

Wetenschappelijke PUBLICATIES

Communicatie artsen | 2015



Geachte collega,

Hierbij stellen wij u de vierde uitgave voor van de bundeling van alle peer-reviewed abstracts van ZOL-artsen gepubliceerd in 2015.

2015 was opnieuw een druk jaar met heel wat realisaties, zo blijkt uit deze uitgebreide lijst van artikels. We zijn bijzonder trots op het wetenschappelijk werk dat onze artsen verrichten in het ziekenhuis.

We zijn tevens erg verheugd met de mogelijkheden die het Limburg Clinical Research Program - een samenwerkingsinitiatief tussen Universiteit Hasselt, ZOL en Jessa Ziekenhuis - ons biedt om onze wetenschappelijke kennis verder uit te bouwen en om te zetten in innovatieve, wetenschappelijk ondersteunde, patiëntenzorg. Innovatie is immers van cruciaal belang om kwalitatieve zorg te garanderen voor al onze patiënten. Nu en in de toekomst.

Wij wensen u veel leesplezier!

Dr. Griet Vander Velpen
Medisch directeur

INHOUDSTAFEL

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DIVISIE 1 (MOEDER - KIND - PLASTISCHE HEELKUNDE)

Int J Colorectal Dis. 2015 Jan;30(1):51-6.

The course of anaemia in children and adolescents with Crohn's disease included in a prospective registry.

Van Biervliet S, Smets F, Hofmann I, Degreef E, Hauser B, Bontems P, Vande Velde S, Arts W, Paquot I, Alliet P, Bossuyt P, Louis E, Baert F, Bauraind O, Rahier JF, Veereman G.

Abstract

AIM: The aim of this study is to determine the prevalence and evolution of anaemia in prospectively followed children and adolescents diagnosed with Crohn's disease (CD).

METHODS: The BELCRO registry (inclusion May 2008-April 2010), describing current clinical treatment practice of children diagnosed with CD, provided data on age, height, body mass index (BMI), paediatric Crohn's disease activity index (PCDAI), therapy and haemoglobin (Hb) at diagnosis 12 and 24 months follow-up. Anaemia was defined as Hb < -2 sd, while severe anaemia was defined as Hb < -4 sd. Patients were classified as child ≤13 and adolescent >13 years of age.

RESULT: Ninety-six were included, 13 dropped out due to insufficient Hb data (37 females/46 males; median age 13.3 years, range 2.2-17.8 years). At diagnosis, the median Hb sd was -2.66 (-8.4; 1.07) and was correlated with the PCDAI (p=0.013). At diagnosis, 51/83 (61%) were anaemic and all had active disease. Hb z-score significantly improved (p<0.0001) but 26/68 (38%) remained anaemic at 12 months and 29/76 (38%) at 24 months of follow-up. The correlation to the PCDAI disappeared. At 24 months, children were more likely to be anaemic. There was no difference in iron dose nor duration of iron supplements between children and adolescents. Iron treatment was more readily given to patients presenting with anaemia. Hb did not differ between patients with (n=28) or without iron supplements. Half of the patients with persisting anaemia were given iron supplements, of which, only three were given intravenously.

CONCLUSION: Anaemia remains an important extra-intestinal manifestation of CD in children. Physicians, lacking optimal treatment strategies, undertreat their patients.

Hum Reprod. 2015 May;30(5):1046-58.

The comprehensiveness of the ESHRE/ESGE classification of female genital tract congenital anomalies: a systematic review of cases not classified by the AFS system.

Di Spiezio Sardo A, Campo R, Gordts S, Spinelli M, Cosimato C, Tanos V, Brucker S, Li TC, Gergolet M, De Angelis C, Gianaroli L, Grimbizis G.

Abstract

STUDY QUESTION: How comprehensive is the recently published European Society of Human Reproduction and Embryology (ESHRE)/European Society for Gynaecological Endoscopy (ESGE) classification system of female genital anomalies?

SUMMARY ANSWER: The ESHRE/ESGE classification provides a comprehensive description and categorization of almost all of the currently known anomalies that could not be classified properly with the American Fertility Society (AFS) system.

WHAT IS KNOWN ALREADY: Until now, the more accepted classification system, namely that of the AFS, is associated with serious limitations in effective categorization of female genital anomalies. Many cases published in the literature could not be properly classified using the AFS system, yet a clear and accurate classification is a prerequisite for treatment.

STUDY DESIGN, SIZE AND DURATION: The CONUTA (CONgenital UTerine Anomalies) ESHRE/ESGE group conducted a systematic review of the literature to examine if those types of anomalies that could not be properly classified with the AFS system could be effectively classified with the use of the new ESHRE/ESGE system. An electronic literature search through Medline, Embase and Cochrane library was carried out from January 1988 to January 2014. Three participants independently screened, selected articles of potential interest and finally extracted data from all the included studies. Any disagreement was discussed and resolved after consultation with a fourth reviewer and the results were assessed independently and approved by all members of the CONUTA group.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Among the 143 articles as-

sessed in detail, 120 were finally selected reporting 140 cases that could not properly fit into a specific class of the AFS system. Those 140 cases were clustered in 39 different types of anomalies.

MAIN RESULTS AND THE ROLE OF CHANCE: The congenital anomaly involved a single organ in 12 (30.8%) out of the 39 types of anomalies, while multiple organs and/or segments of Müllerian ducts (complex anomaly) were involved in 27 (69.2%) types. Uterus was the organ most frequently involved (30/39: 76.9%), followed by cervix (26/39: 66.7%) and vagina (23/39: 59%). In all 39 types, the ESHRE/ESGE classification system provided a comprehensive description of each single or complex anomaly. A precise categorization was reached in 38 out of 39 types studied. Only one case of a bizarre uterine anomaly, with no clear embryological defect, could not be categorized and thus was placed in Class 6 (un-classified) of the ESHRE/ESGE system.

LIMITATIONS, REASONS FOR CAUTION: The review of the literature was thorough but we cannot rule out the possibility that other defects exist which will also require testing in the new ESHRE/ESGE system. These anomalies, however, must be rare.

WIDER IMPLICATIONS OF THE FINDINGS: The comprehensiveness of the ESHRE/ESGE classification adds objective scientific validity to its use. This may, therefore, promote its further dissemination and acceptance, which will have a positive outcome in clinical care and research.

Gynecol Surg. 2015;12(1):3-15.

Options on fibroid morcellation: a literature review.

Brölmann H, Tanos V, Grimbizis G, Ind T, Philips K, van den Bosch T, Sawalhe S, van den Haak L, Jansen FW, Pijnenborg J, Taran FA, Brucker S, Wattiez A, Campo R, O'Donovan P, de Wilde RL; European Society of Gynaecological Endoscopy (ESGE) steering committee on fibroid morcellation.

