-A-9). Children and thymic carcinomas were excluded in this study.

Results:
In total, 398 robotic thymectomies were performed and 130 thymomas (32.7%) were found. Median follow-up time, procedure time and hospitalization were 46 months, 116 minutes and 3 days respectively. In 8.4% of the patients a conversion was performed and in 20.8% a complication was registered. MG was diagnosed before the thymectomy in 89 patients (68.5%). The majority of myasthenic patients with a thymoma went into remission, mostly within 12 to 24 months after thymectomy. No statistical difference was found in the amount of complications, conversions, incomplete resections or death between patients with myasthenia gravis versus non-myasthenic patients. Postoperative radiotherapy was performed in 36 patients (27.7%). The recurrence rate was 9.1%, and recurrences were predominantly found in patients with MG and in B2-thymomas. The five-year thymoma-related survival rate was 97.7% .

Conclusion:
Robotic thymectomy was found safe and feasible in early-stage thymomas and most advanced-stage thymomas. No significant differences were found in surgical- and oncological outcomes between patients with myasthenia gravis and non-myasthenic patients. A national guideline could contribute to the improvement of the oncological follow-up of thymic epithelial tumors in The Netherlands.

Breast-Related and Body-Related Quality of Life Following Autologous Breast Reconstruction is Superior to Implant-Based Breast Reconstruction - a Long-Term Follow-Up Study

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Department of Plastic Surgery

Introduction:
The better survival rates after breast cancer allow for setting of long-term goals, such as quality of life (QoL) and aesthetic outcomes following breast reconstruction. Studies find a higher breast-related QoL and greater satisfaction with breasts following autologous breast reconstruction (ABR) compared to implant-based breast reconstruction (IBBR). However, aesthetic results from donor sites can influence body image. This concern is little addressed in the literature. Therefore, the aim of this study was to compare the long-term breast-related and body-related QoL of women who underwent ABR to women who underwent IBBR.

Methods:
A multicenter, cross-sectional survey was conducted between November and December 2020 among women who underwent postmastectomy breast reconstruction between January 2015 and December 2018. A general questionnaire, the BREAST-Q, and the BODY-Q were used to collect data. Multivariable linear regression was performed to adjust differences in Q-scores for potential confounders.

Results:
In total, 336 patients were included (112 IBBR, 224 ABR). Autologous reconstruction resulted in significantly higher mean scores in all subdomains of the BREAST Q. On the BODY-Q, IBBR scored significantly higher on scars, while ABR scored moderately to significantly higher on all other scales. Despite a lower mean score on Hips & outer thighs in women with Lateral Thigh Perforator (LTP) flap reconstruction, no negative influence on body image was found in these women.

Conclusion:
Long-term breast and body-related outcomes of ABR are superior to IBBR. Donor site aesthetic does not adversely affect body image in women who underwent free flap breast reconstruction.

Serial markers of coagulation and inflammation and the occurrence of clinicalpulmonary thromboembolism inmechanically ventilated patients with SARS-CoV-2 infection; the prospective Maastricht intensive care COVID cohort

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Department of Intensive Care

Introduction:
The incidence of pulmonary thromboembolism is high in SARS-CoV-2 patients admitted to the Intensive Care. Elevated biomarkers of coagulation (fibrinogen and D-dimer) and inflammation (c-reactive protein (CRP) and ferritin) are associated with poor outcome in SARS-CoV-2. Whether the time-course of fibrinogen, D-dimer, CRP and ferritin is associated with the occurrence of pulmonary thromboembolism in SARS-CoV-2 patients is unknown. We hypothesise that patients on mechanical ventilation with SARS-CoV-2 infection and clinical pulmonary thromboembolism have lower concentrations of fibrinogen and higher D-dimer, CRP, and ferritin concentrations over time compared to patients without a clinical pulmonary thromboembolism.

Methods:
In a prospective study, fibrinogen, D-dimer, CRP and ferritin were measured daily. Clinical suspected pulmonary thromboembolism was either confirmed or excluded based on computed tomography pulmonary angiography (CTPA) or by transthoracic ultrasound (TTU) (i.e., right-sided cardiac thrombus). In addition, patients who received therapy with recombinant tissue plasminogen activator were included when clinical instability in suspected pulmonary thromboembolism did not allow CTPA. Serial data were analysed using a mixed-effects linear regression model, and models were adjusted for known risk factors (age, sex, APACHE-II score, body mass index), biomarkers of coagulation and inflammation, and anticoagulants.

Results:
Thirty-one patients were considered to suffer from pulmonary thromboembolism ((positive CTPA (n=27), TTU positive (n=1), therapy with recombinant tissue plasminogen activator (n=3)), and eight patients with negative CTPA were included. After adjustment for known risk factors and anticoagulants, patients with, compared to those without, clinical pulmonary thromboembolism had lower average fibrinogen concentration of -0.9 g/L (95% CI: -1.6 – -0.1) and lower average ferritin concentration of -1045 µg/L (95% CI: -1983 – -106) over time. D-dimer and CRP average concentration did not significantly differ, 561 µg/L (-6212 – 7334) and 27 mg/L (-32 – 86) respectively. Ferritin lost statistical significance, both in sensitivity analysis and after adjustment for fibrinogen and D-dimer.