Abstract

In laparoscopy, specimens have to be removed from the abdominal cavity. If the trocar opening or the vaginal outlet is insufficient to pass the specimen, the specimen needs to be reduced. The pow-

er morcellator is an instrument with a fast rotating cylindrical knife which aims to divide the tissue into smaller pieces or fragments. The Food and Drug Administration (FDA) issued a press release in April 2014 that discouraged the use of these power morcellators. This article has the objective to review the literature related to complications by power morcellation of uterine fibroids in laparoscopy and offer recommendations to laparoscopic surgeons in gynaecology. This project was initiated by the executive board of the European Society of Gynaecological Endoscopy. A steering committee on fibroid morcellation was installed and experienced ESGE members requested to chair an action group to address distinct clinical questions. Clinical questions were formulated with regards to the sarcoma risk in presumed uterine fibroids, diagnosis of sarcoma, complications of morcellation and future research. A literature review on the different subjects was conducted, systematic if appropriate and feasible. It was concluded that the true prevalence of uterine sarcoma in presumed fibroids is not known given the wide range of prevalences (0.45-0.014 %) from meta-analyses mainly based on retrospective trials. Age and certain imaging characteristics such as 'lacunes' suggesting necrosis and increased central vascularisation of the tumour are associated with a higher risk of uterine sarcoma, although the risks remain low. There is not enough evidence to estimate this risk in individual patients. Complications of morcellation are rare. Reported are direct morcellation injuries to vessels and bowel, the development of so-called parasitic fibroids requiring reintervention and the spread of sarcoma cells in the abdominal cavity, which may possibly or even likely upstaging the disease. Momentarily in-bag morcellation is investigated as it may possibly prevent morcellation complications. Because of lack of evidence, this literature review cannot give strong recommendations but offers only options which are condensed in a flow chart. Prospective data collection may clarify the issue on sarcoma risk in presumed fibroids and technology to extract tissue laparoscopically from the abdominal cavity should be perfected.

Facts Views Vis Obgyn. 2015;7(3):153-60.

The European Academy laparoscopic "Suturing Training and Testing" (SUTT) significantly improves surgeons' performance.

Sleiman Z, Tanos V, Van Belle Y, Carvalho JL, [Campo R](#).

Abstract

The efficiency of suturing training and testing (SUTT) model by laparoscopy was evaluated, measuring the suturing skill acquisition of trainee gynecologists at the beginning and at the end of a teaching course. During a workshop organized by the European Academy of Gynecological Surgery (EAGS), 25 participants with three different experience levels in laparoscopy (minor, intermediate and major) performed the 4 exercises of the SUTT model (Ex 1: both hands stitching and continuous suturing, Ex 2: right hand stitching and intracorporeal knotting, Ex 3: left hand stitching and intracorporeal knotting, Ex 4: dominant hand stitching, tissue approximation and intracorporeal knotting). The time needed to perform the exercises is recorded for each trainee and group and statistical analysis used to note the differences. Overall, all trainees achieved significant improvement in suturing time ($p < 0.005$) as measured before and after completion of the training. Similar significantly improved suturing time differences ($p < 0.005$) were noted among the groups of trainees with different laparoscopic experience. In conclusion a short well-guided training course, using the SUTT model, improves significantly surgeon's laparoscopic suturing ability, independently of the level of experience in laparoscopic surgery.

Gynecol Surg. 2014;11(4):273-278.

Hysteroscopic diagnosis and excision of myometrial cystic adenomyosis.

Gordts S, [Campo R](#), Brosens I.

Abstract

In 1908, Cullen described the first cases of cystic adenomyosis in his textbook on adenomyomata. Although not very common, with the introduction of noninvasive imaging techniques such as magnetic resonance imaging (MRI) and 3-D transvaginal

ultrasound, an increasing number of cases have been reported. Patients primarily complain of severe dysmenorrhea, chronic pelvic pain, and dysfunctional uterine bleeding. Currently, it is unclear whether adenomyosis and, more specifically, cystic adenomyosis can be an underlying reason for impaired fertility and reproductive outcome. With the postponement of childbearing, the number of patients with adenomyosis and cystic adenomyosis seeking fertility treatment is increasing. Therefore, in these patients, uterine exploration should include not only the evaluation of the endometrial cavity but also the exploration of the sub-endometrial zone. Indirect imaging techniques, combined with office mini-hysteroscopy, offer the possibility of complete uterine exploration. Two patients with cystic adenomyosis are described in this paper: one had the chief complaint of menorrhagia and the other was referred for evaluation of infertility and severe dysmenorrhea. The aim of these case reports is to present hysteroscopic dissection and ablation of adenomyotic cysts as an alternative procedure for the surgical management of this condition.

Oncol Nurs Forum. 2015 Jul;42(4):E302-9.

The Value of Fatigue Severity to Rule Out Depression in Older Adult Patients With Cancer.

Deckx L, van den Akker M, Vergeer D, van Abbema D, van den Berkmortel F, Linsen L, [de Jonge ET](#), Houben B, van Driel M, Buntinx F.

Abstract

PURPOSE/OBJECTIVES: To evaluate whether fatigue severity can serve as a cue to investigate the presence of depression in older adult patients with cancer.

DESIGN: Cross-sectional observational cohort study.

SETTING: Seven hospitals and general practices in Belgium and the Netherlands.

SAMPLE: 205 older adult patients with cancer and 436 older adults without cancer (aged 70 years or older).

METHODS: The diagnostic accuracy of fatigue as a proxy for depression was evaluated using sensitivity, specificity, and predictive values.

MAIN RESEARCH VARIABLES: Fatigue was measured with a visual analog scale, and depression was measured with the 15-item Geriatric Depression Scale.

FINDINGS: Fifty-six percent of the population experienced fatigue, and 13% were depressed. For fatigue as a cue for depression, sensitivity was 82%, specificity was 47%, positive predictive value was 18%, and negative predictive value was 95%.

CONCLUSIONS: The data confirm that fatigue is a valuable cue to investigate the presence of depression because 82% of depressed participants were correctly identified by fatigue. The assessment of fatigue severity is intuitive, quick, straightforward, and usually already implemented.

IMPLICATIONS FOR NURSING: Identification of depression is difficult in older adult patients with cancer. Instead of experiencing affective symptoms of depression, older adult patients are more likely to disclose somatic symptoms, such as fatigue, which often overlap with cancer-related symptoms. Nurses should be aware of this problem and should be alert for the possibility of depression in older adult patients presenting with fatigue.

Int J Gynecol Cancer. 2015 Jul;25(6):993-9.
Outcome of Epithelial Ovarian Cancer: Time for Strategy Trials to Resolve the Problem of Optimal Timing of Surgery.
Van de Putte G, Oben J, Prenen L, Schobbens JC, Vlasselaer J, Van Holsbeke C, Debrock G, Van Eycken P, de Jonge E.

Abstract

INTRODUCTION: The standard treatment of ovarian cancer is the combination of debulking surgery and chemotherapy. There is an ongoing discussion on which treatment is best: primary debulking surgery (PDS) or neoadjuvant chemotherapy with interval debulking (NACT-IDS). Even a large randomized trial has not settled this issue. We examined whether comparing a specified treatment protocol would not be a more logical approach to answer this type of discussions.

METHODS: A retrospective study of 142 consecutively treated patients according to a fixed protocol between 2000 and 2012 was conducted. Disease-free survival and overall survival were calculated by univari-

ate and multivariate analyses for the whole group and for advanced stages separately. Specific differences between PDS and NACT-IDS were studied. Comparison of results from large databases was made.

RESULTS: Disease-free survival and overall 5-year survival for the whole group were 35% and 50%. For the advanced stages, disease-free survival and overall 5-year survival were 14% and 36%, with a median disease-free and overall survival of 16 and 44 months. Of the 98 women with advanced ovarian carcinoma, 54% of operable patients underwent PDS and 44% underwent NACT-IDS. More patients in the PDS group were optimally (<1 cm) debulked: 80% vs 71%. There was no significant difference in survival between PDS or NACT-IDS. Optimally debulked patients had a significant better overall survival in multivariate analysis with a hazard ratio of 2.1.