Conclusion:
Lower average concentrations of fibrinogen over time were associated with the presence of clinical pulmonary thromboembolism in patients at the Intensive Care, whereas D-dimer, CRP and ferritin were not. Lower concentrations over time may indicate the consumption of fibrinogen related to thrombus formation in the pulmonary vessels.

Evaluating the longitudinal effect of colorectal surgery on health-related quality of life in patients with colorectal cancer

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Introduction:
Health-related quality of life (HRQoL) is negatively affected by colorectal cancer (CRC) and it is being compromised further by treatment modalities and associated adverse effects. The purpose of this study was to evaluate the impact of surgery for CRC on the course of HRQoL from baseline up to two years after diagnosis.

Methods:
In this prospective, population-based cohort study patients with newly diagnosed CRC were included between 2016 and 2019. Patients were recruited from four Dutch hospitals (i.e. Catharina Hospital in Eindhoven, Elisabeth-TweeSteden Hospital in Tilburg, Elkerliek Hospital in Helmond, and Máxima Medical Center in Veldhoven). HRQoL was assessed with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core module C30 over time both between and within subgroups of patients that underwent 1) right-sided colonic resection, 2) left-sided colonic resection, and 3) rectal resection using linear mixed model analyses. Longitudinal data is being collected on baseline (before start of treatment), four weeks postoperatively, and one and two years after diagnosis.

Results:
The study included 415 patients of whom 148 patients underwent right-sided colonic resection (36%), 147 left-sided colonic resection (35%), and 120 rectal resection (29%). Overall, HRQoL scores generally deteriorated after surgery but restored to approximately baseline level at one year after diagnosis in most of the domains. Impact of surgery seems to be more prominent in patients who underwent rectal resection, as they experienced more pain symptoms and worse role and social functioning at four weeks after surgery. Finally, among patients who underwent left-sided and rectal resection, physical functioning did not return to baseline level during follow-up.

Conclusion:
This study showed several differences (between-group and within-group) in HRQoL according to surgery type. The results of the current study enable clinicians in daily clinical practice to inform CRC surgical patients on the course of specific HRQoL domains up to two years after diagnosis. In addition to other clinical treatment outcomes (e.g. postoperative complications, survival), HRQoL should be discussed thoroughly on a routine basis and is to date perhaps somewhat underexposed in the consultation room.

Learning Curve of Sensory Nerve Coaptation in Autologous Breast Reconstruction - A Retrospective Cohort Study

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Department of Plastic Surgery

Introduction:
Microsurgical sensory nerve reconstruction in breast reconstructions using the body's own tissue involves connecting a nerve from the donor tissue to a nerve in the chest area. The procedure potentially enhances sensation in the reconstructed breast. It is unknown whether succes ratios increase along with the surgeon's experience with the technique - and thus, whether the procedure is subject to a learning curve. In this retrospective cohort study, we evaluated for four senior microsurgeons in our team whether - collectively and per surgeon - a relationship exists between the cumulative number of performed nerve reconstuctions and succes rates.

Methods:
We identified all consecutive sensory nerve coaptations performed by four reconstructive surgeons in deep inferior epigastric perforator (DIEP)- or lateral thigh perforator (LTP)-flap autologous breast reconstructions from March 2015 to August 2018 in the Maastricht University Medical Hospital. We excluded procedures of which operative reports were unavailable. 'Succes' was defined as a completed nerve reconstruction, still intact at the end of the operation. This surrogate for technical competence was plotted as a funtion of case number using multiple logistic regression analysis, resulting in specification of a learning curve for the procedure.

Results:
In the study period, 546 breast reconstructions using the body's own tissue were performed. In 250 cases (44.3%), a nerve reconstruction was completed; the succes ratio increased along with case number (OR 1.03; 95% CI 1.01-1.04; p=0.001). The total success ratio per surgeon varied considerably (43-91%). Variables negatively associated with the odds of a completed nerve reconstruction were patient BMI, rib resection, and intraoperative complications. These three factors are measures for the overall difficulty of the operation.

Conclusion:
The number of successful nerve reconstructions increased along with case number, which indicates presence of a learning effect. The negative association between the complicating factors BMI, rib resection, and intraoperative complications implies that during a technically challenging operation, nerve reconstruction degrades on the surgeon's priority list. Based on the data in our cohort, nerve reconstruction in breast reconstruction seems subject to a learning process. However, the odds of a successful nerve reconstruction seems to depend even stronger on the overall difficulty of the operation.

Chemosensory function in COPD patients

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Introduction:
Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease characterized by persistent airflow limitation. Malnutrition and muscle wasting are highly prevalent in COPD and even predict mortality in COPD patients, whilst optimizing nutritional status improves COPD outcomes. Although chemosensory function is an important determinant of nutritional, research into taste and smell function is limited in this population. In this observational pilot study, we aim to establish if COPD patients have impaired smell and taste (i.e. chemosensory) function.