DISCUSSION: Outcome of treatment according to a fixed protocol with a mixture of PDS and NACT-IDS was similar to results from large databases. We hypothesize that comparison of a specific strategy may yield more useful results than awaiting the perfect randomized trial.

Prenat Diagn. 2015 Dec;35(13):1347-52.
Contingent non-invasive prenatal testing: an opportunity to improve non-genetic aspects of fetal aneuploidy screening.

Gyselaers W, Hulstaert F, Neyt M.

Abstract

BACKGROUND: Several countries today struggle with suboptimal performances in many aspects of the fetal aneuploidy screening process and consider introducing non-invasive prenatal screening (NIPT) as a solution. In this study, costs and benefits of different scenarios for contingent NIPT screening in Belgium are evaluated with respect to partial redistribution of the national screening budget into quality improving measures for those screening activities that will be maintained when full NIPT screening is implemented.

METHODS: Data from the Belgian National Institute for Health and Disability Insurance and the Study Centre for Perinatal Epidemiology were used in modeled calculations of medical and economic impact of

NIPT after prior conventional screening (1) at thresholds 1:300 and 1:600, and (2) at current and improved screening sensitivity.

RESULTS: Contingent NIPT screening under current screening conditions would maintain today's 7.9(0)/000 live birth prevalence of Down syndrome (LBPD) at an 11% reduction of overall short-term costs. Lowering the screening threshold to 1:600 or increasing sensitivity by 10% would reduce LBPD to 7(0)/000 at a maximum 3% increase of overall short-term costs.

CONCLUSION: Today, in Belgium and in many other countries, full NIPT screening is considered too expensive for immediate introduction into the national fetal aneuploidy screening program. Contingent NIPT screening is both clinically and economically beneficial. A temporary contingent NIPT protocol allows for reinvesting economic savings into optimization of those screening aspects, which are to be maintained in parallel to full NIPT screening.

Epigenetics. 2015;10(6):536-44.

Placental mitochondrial methylation and exposure to airborne particulate matter in the early life environment: An ENVIRONAGE birth cohort study.

Janssen BG, Byun HM, Gyselaers W, Lefebvre W, Baccarelli AA, Nawrot TS.

Abstract

Most research to date has focused on epigenetic modifications in the nuclear genome, with little attention devoted to mitochondrial DNA (mtDNA). Placental mtDNA content has been shown to respond to environmental exposures that induce oxidative stress, including airborne particulate matter (PM). Damaged or non-functioning mitochondria are specifically degraded through mitophagy, exemplified by lower mtDNA content, and could be primed by epigenetic modifications in the mtDNA. We studied placental mtDNA methylation in the context of the early life exposome. We investigated placental tissue from 381 mother-newborn pairs that were enrolled in the ENVIRONAGE birth cohort. We determined mtDNA methylation by bisulfite-pyrosequencing in 2 regions, i.e., the D-loop control region and 12S rRNA (MT-RNR1), and measured mtDNA content by qPCR. PM_{2.5} exposure was

calculated for each participant's home address using a dispersion model. An interquartile range (IQR) increment in PM2.5 exposure over the entire pregnancy was positively associated with mtDNA methylation (MT-RNR1: +0.91%, $P = 0.01$ and D-loop: +0.21%, $P = 0.05$) and inversely associated with mtDNA content (relative change of -15.60%, $P = 0.001$) in placental tissue. mtDNA methylation was estimated to mediate 54% [$P = 0.01$ (MT-RNR1)] and 27% [$P = 0.06$ (D-loop)] of the inverse association between PM2.5 exposure and mtDNA content. This study provides new insight into the mechanisms of altered mitochondrial function in the early life environment. Epigenetic modifications in the mitochondrial genome, especially in the MT-RNR1 region, substantially mediate the association between PM2.5 exposure during gestation and placental mtDNA content, which could reflect signs of mitophagy and mitochondrial death.

Environ Health Perspect. 2015 Aug;123(8):834-40.

In Utero Fine Particle Air Pollution and Placental Expression of Genes in the Brain-Derived Neurotrophic Factor Signaling Pathway: An ENVIRONAGE Birth Cohort Study.

Saenen ND, Plusquin M, Bijlens E, Janssen BG, Gyselaers W, Cox B, Fierens F, Molenberghs G, Penders J, Vrijens K, De Boever P, Nawrot TS.

Abstract

BACKGROUND: Developmental processes in the placenta and the fetal brain are shaped by the same biological signals. Recent evidence suggests that adaptive responses of the placenta to the maternal environment may influence central nervous system development.

OBJECTIVES: We studied the association between in utero exposure to fine particle air pollution with a diameter $\leq 2.5 \mu\text{m}$ (PM2.5) and placental expression of genes implicated in neural development.

METHODS: Expression of 10 target genes in the brain-derived neurotrophic factor (BDNF) signaling pathway were quantified in placental tissue of 90 mother-infant pairs from the ENVIRONAGE birth cohort

using quantitative real-time polymerase chain reaction. Trimester-specific PM2.5 exposure levels were estimated for each mother's home address using a spatio-temporal model. Mixed-effects models were used to evaluate the association between the target genes and PM2.5 exposure measured in different time windows of pregnancy.

RESULTS: A $5\text{-}\mu\text{g}/\text{m}^3$ increase in residential PM2.5 exposure during the first trimester of pregnancy was associated with a 15.9% decrease [95% confidence interval (CI): -28.7, -3.2%, $p = 0.015$] in expression of placental BDNF at birth. The corresponding estimate for synapsin 1 (SYN1) was a 24.3% decrease (95% CI: -42.8, -5.8%, $p = 0.011$).

CONCLUSIONS: Placental expression of BDNF and SYN1, two genes implicated in normal neurodevelopmental trajectories, decreased with increasing in utero exposure to PM2.5. Future studies are needed to confirm our findings and evaluate the potential relevance of associations between PM2.5 and placental expression of BDNF and SYN1 on neurodevelopment. We provide the first molecular epidemiological evidence concerning associations between in utero fine particle air pollution exposure and the expression of genes that may influence neurodevelopmental processes.

Reproductieve geneeskunde, Gynaecologie en obstetrie anno 2015; 559-563

Effecten van leefstijlinterventies tijdens de zwangerschap bij obese vrouwen.

A. Bongaerts, R. Devlieger, E. Nuyts, I. Witters, W. Gyselaers, B. Van den Bergh

Tijdschrift voor Geneeskunde, 2015, 71(9).

De moeilijke, maar noodzakelijke diagnostiek van foetale alcohol spectrumstoornissen.

M. Finoulst, P. Vankrunkelsven, W. Gyselaers

Vrouwen die te veel drinken tijdens de zwangerschap, riskeren foetaal alcohol syndroom. Er wordt geschat dat in België jaarlijks 240 baby's geboren worden met afwijkingen door alcoholmisbruik. Heel veel dokters zijn nauwelijks op de hoogte, zegt de belangengroep.

Tijdschrift voor Geneeskunde, 2015, 71(22)

Maternale cardiovasculaire veranderingen in de vroege zwangerschap.