Methods:
Based on power calculations (for a medium effect size and statistical power of 80%) we will include a total of 104 participants, 52 COPD patients and 52 age- and gender-matched controls. Currently, COPD patients, visiting the outpatient clinic of the MUMC+ (Maastricht), VieCuri (Venlo) hospital are recruited as participants and their partners as healthy controls. Participants complete our newly developed chemosensory questionnaire, investigating their perceived (subjective) taste and smell function, COPD status measured by COPD Assessment Test (CAT) and demographic characteristics.
During the study visit, we objectively evaluate smell function by performing a threshold and identification test with Sniffin' Sticks and taste function with a threshold test for the basic tastants, sweet, sour, salt and bitter, using Taste Strips. Lung function by means of spirometry is obtained in all participants.

Results:
Participants are currently being recruited and tested. The study is expected to be completed by September 2021. Nonetheless, preliminary results already suggest that smell, but not taste, function is impaired in COPD patients relative to healthy controls.

Conclusion:
Our preliminary data suggest that smell function seems to be impaired in COPD patients compared to controls, but this has yet to be confirmed in the complete dataset. COPD associated hyposmia may decrease patients' food enjoyment and thus further undermines adequate nutritional intake.

Bariatric surgery in youth: the perspective of Dutch pediatricians, parents and adolescents

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Introduction:
The worldwide prevalence of youth with severe obesity has increased substantially in the last decades. Recent studies have indicated that bariatric surgery is effective for the treatment of youth with severe obesity. However, the attitudes of pediatricians, parents and adolescents regarding this topic remains unclear. Therefore, the aim of this study was to assess the current thoughts and beliefs of Dutch pediatricians, parents and adolescents regarding bariatric surgery in youth.

Methods:
An online survey containing twenty questions on bariatric surgery in youth was distributed to pediatricians of the Dutch Society of Pediatrics. Parents and adolescents who participated in an interdisciplinary care program for overweight, obesity and severe obesity filled out an online survey of twelve questions during their follow-up visits regarding bariatric surgery in youth.

Results:
One hundred and twenty-one pediatricians, 49 parents and 19 adolescents completed the surveys. Seventy-two pediatricians (59.5%) considered bariatric surgery to be an effective treatment for youth with severe obesity when conventional treatment fails, and intent to refer patients for bariatric surgery. The most frequently suggested conditions for bariatric surgery were a minimum age of 16 years (n = 59, 48.7%), a BMI threshold of 40 kg/m2 (n = 51, 42.2%), and a minimum Tanner stage of IV (n = 59, 48.8%).
Thirty parents (61.2%) and fourteen adolescents (73.7%) responded that bariatric surgery should become available for youth with severe obesity.

Conclusion:
Dutch pediatricians, parents and adolescents increasingly accept bariatric surgery as a treatment modality in youth with severe obesity who do not respond successfully to lifestyle intervention.
Whether pediatricians will actually refer for bariatric surgery remains to be seen when this treatment option will be implemented in the Netherlands.

Artificial intelligence in (gastroenterology) healthcare – Doctors' and patients' perspective (interim analysis)

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Department of Gastroenterology

Introduction:
Artificial intelligence (AI) is the ability to solve complex problems with help of computers and algorithms. For instance, in image-based procedures widely used in medicine, pattern recognition is used by automatically extracting relevant imaging features. AI is rapidly becoming integrated and used in medical fields to improve healthcare. Aim of this study was to investigate the knowledge and opinion of gastroenterologists and patients with gastrointestinal diseases on the use of AI in healthcare.

Methods:
We conducted a prospective survey study among gastroenterologists and gastroenterology fellows working in Dutch hospitals, and among gastroenterology patients at the Maastricht University Medical Center and Catharina Hospital Eindhoven, the Netherlands, from April 2020 to June 2021.

Results:
In this interim analysis, 80 gastroenterologists and 246 patients participated. 68.8% (n = 55) of doctors used medical applications (apps) in their current clinical practice. 94.2% (n = 228) of patients were familiar with device use (a.o. computers and smartphones), compared to 43.9% (n = 101) for medical device use. On a 5-point Likert-scare, patients preferred their doctors to use AI (3.8 [SD 1.0]) and doctors were willing to use AI for their patients (4.4 [SD 0.7]). Both doctors and patients do believe that the quality of care will increase with the aid of AI, but doctors are more convinced (81.3%) than patients (64.5%, P=0.02). The expectation of doctors is that AI will have a place in healthcare within 5.2 years (range 1-15, SD 3.0), patients expect this within 5.9 years (range 0-25, SD 4.5, P=0.17). Doctors and patients agreed on the most important advantages of AI in healthcare: improving quality of care (90.0% doctors vs. 66.7% patients), time saving (55.0% doctors vs. 39.6% patients), and faster diagnostics and shorter waiting times (51.2% doctors vs. 66.7% patients). The most important disadvantage for doctors was insufficiently developed IT infrastructures (56.3%), were this was the potential loss of personal contact with healthcare professionals for patients (70.9%).