I. Bollen, L. Broekx, S. Vonck, A. Staelens, D. Lamsens, W. Gyselaers

Samenvatting

In de vroege zwangerschap ondergaat het maternale cardiovasculaire systeem grondige veranderingen. Er is een daling van de totale perifere weerstand („total peripheral resistance” – TPR). Door deze daling zal de nabelasting („afterload”) van het hart afnemen, waardoor het slagvolume stijgt. Ook zorgt de daling van de TPR voor een status van relatieve hypovolemie, waardoor de hartslag stijgt en volumeherstellende mechanismen worden geactiveerd. Hierdoor wordt de voorbelasting („preload”) naar het hart ook hoger, en neemt het hartdebiet toe. Doordat het plasmavolume sneller toeneemt dan het volume rode bloedcellen, is er een fysiologische anemie. De renale vasculatuur dilateert, waardoor de renale bloedstroom en de glomerulaire filtratiesnelheid stijgen. Een inadequate maternale cardiovasculaire aanpassing is meermaals gerapporteerd bij pre-eclampsie en/of intra-uteriene groeirestrictie (IUGR). Pre-eclampsie en IUGR zijn belangrijke oorzaken van perinatale morbiditeit en mortaliteit. Maternale cardiovasculaire maladaptaties kunnen worden opgespoord met verschillende niet-invasieve technieken. Dopplerechografie en impedantiecardiografie zijn hier voorbeelden van. Dit artikel geeft een overzicht van de verschillende cardiovasculaire aanpassingen in de vroege zwangerschap en de mogelijkheden en beperkingen van de niet-invasieve methoden om deze aanpassingen te evolveren.

J. Metarn. Fetal Neonatal Med, 2015 Feb, 28(3); 311-315

Maternal venous hemodynamics assessment for prediction of pre-eclampsia should be longitudinal.

T. Mesens, K. Tomsin, J. Oben, A. Staelens, W. Gyselaers

Ultrasound obstet gynecol., 2015 apr.,

45(4); 421-426

Maternal venous Doppler characteristics are abnormal in pre-eclampsia but not in gestational hypertension.

W. Gyselaers, A. Staelens, T. Mesens, K. Tomsin, J. Oben, S. Vonck, L. Verresen, G. Molenberghs

Cell transplant, 2015, 24(10); 2077-2098

Human wharton's jelly-derived stem cells display immunomodulatory properties and transiently improve rat experimental autoimmune encephalomyelitis.

R. Donders, M. Vanheusden, JF Bogie, S. Ravanidis, K. Thewissen, P. Stinissen, W. Gyselaers, JJ. Hendriks, N. Hellings

Prenat. Diagn, 2015 dec, 35(13); 1347-1352

Contingent non-invasive prenatal testing: an opportunity to improve non-genetic aspects of fetal aneuploidy screening.

W. Gyselaers, F. Hulstaert, M. Neyt

Environ Int. 2015 Nov;84:154-60.

Human exposure to endocrine disrupting chemicals and fertility: A case-control study in male subfertility patients.

Den Hond E, Tournaye H, De Sutter P, Ombelet W, Baeyens W, Covaci A, Cox B, Nawrot TS, Van Larebeke N, D'Hooghe T.

Abstract

BACKGROUND: Dioxins, PCBs, chlorinated pesticides, brominated flame retardants, bisphenol A, triclosan, perfluorinated compounds and phthalates are known as endocrine disrupting chemicals (EDCs).

OBJECTIVES: The aim of our study was to investigate whether higher exposure to EDCs is associated with increased subfertility in men.

METHODS: We measured biomarkers of exposure in 163 men, recruited through four fertility clinics. According to WHO guidelines, we used a total motility count (TMC) of 20 million as cut-off value. We assigned patients to the case group when two semen samples - collected at least one week apart - had a TMC<20 and to the control group when both samples had a TMC≥20. To estimate the risk of subfertility and alteration in sex hormone

concentrations we used multivariable-adjusted analysis, using logistic and linear regressions, respectively.

RESULTS: For an IQR increase in serum oxychlordane, the odds ratio for subfertility was 1.98 (95% CI: 1.07; 3.69). Furthermore, men with serum levels of BDE209 above the quantification limit had an odds of 7.22 (1.03; 50.6) for subfertility compared with those having values below the LOQ. Urinary levels of phthalates and triclosan were negatively associated with inhibin B and positively with LH. Urinary bisphenol A correlated negatively with testosterone levels.

CONCLUSIONS: Our study in men showed that internal body concentrations of endocrine disrupting chemicals are associated with an increased risk of subfertility together with alterations in hormone levels. The results emphasize the importance to reduce chemicals in the environment in order to safeguard male fertility.

Facts Views Vis Obgyn. 2015;7(2):137-43.

Artificial insemination history: hurdles and milestones.

Ombelet W, Van Robays J.

Abstract

Artificial insemination with homologous (AIH) or donor semen (AID) is nowadays a very popular treatment procedure used for many subfertile women worldwide. The rationale behind artificial insemination is to increase gamete density at the site of fertilisation. The sequence of events leading to today's common use of artificial insemination traces back to scientific studies and experimentation many centuries ago. Modern techniques used in human artificial insemination programmes are mostly adapted from the work on cattle by dairy farmers wishing to improve milk production by using artificial insemination with sperm of selected bulls with well chosen genetic traits. The main reason for the renewed interest in artificial insemination in human was associated with the refinement of techniques for the preparation of washed motile spermatozoa in the early years of IVF. The history of artificial insemination is reviewed with particular interest to the most important hurdles and milestones.

Fertility reproduction and sexuality volume 31, 2015, Chapter 5, edited by Kate Hampshire and Bob Simpson. Assisted reproductive technologies in the third phase.

Global access to reproductive technologies and infertility care in developing countries.

W. Ombelet

Horm Res Paediatr. 2015;83(5):361-4.

Short Stature in KBG Syndrome: First Responses to Growth Hormone Treatment.

Reynaert N, Ockeloen CW, Säwendahl L, Beckers D, Devriendt K, Kleefstra T, Carrels CE, Grigeliuniene G, Nordgren A, Francois I, de Zegher F, Casteels K.

Abstract

BACKGROUND: KBG syndrome is a rare disorder characterized by intellectual disability and associated with macrodontia of the upper central incisors, specific craniofacial findings, short stature and skeletal anomalies. Genetic corroboration of a clinical diagnosis has been possible since 2011, upon identification of heterozygous mutations in or a deletion of the ANKRD11 gene.

METHODS: We summarized the height data of 14 adults and 18 children (age range 2-16 years) with a genetically confirmed diagnosis of KBG syndrome. Two of these children were treated with growth hormones.

RESULTS: Stature below the 3rd centile or -1.88 standard deviation score (SDS) was observed in 72% of KBG children and in 57% of KBG adults. Height below -2.50 SDS was observed in 62% of KBG children and in 36% of KBG adults. The mean SDS of height in KBG children was -2.56 and in KBG adults -2.17. Two KBG children on growth hormone therapy increased their height by 0.6 and 1 SDS within 1 year, respectively. The former also received a gonadotropin-releasing hormone agonist due to medical necessity.

CONCLUSION: Short stature is prevalent in KBG syndrome, and spontaneous catch-up growth beyond childhood appears limited. Growth hormone intervention in short KBG children is perceived as promising.

Int J Pediatr Endocrinol. 2015;2015(1):7.
Congenital nystagmus and central hypothyroidism.

Reynaert N, Braat E, de Zegher F.