Conclusion:
Generally, gastroenterologists and patients are positive towards AI. For optimal application of AI in healthcare, trust of doctors and patients in AI has to be further built, making qualitative research and validation of AI highly important.

Field-testing a patient decision aid for patients with superficial basal cell carcinoma

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Introduction:
Treatment options for superficial basal cell carcinoma (sBCC) are surgical excision, imiquimod cream, 5-fluorouracil cream, and photodynamic therapy. These treatments all have an acceptable efficacy but differ in aspects like cosmetic outcome, practical issues, and side-effects. The treatment decision is thus preference-sensitive. To aid patients and physicians in (shared) decision making, we developed and field-tested a patient decision aid (PDA). We hypothesized that patients that use the PDA will have decreased decisional conflict, more knowledge of diagnosis and treatment options and are happier with their decision post-treatment.

Methods:
A prospective multicentre pre- and post-implementation study was performed amongst patients with a newly diagnosed sBCC. The pre-implementation group did not use the PDA, the post-implementation group did. The primary outcome was decisional conflict measured on the decisional conflict scale (DCS) (before and 3 months post-treatment) in total and on subscales of 'uncertainty', 'informed decision', and 'contributing factors'. A score over 25 meant high decisional conflict. Knowledge of disease and treatment options was tested with a knowledge questionnaire. Median scores on the decisional conflict scale were compared between groups using the Mann-Whittney-U test. Descriptive statistics were used for the other outcomes.

Results:
276 patients were included between july 2018 and January 2021. The overall median score of the pre-implementation group on the DCS was 19.5 versus 16.4 post-implementation (p=0.603). On the subscale 'contributing factors' patients felt significantly more supported in their decision after using the PDA (25 pre- and 8.3 post-implementation, p=0.001). On the subscale of 'informed decision', decisional conflict seemed increased in the post-implementation group (8.3 vs. 16.7, p=0.271). Knowledge did not differ between the two groups. 71.6% of patients felt the PDA had added value and 86% would recommend using the PDA to family and friends.

Conclusion:
Since the decisional conflict for the treatment decision of sBCC was already low in the pre-implementation group, there was little room for improvement. Still, patients that used the PDA felt more supported in their decision and were mostly of the opinion that the PDA had added value. We conclude that a PDA for sBCC can contribute to a personalized decision in a selected group of patients.

The effects of verapamil, hydralazine and doxazosin on renin, aldosterone and the ratio thereof

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Introduction:
Hydralazine, alpha-blockers such as doxazosin and verapamil are currently recommended by the Endocrine Society as acceptable bridging antihypertensives for those in whom full cessation of antihypertensive medication is infeasible but nonetheless require screening for Primary Aldosteronism. This is under the assumption that these drugs cause minimal to no effect on the aldosterone-to-renin ratio, the most widely used screening test for Primary Aldosteronism. However, scant evidence is available regarding their effects on said ratio.

Methods:
In the present study, therefore, we assessed the change in aldosterone, renin and aldosterone-to-renin ratio values in otherwise healthy essential hypertensive participants before and after hydralazine (n=26), doxazosin (n=20) and verapamil (n=15) treatment. All samples were taken under highly standardised conditions.

Results:
Hydralazine resulted in a borderline significant rise in active plasma renin concentration (19 vs 25, p=0.067) and a significant fall in the aldosterone-to-renin ratio (38 vs 24, p=0.017). Doxazosin caused declines in both plasma aldosterone concentration (470 vs 330, p=0.028) and the aldosterone-to-renin ratio (30 vs 20, p=0.020). Our data show that verapamil did not significantly affect any of our outcome variables.

Conclusion:
Based on our findings, we conclude that the assumption that these drugs can be used with little consequence to the aldosterone-to-renin is false. While it is possible that they are indeed the best option when full antihypertensive cessation is infeasible, the potential effects of these drugs must still be taken into account when interpreting the aldosterone-to-renin ratio.

Are you prepared?

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Department of Internal Medicine

Introduction:
That young doctors experience stress and burn out is an increasingly big problem. One of the issues that contribute to this stress is working in the Emergency Department (ED) during shifts. Young doctors "should just do it", because "with others it went well too". Little is known about how well prepared the doctors really feel before doing their first shifts, how much stress these shifts cause, and what it takes to better prepare doctors for their first shifts.

Methods:
The data was collected through an anonymous internet survey among doctors containing questions about how well prepared doctors felt for their first shifts. We asked how well prepared they felt before and how much stress they experienced during their first shifts. In addition, we asked how well prepared they felt with regard to 6 different domains: Responsibility, Leadership in the acute setting, Care for critically ill patients, Physician distress (e.g. workload), Emotional stress (e.g. sleep deprivation) and Logistics. Last, we asked after how many weeks they had their first shift and whether they had an training in the ABCDE methodology before their shifts.