Abstract

We observed a male newborn with bilateral nystagmus and central hypothyroidism without hypoprolactinemia due to a deletion of chromosome band Xq26.1q26.2, containing FRMD7 and IGSF1. These two loss-of function mutations are known to cause, respectively, congenital nystagmus and the ensemble of central hypothyroidism, hypoprolactinemia and testicular enlargement. These latter two features may not yet be present in early life.

Environ health perspect 2016 May, 124(5); 659-665

Prenatal ambient air pollution, placental mitochondrial DNA content and birth weight in the INMA (Spain) and ENVIRONAGE (Belgium), birth cohorts.

DB. Clemente, M. Casas, N. Vilahur, H. Begiristain, M. Bustamante, AE. Carsin, MF. Fernández MF, F. Fierens, W. Gyselaers, C. Iñiguez, BG. Janssen, W. Lefebvre, S. Llop, N. Olea, M. Pedersen, N. Pieters, L. Santa Marina, A. Souto, A. Tardón, C. Vanpoucke, M. Vrijheid, J. Sunyer, TS. Nawrot

Clin. Exp. Pharmacol. Physiol. 2015 oct, 42(10); 1036-1044

Type-specific orthostatic hemodynamic response of hypertensive diseases in pregnancy.

AS. Staelens, S. Vonck, T. Mesens, K. Tomsin, G. Molenberghs, W. Gyselaers

BMJ. 2015 Sep 23;351:h4579.

Defining safe criteria to diagnose miscarriage: prospective observational multicentre study.

Preisler J, Kopeika J, Ismail L, Vathanan V, Farren J, Abdallah Y, Battacharjee P, Van Holsbeke C, Bottomley C, Gould D, Johnson S, Stalder C, Van Calster B, Hamilton J, Timmerman D, Bourne T.

Abstract

OBJECTIVES: To validate recent guidance changes by establishing the performance of cut-off values for embryo crown-rump length and mean gestational sac diameter

to diagnose miscarriage with high levels of certainty. Secondary aims were to examine the influence of gestational age on interpretation of mean gestational sac diameter and crown-rump length values, determine the optimal intervals between scans and findings on repeat scans that definitively diagnose pregnancy failure.)

DESIGN: Prospective multicentre observational trial.

SETTING: Seven hospital based early pregnancy assessment units in the United Kingdom.

PARTICIPANTS: 2845 women with intrauterine pregnancies of unknown viability included if transvaginal ultrasonography showed an intrauterine pregnancy of uncertain viability. In three hospitals this was initially defined as an empty gestational sac <20 mm mean diameter with or without a visible yolk sac but no embryo, or an embryo with crown-rump length <6 mm with no heartbeat. Following amended guidance in December 2011 this definition changed to a gestational sac size <25 mm or embryo crown-rump length <7 mm. At one unit the definition was extended throughout to include a mean gestational sac diameter <30 mm or embryo crown-rump length <8 mm.

MAIN OUTCOME MEASURES: Mean gestational sac diameter, crown-rump length, and presence or absence of embryo heart activity at initial and repeat transvaginal ultrasonography around 7-14 days later. The final outcome was pregnancy viability at 11-14 weeks' gestation.

RESULTS: The following indicated a miscarriage at initial scan: mean gestational sac diameter ≥ 25 mm with an empty sac (364/364 specificity: 100%, 95% confidence interval 99.0% to 100%), embryo with crown-rump length ≥ 7 mm without visible embryo heart activity (110/110 specificity: 100%, 96.7% to 100%), mean gestational sac diameter ≥ 18 mm for gestational sacs without an embryo presenting after 70 days' gestation (907/907 specificity: 100%, 99.6% to 100%), embryo with crown-rump length ≥ 3 mm without visible heart activity presenting after 70 days' gestation (87/87 specificity: 100%, 95.8% to 100%). The following were indicative of miscarriage at a repeat scan: initial scan and repeat scan after seven

days or more showing an embryo without visible heart activity (103/103 specificity: 100%, 96.5% to 100%), pregnancies without an embryo and mean gestational sac diameter <12 mm where the mean diameter has not doubled after 14 days or more (478/478 specificity: 100%, 99.2% to 100%), pregnancies without an embryo and mean gestational sac diameter ≥ 12 mm showing no embryo heartbeat after seven days or more (150/150 specificity: 100%, 97.6% to 100%).

CONCLUSIONS: Recently changed cut-off values of gestational sac and embryo size defining miscarriage are appropriate and not too conservative but do not take into account gestational age. Guidance on timing between scans and expected findings on repeat scans are still too liberal. Protocols for miscarriage diagnosis should be reviewed to account for this evidence to avoid misdiagnosis and the risk of terminating viable pregnancies.

PLoS One.2015, 3(10); 3

Patient-specific modeling of regional antibiotic concentration levels in airways of patients with cystic fibrosis: are we dosing high enough?

AC. Bos, C. Van Holsbeke, JW de Backer, M. van Westreenen, HM Janssens, WG Vos, HA. Tiddens

J Thromb Haemost. 2015 May;13(5):755-67.

Pituitary adenylate cyclase-activating polypeptide deficiency associated with increased platelet count and aggregability in nephrotic syndrome.

Eneman B, Freson K, van den Heuvel L, van Hoyweghen E, Collard L, Vande Walle J, van Geet C, Levtchenko E.

Abstract

BACKGROUND: Pituitary adenylate cyclase-activating polypeptide (PACAP) was recently identified as an inhibitor of megakaryopoiesis and platelet aggregability.

OBJECTIVE: We studied PACAP levels in children with nephrotic syndrome (NS), which is associated with thrombocytosis, platelet hyperaggregability, and an increased risk of thrombosis.

PATIENTS/METHODS: In four children with congenital NS (CNS) and 24 children with idiopathic NS (INS), plasma and urine

levels of PACAP and ceruloplasmin were measured, as were platelet counts and platelet aggregation responses to collagen. In CNS patients, in vitro megakaryopoiesis and nuclear factor- κ B expression in platelet lysates were also measured. All tests were performed during the nephrotic state and the non-nephrotic state.

RESULTS: Urinary losses of PACAP and ceruloplasmin were observed during the nephrotic state, and disappeared during the non-nephrotic state. Plasma PACAP deficiency was more pronounced in CNS patients than in INS patients. Thrombocytosis was observed in all CNS patients and in 11 of 29 INS patients during the nephrotic state. During the PACAP-deficient state, in vitro megakaryopoiesis was increased for CNS patients, and this effect could be reversed by the addition of recombinant PACAP. Platelet hyperaggregability was observed during the nephrotic state in both CNS and INS patients. In INS patients, the addition of recombinant PACAP to patients' platelets was studied, and resulted in decreased aggregation during the nephrotic state. Platelet aggregation correlated inversely with plasma PACAP levels, but not with serum albumin levels.

CONCLUSIONS: We demonstrate urinary losses of PACAP and plasma PACAP deficiency in children with NS, associated with thrombocytosis and platelet hyperaggregability.

Eur J Paediatr Neurol. 2015 Mar;19(2):114-21.
Outcome of 12 antenatally diagnosed fetal arachnoid cysts: case series and review of the literature.

De Keersmaecker B, Ramaekers P, Claus F, Witters I, Ortibus E, Naulaers G, Van Calenberg F, De Catte L.