Results:
A total of 301 doctors from different specialties responded to the survey. In total, 11.7% felt sufficiently prepared for their shifts. With regard to the following domains many doctors felt unprepared: Leadership (45.5%), Physician distress (39.9%) and Care for critically ill patients (38.1%). The mean stress level before the first shift was 6.9 on a scale from 1 to 10. Last, 31.9% of the respondents had their first shift within four weeks of starting their first job as a doctor. Doctors who started the shifts earlier (<6 weeks) felt significantly (58.3 % vs 27.8%, $p<0.001$) less often prepared than physicians who start the shifts later.
Physicians who had not followed a training in the ABCDE methodology felt significantly less often prepared (45.0% vs 23.8%, $p= 0.005$) than those who did.

Conclusion:
Doctors are not well enough prepared for their shifts. Let’s prepare them better: don’t schedule them too soon and train them.

Mass Spectrometry Imaging Provides Novel Insights into the Complex Pathways Underlying Intestinal Anastomotic Healing in Rats

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Department of Surgery

Introduction:
The creation of an intestinal anastomosis is one of the most commonly performed procedures in colorectal surgery. Despite advancements in surgical technique and perioperative care, intestinal anastomoses have a 10-15% risk of leakage, causing severe morbidity, and even mortality. The lack of a thorough understanding of the pathways underlying anastomotic healing (AH) has most likely led to the inability to reduce the incidence of anastomotic leakage (AL) thus far. Most conventional techniques struggle to deal with the complexity of AH and provide no spatial information about the involved pathways. To enable a sustainable reduction of the AL incidence, we aimed to elucidate these pathways in an animal model of AH using the novel label-free molecular imaging technique: mass spectrometry imaging (MSI).

Methods:
28 Wistar rats underwent colonic transsection and primary anastomosis. After surgery, groups of 4 rats each were sacrificed on 7 consecutive time-points (6, 12, 24, 48, 72, 120, and 168 hours). The harvested intestinal anastomotic tissue sections were analyzed by matrix-assisted laser desorption/ionization (MALDI)-MSI. Molecular identification was verified by tandem MS. Subsequently, the same tissue sections were histopathologically stained, evaluated, and scored by an experienced animal pathologist. Histological scores were correlated to the MSI data.

Results:
Preliminary results showed that MALDI-MSI was capable of discriminating mucosal, submucosal, and muscular intestinal layers by differential expression of characteristic lipids throughout these layers. Lipid profiles of all intestinal layers evoluated over time and showed the greatest changes in lipid expression around 24-48 hours, dividing the first 7 days of AH in three distinctive phases. These findings correlated to the scored histopathological changes. Ongoing tandem MS analysis will verify the identified characteristic lipids. Placing these lipids in known lipid interaction networks will help to reconstruct the biochemical processes involved in AH.

Conclusion:
The lipid composition of the different histological layers of the intestine is highly distinct and fluctuates over time in an animal model of intestinal AH, stressing the importance of spatiotemporal context when studying the complex processes underlying AH. Additionally, this study highlights the significant potential of MSI to enable comprehensive studies into AH, bringing us one step closer to the prevention of AL

Semi-arts categorie

Predicting Non-Responsiveness to Iron Therapy in Anaemic Children with Inflammatory Bowel Disease

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Department of Paediatrics

Introduction:
A considerable proportion of patients with inflammatory bowel disease (IBD) fail to respond to iron therapy, but it remains difficult to identify non-responders at baseline with currently used iron indicators. The identification of iron therapy (non)responsiveness in the IBD population is relevant since ineffective therapy leads to delay in treatment and unnecessary exposure to iron. We evaluated commonly used iron indicators (ferritin and transferrin saturation [TSAT]) and emerging biomarkers (soluble transferrin receptor [sTfR] and hepcidin levels) at baseline to predict non-responsiveness to iron therapy.

Methods:
We performed a prospective multi-centre cohort study among paediatric patients with IBD and anaemia. We assessed iron indicators, sTfR, and hepcidin at baseline and again one month after the initiation of oral or intravenous iron therapy. Haemoglobin (Hb) z-scores (difference to mean expressed in standard deviations [SD]) were calculated correcting for age and gender according to international guidelines. The primary outcome was based on the change of Hb z-score (one month after treatment vs. baseline) divided by baseline SD, where non-responsiveness was defined as a standardised change score of less than 1. Baseline values of ferritin and TSAT were used to construct a basic logistic regression model. Hepcidin, sTfR, or both (respectively models [M] 1, 2, and 3) were then added to the basic prediction model.

Results:
Of 40 anaemic IBD patients (mean age 14.1 years; mean Hb z-score -3.1), sixteen (40%) were non-responsive to iron therapy after one month. The basic prediction model yielded an area under the curve (AUC) of 0.69 (95% Confidence Interval [CI] 0.52-0.85). Adding sTfR, hepcidin or both to the model increased the AUC to 0.78 (95% CI 0.63-0.93) (M1), 0.82 (95% CI 0.68-0.96) (M2), and 0.90 (95% CI 0.80-0.99) (M3), respectively. For model 3, sensitivity and specificity at the optimal cut-off value were 94% and 71%, respectively, with a positive predictive value of 68%.

Conclusion:
A diagnostic strategy that involves baseline ferritin, transferrin saturation, sTfR, and hepcidin correctly predicts non-responsiveness to iron therapy in 68% of cases. As a result, clinicians may personalise iron therapy in pediatric IBD patients preventing toxicity.