Abstract

OBJECTIVES: To investigate the natural history, associated abnormalities and outcome of 12 fetuses with arachnoid cyst diagnosed antenatally by ultrasound and magnetic resonance imaging and to compare the outcome with cases in the literature.

METHODS: A retrospective study of all cases of antenatally detected fetal arachnoid cysts was performed in patients referred to a tertiary unit between 2007 and 2013. Associated abnormalities, pregnancy out-

come and postnatal follow-up were analyzed. All papers about prenatally diagnosed arachnoid cysts, of the last 30 years, were evaluated (search terms in Pubmed: "prenatal diagnosis", "Arachnoid Cysts").

RESULTS: Fetal arachnoid cysts were diagnosed in 12 fetuses, 9 were females. The mean gestational age of diagnosis was 28 1/7 (range 19 1/7-34 2/7 weeks). A total of 9 cases were supratentorial, 3 were located in the posterior fossa. In 10 cases a fetal MRI was performed which confirmed brain compression in 4 out of 5 supratentorial arachnoid cyst. MRI did not reveal other malformations nor signs of nodular heterotopia. Only one fetus presented with additional major anomalies (bilateral ventriculomegaly of >20 mm and rhombencephalosynapsis) leading to a termination of pregnancy. Two neonates underwent endoscopic fenestration of the arachnoid cyst in the first week of life with no additional intervention in childhood. All but one (10/11) had a favorable postnatal outcome. This child suffered from visual impairment at autism was diagnosed at the age of 5. One child had a surgical correction of strabismus later in childhood. In one child the infratentorial arachnoid cyst regressed spontaneously on ultrasound and MRI in the postnatal period.

CONCLUSIONS: The majority of arachnoid cysts in this series are of benign origin and remain stable. Based on the current series and the review of the literature, in the absence of other associated anomalies and when the karyotype is normal, the postnatal overall and neurological outcome is favorable. Large suprasellar arachnoid cysts however, may cause visual impairment and endocrinological disturbances. Rarely associated cerebral or cerebellar malformations are present. Modern postnatal management of suprasellar arachnoid cyst consists of endoscopic cystoventriculostomy.

J Matern Fetal Neonatal Med. 2015 Jun;28(9):1026-31.

Population-specific serum creatinine centiles in neonates with posterior urethral valves already predict long-term renal outcome.

Lemmens AS, Mekahli D, Devlieger R, Levchenko E, Allegaert K.

Abstract

INTRODUCTION: The lowest serum creatinine (nadir Scr, cut-off 1 mg/dl) during infancy predicts subsequent renal outcome in posterior urethral valve (PUV) infants, but early, neonatal values may be useful to guide care. We aimed to explore correlations between neonatal Scr values and long-term renal outcome.

METHODS: Retrospective evaluation of records of 39 PUV patients, treated in the University Hospitals Leuven (2001-2011). Scr measurements were collected and associations (Mann-Whitney U, Spearman) to predict unfavorable renal outcome [GFR <60 ml/min/1.73 m² at 2 years] were explored.

RESULTS: Unfavorable renal outcome at the last follow-up was observed in 7/36 patients (19%). Besides the nadir Scr at a median age of 5 months, also the peak Scr and Scr between days 9 and 42 correlated significantly with renal outcome. By introducing "centiles" for neonatal Scr values in this PUV cohort, the 75th Scr percentile in this PUV cohort was highly predictive for unfavorable renal outcome.

CONCLUSIONS: Besides the nadir Scr, early neonatal Scr values (peak, days 9-42, PUV cohort-specific 75th centile) also predicted unfavorable renal outcome. The introduction of PUV disease specific reference Scr centiles may be helpful to facilitate earlier prediction and guide counseling, but necessitates external validation.

Eur J Med Genet. 2011 May-Jun;54(3):236-40.
Circumferential skin creases, cleft palate, typical face, intellectual disability and growth delay: "circumferential skin creases Kunze type".

Wouters L, Rodriguez Rodriguez CM, Dapena EP, Poorten VV, Devriendt K, Van Esch H.

Abstract

Congenital symmetrical circumferential skin creases are a rare feature, often described as the "Michelin Tire Baby" syndrome and in general having a good prognosis. In some patients however, the circumferential skin creases are associated with other congenital malformations. We describe 2 unrelated patients presenting with multiple circumferential skin creases, growth retardation, developmental de-

lay, a typical facial appearance and cleft palate. In literature, 6 patients with an almost identical clinical phenotype have been described. This well recognizable syndrome should be distinguished from the "Michelin Tire Baby" syndrome and we therefore propose the term "circumferential skin creases Kunze type".

BMC Fam Pract. 2015 Mar 3;16:30.

Geriatric screening tools are of limited value to predict decline in functional status and quality of life: results of a cohort study.

Deckx L, van den Akker M, Daniels L, De Jonge ET, Bulens P, Tjan-Heijnen VC, van Abbema DL, Buntinx F.

Abstract

BACKGROUND: Geriatric screening tools are increasingly implemented in daily practice, especially in the oncology setting, but also in primary care in some countries such as the Netherlands. Nonetheless, validation of these tools regarding their ability to predict relevant outcomes is lacking. In this study we evaluate if geriatric screening tools predict decline in functional status and quality of life after one year, in a population of older cancer patients and an older primary care population without cancer with a life expectancy of at least six months.

METHODS: Older cancer patients and a general older primary care population without a history of cancer (≥ 70 years) were included in an on-going prospective cohort study. Data were collected at baseline and after one-year follow-up. Functional decline was based on the Katz Index and Lawton IADL-scale and was defined as deterioration on one or more domains. Decline in quality of life was measured using the global health related subscale of the EORTC QLQ-C30, and was defined as a decline ≥ 10 points. The selected geriatric screening tools were the abbreviated Comprehensive Geriatric Assessment, Groningen Frailty Indicator, Vulnerable Elders Survey-13, and G8. We calculated sensitivity, specificity, predictive values, and odds ratios to assess if normal versus abnormal scores predict functional decline and decline in quality of life.

RESULTS: One-year follow-up data were

available for 134 older cancer patients and 220 persons without cancer. Abnormal scores of all screening tools were significantly associated with functional decline. However, this was only true for older persons without cancer, and only in univariate analyses. For functional decline, sensitivity ranged from 54% to 71% and specificity from 33% to 66%. For decline in quality of life, sensitivity ranged from 40% to 67% and specificity from 37% to 54%.

CONCLUSION: In older persons with a relatively good prognosis, geriatric screening tools are of limited use in identifying persons at risk for decline in functional status or quality of life after one year. Hence, a geriatric screening tool cannot be relied on in isolation, but they do provide very valuable information and may prompt physicians to also consider different aspects of functioning.

Fact Views Vision in Obgyn, 2015, 7(4); 251-256

Improving systemic breast cancer therapy: time to look beyond the primary tumor?

E. Vandendriessche, G. Van De Putte, R. Van Den Broecke, E.T.M. De Jonge

Abstract

AIM: Intra and inter tumour heterogeneity is a known feature in cancer because tumour cells undergo changes at genetic and epigenetic level as they spread from their primary tumour site. Adjuvant treatment protocols in breast cancer are currently based on the biological characteristics of the primary tumour, which in most cases has been removed surgically. Considering tumour heterogeneity in metastases we examined the present status of knowledge regarding measurable differences in tumour profiling between the primary breast tumour and its synchronous axillary lymph node metastases (ALNM) and if so whether adjuvant therapy directed towards the tumour characteristics of the ALNM instead of those of the primary tumour is more effective. **Methods:** We performed a literature search in Pubmed with the following MeSH headings: HUMAN and BREAST NEOPLASMS and RECEPTORS and ErbB-2. **Results:** A significant change in tumour features was seen in metachro-

nous metastases. In contrast, a high concordance of biomarker expression was reported between a primary breast tumour and its synchronous ALNM. **Conclusion:** Tumour heterogeneity is a challenge for targeted therapy. A poor response can be explained by the diversity of tumour cells. The biological profile of synchronous ALNM measured by oestrogen (ER), progesterone (PR) and her-2-neu receptor status does not differ from the primary breast tumour and is not predictive of the tumour profile in metachronous metastasis. New techniques, such as profiling of circulating tumour cells or tumour behaviour in xenografts, are promising in directing more effective adjuvant therapy.

DIVISIE 2 (THORAX - NEFROLOGIE - CARDIOLOGIE)

J Cardiovasc Med (Hagerstown). 2015 Nov 21.

Antegrade wire escalation for chronic total occlusions in coronary arteries: simple algorithms as a key to success.

Maeremans J, Knaapen P, Stuijzand WJ, Kayaert P, Pereira B, Barbato E, Dens J.

Abstract

AIMS: Antegrade wire escalation (AWE) remains the method of choice for tackling chronic total occlusions (CTOs), especially for lesions with low J-CTO score. To increase the number of operators which treat CTOs and increase AWE success rates, there is a need for a clear, algorithmic approach. We report the results of a simple AWE algorithm with new guidewire technology in coronary CTOs.

METHODS: Hundred consecutive CTO lesions selected for AWE as the primary strategy were included in five Benelux centers. The algorithm follows a step-wise increase in guidewire tip load. Lesions were categorized according to the J-CTO score. Primary endpoint was successful guidewire crossing.

RESULTS: No differences in baseline demographics were present between successful and unsuccessful procedures. Overall, in 75% of the lesions AWE resulted in successful crossing. AWE success rates in easy, intermediate, difficult and very difficult CTOs were 83, 86, 71 and 43%, respectively. 46% could be crossed using a soft guidewire only. An additional success of 34 and 60% could be reached with an intermediate and stiff guidewire, respectively. Adding additional techniques resulted in 88% overall success. Procedure and fluoroscopy times, radiation doses and use of contrast were within highly acceptable ranges (67 ± 39 min, 27 ± 19 min, 1.7 ± 1.3 Gy, 264 ± 123 ml).

CONCLUSION: The algorithm and new wire technologies led to high success rates. AWE as a standalone procedure is highly successful in J-CTO 0-1. Low- and intermediate-volume CTO operators should try to implement a systematic approach in their CTO procedures, especially for lesions with low J-CTO scores. Adding additional techniques further increases these success rates.

Am J Cardiol. 2015 Dec 1;116(11):1774-80.

Myths to Debunk to Improve Management, Referral, and Outcomes in Patients With Chronic Total Occlusion of an Epicardial Coronary Artery.

Azzalini L, Vo M, Dens J, Agostoni P.

Abstract

A chronic total occlusion (CTO) is defined as an occlusive (100% stenosis) coronary lesion with antegrade Thrombolysis In Myocardial Infarction 0 flow for at least 3 months. CTOs are common in patients referred for coronary angiography (up to 33%) and are associated with angina, impaired quality of life, and reduced survival. Unfortunately, CTO percutaneous coronary intervention continues to be underperformed worldwide (10% to 15% at most institutions, ~30% where expert operators are available). The aim of this study was to address common fallacies pertaining to CTOs among cardiologists by providing a concise review of pertinent previously published reports along with an update on safety and efficacy of state-of-the-art CTO percutaneous coronary intervention techniques.

Acta Cardiol. 2015 Jun;70(3):265-73.

Determinants and impact of the natriuretic response to diuretic therapy in heart failure with reduced ejection fraction and volume overload.

Verbrugge FH, Dupont M, Bertrand PB, Nijst P, Penders J, Dens J, Verhaert D, Vandervoort P, Tang WH, Mullens W.

OBJECTIVE: The objective of this study was to investigate determinants of the natriuretic response to diuretics in decompensated heart failure (HF) and the relationship with decongestion, neurohumoral activation and clinical outcome in the contemporary era of HF management.

METHODS AND RESULTS: In this prospective, single-centre cohort study, consecutive patients with decompensated HF (n = 54) and left ventricular ejection fraction 45% received protocol-driven diuretic therapy until complete disappearance of congestion signs. Urine was collected during three consecutive 24-h intervals. Natriuretic response was defined as absolute natriuresis (mmol) per mg of intravenous

bumetanide administered. Natriuresis was 146 mmol (76-206 mmol), 74 mmol (37-167 mmol) and 74 mmol (53-134 mmol) per mg intravenous bumetanide administered during the first, second and third 24-h interval, respectively. Diastolic blood pressure ($\beta = 23.048 \pm 10.788$; P-value = 0.036), plasma aldosterone ($\beta = -25.722 \pm 11.560$; P-value = 0.029), and combination therapy with acetazolamide ($\beta = 103.241 \pm 40.962$; P-value = 0.014) were independent predictors of the natriuretic response. Patients with a stronger natriuretic response demonstrated more pronounced decreases in plasma NT-proBNP levels (P-value = 0.025), while a weaker response was associated with higher peak plasma aldosterone levels (P-value = 0.013) and plasma renin activity (P-value = 0.033). Natriuresis per loop diuretic dose predicted freedom from all-cause mortality or HF readmissions, independently of baseline renal function (HR 0.40, 95% CI 0.16-0.98; P-value = 0.045).

CONCLUSIONS: More effective natriuresis in decompensated HF patients with reduced ejection fraction and volume overload is associated with better decongestion, less neurohumoral activation and predicts favourable clinical outcome independently from renal function per se. Acetazolamide warrants further evaluation in large prospective trials to increase the natriuretic response to loop diuretics.

Catheter Cardiovasc Interv. 2015 Sep;86(3):528-35.

Midterm clinical outcome following Edwards SAPIEN or Medtronic CoreValve transcatheter aortic valve implantation (TAVI): Results of the Belgian TAVI registry.

Collas VM, Dubois C, Legrand V, Kefer J, De Bruyne B, Dens J, Rodrigus IE, Herijgers P, Bosmans JM; Belgian TAVI Registry Participants.

Abstract

OBJECTIVE: To assess midterm (3 years) clinical outcomes of transcatheter aortic valve implantation (TAVI) in Belgium using the Edwards SAPIEN valve or the Medtronic CoreValve transcatheter heart valve (THV).

BACKGROUND: Medium and long term

follow-up data of both THVs are still relatively scarce, although of great clinical relevance for a relatively new but rapidly expanding treatment modality. Therefore, reporting mid- and long term clinical outcome data, coming from large "real world" national registries, remains contributive.

METHODS: Between December 2007 and March 2012, 861 "real world" patients who were not candidates for surgical aortic valve replacement as decided by the local heart teams, underwent TAVI at 23 sites. Eleven sites exclusively used SAPIEN THV (n=460), while 12 exclusively used CoreValve THV (n=401). Differences in clinical outcomes by valve system were assessed, according to access route and baseline EuroSCORE risk profile (<10%: low, 10-20%: intermediate and >20%: high risk).