Semi-arts categorie

Identification of pathogenic bacteria during abdominal sepsis using exhaled breath analysis.

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Introduction:
Sepsis is a life-threatening condition and early diagnosis is often difficult. Identifying the causative bacteria can take several days. Early diagnosis is important for a life-saving treatment. Volatile organic components (VOCs) in exhaled breath might be a non-invasive and rapid diagnostic tool. The main objective of this animal experiment is to examine whether VOCs in exhaled breath can be used to diagnose an early stage of abdominal sepsis. The second aim is to define bacteria specific VOC profiles.

Methods:
Abdominal sepsis was induced in male C57BL/6 mice (aged 8-10 weeks) by an intraperitoneal injection with 200uL of 10^8 CFUs/ml Escherichiae coli (n=20) or 10^9 CFUs/ml Enterococcus faecalis (n=20). Breath was collected by a custom-made sampling device prior to sepsis induction, 1, 3, 6 hours thereafter and at the end. VOCs were stored on stainless steel desorption tubes (1TD/Carbopack X) and analyzed by gas chromatography time-of-flight mass spectrometry (GC-tof-MS). Analysis was performed by a Random Forest technique and visualized by means of Principal Coordinate Analysis (PCoA). IL-6 was determined in plasma at 6 hours after sepsis and at the end of the experiment using Luminex.

Results:
Analysis shows changes in VOC profiles even before mice showed clinical symptoms. Thirty VOCs were identified for the development of sepsis over time induced by E. Coli and 42 VOCs for E. Faecalis. In both groups the IL-6 concentration increased up to 34932 pg/ml for E. Coli and 36467 pg/ml for E. Faecalis, indicating an active sepsis. After 6 hours the concentration decreased again. Moreover, based on 50 VOCs, distinction of sepsis induced by E. Coli or E. Faecalis is possible.

Conclusion:
This study shows the possibility to detect changes in VOCs in exhaled breath during the development of an abdominal sepsis, and the possibility to discriminate Escherichiae coli and Enterococcus faecalis. This is a step towards clinical research so VOCs can be implemented as a non-invasive and rapid diagnostic tool for human diseases in the future.

Semi-arts categorie

Vestibular Assessment in Children with Sensorineural Hearing Loss

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Introduction:
30-70% of children with sensorineural hearing loss (SNHL) demonstrate a vestibular hypofunction (VH) due to the anatomical proximity of the cochlea and vestibular system. Even children with unilateral SNHL are at risk of bilateral VH. Vestibular assessment in children with SNHL is not standard yet, but critical for early vestibular rehabilitation therapy to promote (motor) development and to locate the optimal side for cochlear implantation. The aim was to assess vestibular function, evaluate the vestibular tests available and provide a clinical recommendation for this population.

Methods:
The retrospective single-center preliminary study included 45 children (90 ears) with SNHL aged 0-18 years. Video head impulse test (vHIT), cervical evoked myogenic potentials (cVEMP), rotary chair test and caloric test were applied to test vestibular function. At least two vestibular tests were performed per patient. VH was diagnosed based on expert opinion, combining vestibular test results and clinical presentation, due to the lack for a golden standard.

Results:
The cohort with mean age 4.92 (SD 3.76) showed SNHL with mean hearing loss of 69 dB. VH was clinically diagnosed in 33%, of which 8 participants diagnosed with bilateral VH and 7 with unilateral VH. Diagnostic accuracy was found to be 93% for caloric test, 91% for vHIT, 79% for cVEMP, and 75-79% for rotary chair (depending on method). When combining multiple tests, optimal diagnostic accuracy was achieved with cVEMP and vHIT (94%).

Conclusion:
The clinical recommendation based on this preliminary study is to implement vHIT and cVEMP as a first assessment in children with unilateral and bilateral SNHL. These tests can non-invasively assess vestibular function of the horizontal semicircular canals and saccule respectively. In the future, cochlear implantation could be combined with vestibular implantation (under development) in children with both SNHL and VH.

Semi-arts categorie

The long term follow-up of micro-nutritional status in children with celiac disease

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Introduction:
Celiac disease (CD) is a chronic, autoimmune-mediated enteropathy that is triggered by dietary gluten in genetically susceptible individuals. If untreated, micro-nutritional deficiencies due to malabsorption can lead to clinical complications. Following a lifelong gluten free diet (GFD) is the only available treatment to manage CD, however the GFD itself can also be a risk factor for the development of micro-nutritional deficiencies due to incompleteness of nutrients. Evidence on the necessity of following up nutrient levels in children with CD is scarce and standardized evidence-based protocols are lacking. Specifically, there is little information about the occurrence and duration of nutrient deficiencies during the long-term follow-up of children with CD.

Methods:
This retrospective chart review included 130 children (age 0-18 years) that visited the MUMC+. All children were diagnosed with CD according to the ESPGHAN (European Society for Pediatric Gastroenterology, Hepatology and Nutrition) guidelines. They have been subjected to treatment and follow-up of CD, including a GFD as well as annual serologic tests.
This study aims to investigate whether routinely monitoring micro-nutritional deficiencies during the long-term follow-up of paediatric CD is clinically relevant. The frequency of micronutrient deficiencies and their possible prediction factors were investigated. The study focussed on newly developed deficiencies after normalization of serological micro-nutritional levels after starting a GFD. For statistical analysis, descriptive statistics and unpaired t-tests were used.

Results:
Deficiencies of vitamin B6 and calcium were not observed in children at any time-point during follow-up. Of all patients with available long-term follow-up measurements with a range of 3-16 years of follow-up, deficiencies of iron, ferritin, vitamin D, vitamin B12, folate and zinc were observed in 18/52, 11/52, 17/44, 3/65, 8/60, 4/43 children, respectively.

Conclusion:
Based on the results, this study showed that deficiencies during the long-term follow-up are frequent for iron and vitamin D. Therefore, long-term follow-up of these nutrients, seems to be clinically relevant to avoid clinical consequences during a child's growth. Additionally, children with CD following a GFD have a very low chance to develop deficiencies of vitamin B6 and calcium during follow-up. Therefore, the clinical value of following-up these micro-nutrients is still debatable

Semi-arts categorie

Added value of OCT for diagnosing recurrent BCC after non-invasive treatment

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Department of Dermatology

Introduction:
The development of non-invasive treatments for superficial basal cell carcinoma (sBCC) enhanced the need for non-invasive diagnostics and monitoring, such as optical coherence tomography (OCT). This need is enhanced because biopsies may be painful and have a small risk of bleeding, scarring and infection.

Methods:
This explorative cohort study included patients who received topical treatment with imiquimod, 5-fluorouracil or photodynamic therapy for sBCC, within 2 years post treatment. Clinical and dermoscopic evaluation (CDE) as well as OCT were used to evaluate suspicion for recurrent basal cell carcinoma (BCC). Primary objective was to evaluate whether adjunct use of OCT increased the detection rate of recurrent BCC. Diagnostic accuracy for CDE and OCT were calculated and displayed as areas under the curve (AUC). OCT images were evaluated by two investigators with varying experience (FA = expert, TW = novice) Furthermore, we examined whether OCT could correctly predict BCC subtypes.

Results:
In this study 6 out of 29 patients underwent a biopsy. 4 out of 6 patients had a recurrent BCC. CDE correctly predicted 2, and missed 2 recurrences (AUC=0.750). FA correctly predicted all 4 recurrences (AUC=1.000). TW correctly predicted 3, and missed 1 recurrence (AUC=0.875). Differences in AUC were not statistically significant.

Conclusion:
Addition of OCT to DCE raised the AUC from 0.750 to 1.000 (p=0.083) when interpreted by an OCT expert. No unnecessary biopsies were obtained due to incorrect OCT diagnosis. The researchers correctly predicted BCC subtype for all 4 histologically confirmed subtypes. Due to the low number of biopsies, these numbers should be interpreted with caution. OCT correctly predicted 2 subclinical recurrences indicating that additional use of OCT may be of interest for diagnosing recurrent BCC after non-invasive treatment of sBCC in the future. This study will be extended to increase the number of participants.

Semi-arts categorie

Better COVID-19 survival in females, independent of age, disease severity, comorbidities, and treatment

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Department of Intensive Care

Introduction:
It is unknown whether better survival rates in female Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) patients compared to male patients can be explained by differences in age, disease severity, comorbidities, risk factors, or anti-infection/inflammatory therapy administration. Therefore, we investigated the association between sex and Intensive Care Unit (ICU) survival, weighing these variables.

Methods:
In this multicentre observational cohort study, all patients with SARS-CoV-2 pneumonia admitted to seven ICUs in the Euregio Meuse-Rhine, one region across Belgium, the Netherlands and Germany, and requiring vital organ support during the first pandemic wave were included. With a random intercept for a centre, mixed-effects logistic regression was used to investigate the association between sex and ICU survival. Models were adjusted for age, APACHE II score, comorbidities, and anti-infection/inflammatory therapy. Interaction terms were added to the models to investigate effect modification by country.

Results:
A total of 551 patients (29% were females) were included. Mean age was 65.4 ± 11.2 years. Females were more often obese and smoked less frequently than males (p-value <0.001 and 0.042, respectively). APACHE II scores of females and males were comparable. Overall, ICU mortality was 12% lower in females than males (27% vs 39% respectively, p-value <0.01) with an odds ratio (OR) of 0.62 (95%CI 0.39-0.96) after adjustment for age and APACHE II score, 0.63 (95%CI 0.40-0.99, p-value 0.044) after additional adjustment for comorbidities, and 0.63 (95%CI 0.39-0.99, p-value 0.047) after adjustment for anti-infection/inflammatory therapy. No effect modification by country was found (p-values for interaction >0.23).

Conclusion:
ICU survival in female SARS-CoV-2 patients was higher than in male patients, independent of age, disease severity, smoking, obesity, comorbidities, anti-infection/inflammatory therapy, and country. Sex-specific biological mechanisms may play a role, emphasising the need to address diversity, such as more sex-specific prediction, prognostic, and therapeutic approach strategies.

Semi-arts categorie

Predicting primary tumour response to neoadjuvant systemic therapy in breast cancer patients using PET/MRI.

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Department of Surgery

Introduction:
This study aims to explore whether hybrid 18F-FDG PET /MRI can accurately predict pathological response of the primary tumor to neoadjuvant systemic therapy (NST) in breast cancer patients. Accurately detecting response could result in an optimal systemic treatment and could select patients for minimal invasive surgery.

Methods:
This single centre study included 33 female patients between February 2015 and January 2016. Patients were diagnosed with histopathologically proven invasive breast cancer and were considered candidates for neoadjuvant systemic therapy. All patients were subjected to a dedicated breast 18F-FDG PET/MRI before, during and after NST. A total of 99 scans were achieved. PET and MR images were reviewed by a nuclear medicine physician and a radiologist, respectively, dedicated to breast cancer. Tumor size, maximum standardized uptake values (SUVmax), and mean apparant diffusion coefficient (ADC) were measured on each scan and their relative change was calculated. The diagnostic performance of each parameter to predict pCR was assessed. Patient and tumour characteristics were compared between response groups using logistic regression analysis.

Results:
Of the 33 patients, 12 (36.4%) patients achieved pCR. There was a statistically significant difference between the tumour subtypes (p-value 0.009) of which HER2 positive patients had a 13.3 times higher chance to achieve pCR. The hybrid parameter SUVmax divided by ADC measured on the second PET/MRI halfway through NST showed the highest diagnostic potential to predict pCR with a sensitivity, specificity, and AUC of 91.7%, 52.4%, and 0.700. SUVmax on the second as well as tumour size on the third PET/MRI yielded AUCs of 0.627 and 0.672, respectively. The ROC curves of the parameters were not statistically significant.

Conclusion:
The PET/MRI shows to be a promising technique in predicting pCR of the primary tumour after neoadjuvant systemic therapy and has the potential to improve sensitivity and specificity by combining PET and MRI parameters. Therefore, it can be used to optimize the neoadjuvant systemic therapy and determine minimal invasive surgery.

Semi-arts categorie

Stereo-Electroencephalography-Guided Radiofrequency Thermocoagulation Affects Brain Network Connectivity in Epilepsy Patients

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Department of Neurology

Introduction:
Stereo-electroencephalography (SEEG) is an invasive diagnostic method to identify the epileptogenic zone (EZ) and network in drug-resistant epilepsy. In selected patients, SEEG-guided radiofrequency thermocoagulation (RFTC) can be employed therapeutically by lesioning of the EZ. Little is known on the effect of focal RFTC on distant large-scale brain network connectivity. This study investigates whether brain responses to repetitive electrical stimulation are affected by RFTC.

Methods:
Patients who underwent SEEG-guided RFTC and 1Hz bipolar repetitive electrical stimulation for 30s before and immediately after RFTC were retrospectively selected. Stimulations were performed on selected electrode channels deemed clinically relevant.
Measure of effective brain connectivity was expressed as root-mean-square (RMS) of the cortico-cortical evoked potentials (CCEPs) following stimulation. RMS was calculated in the 15-300ms interval after stimulation. Pre-stimulus period -200- -15ms was used for baseline correction. RMS was compared across all non-artifactual channels before and after RFTC using a T-test (Bonferroni corrected $P<0.05$). As stimulation amplitude (range: 4-10mA) was kept identical, changes in RMS were attributed to RFTC. Electrode contact pairs were categorized as C=coagulated-coagulated, H=coagulated and non-coagulated or N=both non-coagulated. The data was divided in nine categories based on the stimulating and recording contact pair combinations (C-C, C-H, C-N, H-C etc.). Number of CCEPs with significant changes in RMS was compared to the total number of analyzed CCEPs, per category and per patient.

Results:
Ten patients fulfilled the inclusion criteria. A median of 8 (range 4-16) electrodes, comprising 109 (54-191) contact points, were implanted. On average, 8 (range 3-33) contact points per patient were coagulated. A median of 4 (0-13) C, 1 (0-3) H and 18 (3-44) N stimulated contact pairs per patient could be analyzed following artifact removal (260/295 (88%) unique stimulations).
The percentage of significant CCEP changes ranged from 82.1% in H-C to 23.7% in N-N. RFTC can induce both significant in- and decreases in CCEP RMS.

Conclusion:
Our findings show that RFTC can influence connectivity between the coagulated site and remote regions. Interestingly, focal RFTC affects interactions between non-coagulated brain sites distant from the coagulated lesion(s). Our study adds new insights about the influence of a focal ablative procedure on large-scale brain network communication.

Semi-arts categorie

Added value of OCT for diagnosing recurrent BCC after non-invasive treatment

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Department of Dermatology

Introduction:
The development of non-invasive treatments for superficial basal cell carcinoma (sBCC) enhanced the need for non-invasive diagnostics and monitoring, such as optical coherence tomography (OCT). This need is enhanced because biopsies may be painful and have a small risk of bleeding, scarring and infection.

Methods:
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