RESULTS: Overall cumulative survival at 3 years was 51% for SAPIEN vs. 60% for CoreValve (P=0.021). In transfemorally treated patients, SAPIEN and CoreValve had similar survival at 3 years for each of the baseline EuroSCORE cohorts (low risk: 72% vs. 76%, P=0.45; intermediate risk: 62% vs. 59%, P=0.94; high risk: 48% vs. 53%, P=0.65).

CONCLUSION: Cumulative midterm 3 year survival after transfemoral TAVI in "real world" patients refused for surgery with similar baseline EuroSCORE risk profile is not different between SAPIEN or CoreValve.

Eur J Heart Fail. 2015 Mar;17(3):320-8.

Pulmonary vascular response to exercise in symptomatic heart failure with reduced ejection fraction and pulmonary hypertension.

Verbrugge FH, Dupont M, Bertrand PB, Nijst P, Grieten L, Dens J, Verhaert D, Janssens S, Tang WH, Mullens W.

Abstract

AIMS: To study pulmonary vascular response patterns to exercise in heart failure with reduced ejection fraction (HFrEF) and pulmonary hypertension (PH).

METHODS AND RESULTS: In this prospective single-centre cohort study, consecutive symptomatic HFrEF patients (n = 40) with mean pulmonary arterial pressure (MPAP) ≥ 25 mmHg, pulmonary artery wedge pressure (PAWP) >15 mmHg, and cardiac index <2.5 L/min.m(2), received

protocol-driven titrated sodium nitropruside (SNP) and diuretics to reach mean arterial blood pressure 65-75 mmHg and PAWP ≤ 15 mmHg. Patients performed symptom-limited supine bicycle testing under continued SNP administration. Afterwards, SNP was gradually withdrawn, renin-angiotensin system blockers up-titrated, and hydralazine added to maintain haemodynamic targets. Subsequently, bicycle testing was repeated. Patients presented with pulmonary vascular resistance (PVR) = 3.8 ± 1.4 Wood Units at rest, decreasing to 2.9 ± 0.9 Wood Units after decongestion, with PH was completely reversed (MPAP <25 mmHg) in 22%. From rest to maximal exercise, the cardiac index did not change significantly (P = 0.334 under SNP; P-value = 0.552 under oral therapy). A dynamic exercise-induced PVR increase >3.5 Wood Units was noted in 19 patients (48%) under oral therapy vs. five (13%) under SNP. Such exercise-induced PVR increase was associated with a 33% relative decrease in right ventricular stroke work index (P = 0.037).

CONCLUSIONS: Even after thorough decongestion and under continuous after-load reduction, PH secondary to HFrEF is completely reversible in only a minority of patients. Others demonstrate an exercise-induced PVR increase, associated with impaired right ventricular stroke work, which might be ameliorated by nitric oxide donor support.

Neth Heart J. 2015 Feb;23(2):124-9.

Ultra-thin strut cobalt chromium bare metal stent usage in a complex real-world setting. (SOLSTICE registry).

Suttorp MJ1, Stella PR, Dens J, McKenzie JM, Park KS, Frambach P; SOLSTICE investigators.

Abstract

AIM: To report clinical follow-up at 6 months after implantation of the ultra-thin strut cobalt chromium SolarFlex stent in a real-world setting.

METHODS AND RESULTS: Patients (n=240) with single or multiple vessel coronary artery disease undergoing percutaneous coronary intervention (PCI) at four sites in Europe were enrolled in the SOLSTICE (SolarFlex Stent in Routine

Clinical Practice) registry. Follow-up at 6 months was 100 %. Diabetes was present in 29 % of the patients, 30 % presented with acute myocardial infarction and 17 % had unstable angina. Of the patients, 27 % had previously undergone PCI or coronary artery bypass surgery. Lesion complexity was high (50 % B2+C type lesions). Device success was achieved in 99.7 % of cases and the major adverse cardiac event (MACE) rate was 5.8 % at 6 months of follow-up. Target lesion revascularisation (TLR) was 5.0 % at 6 months.

CONCLUSIONS: The SOLSTICE registry showed that in a complex real-world setting the SolarFlex bare metal stent, with ultra-thin struts and customised scaffolding, provided low clinical MACE and TLR rates. These results provide support for the use of the latest generation bare metal stent in contemporary European practice.

Catheter Cardiovasc Interv. 2015 Feb 1;85(2):207-15.

Two-year safety and effectiveness of the platinum chromium everolimus-eluting stent for the treatment of small vessels and longer lesions.

Teirstein PS, Meredith IT, Feldman RL, Rabinowitz AC, Cannon LA, Lee TC, Dens J, Dubois CL, Mooney MR, Pompili VJ, Saito S, Allocco DJ, Dawkins KD, Stone GW.

Abstract

OBJECTIVES: To report 1- and 2-year clinical outcomes of patients receiving platinum chromium everolimus-eluting stents (PtCr-EES) in the prospective, single-arm PLATINUM small vessel (SV) and long lesion (LL) studies.

BACKGROUND: Small vessel diameter and long lesion length are independently associated with increased risk of adverse cardiac events after drug-eluting stent implantation.

METHODS: The PLATINUM SV study enrolled 94 patients with coronary artery lesions in vessels ≥ 2.25 mm to <2.50 mm in diameter and ≤ 28 mm in length. The PLATINUM LL study enrolled 102 patients with lesions >24 to ≤ 34 mm long in vessels ≥ 2.50 to ≤ 4.25 mm in diameter. The primary endpoint for both studies was target lesion failure (TLF) at 1 year compared to a prespecified performance

goal based on outcomes with the TAXUS Express paclitaxel-eluting stent in small vessels and long lesions.

RESULTS: One-year TLF rates with the PtCr-EES were significantly ($P < 0.001$) lower than the predetermined performance goals: 2.4% versus 21.1% in the SV cohort and 3.2% versus 19.4% in the LL cohort. Cumulative rates of TLF to 2 years were 4.7% in the SV cohort and 8.8% in the LL cohort. No myocardial infarction or ARC definite/probable stent thromboses occurred in either cohort through 2-year follow-up.

CONCLUSIONS: The clinical efficacy and safety outcomes observed in these small vessel and long lesion cohorts support the use of the PtCr-EES in the treatment of small diameter vessels and long lesions.

Acta Cardiol. 2015 Oct;70(5):565-72.

Heart rate reduction and exercise performance in recent onset heart failure with reduced ejection fraction: arguments for beta-blocker hypo-response.

Verbrugge FH, Vrijnsen J, Vercammen J, Grieten L, Dupont M, Mullens W.

Abstract

OBJECTIVE: Beta blockers reduce all-cause mortality and readmissions in heart failure with reduced ejection fraction (HFrEF), which may be explained by their effect on heart rate (HR). This study assessed the impact of HR reduction with beta blockers on exercise capacity in recent onset HFrEF.

METHODS AND RESULTS: Fifty consecutive patients with recent onset HFrEF (<30 days) performed a standardized exercise protocol with respiratory gas analysis at baseline as well as after 6 and 12 months. Patients participated in a quality of care programme aiming to achieve guideline-recommended target doses for beta-blocker therapy. At baseline, 6 and 12 months, 36%, 70% and 62% of patients, respectively, had a resting HR<70 bpm. Beta-blocker dose after 12 months was comparable in patients with resting HR<70 versus ≥ 70 bpm (P value=0.631). However, with similar dose uptitration, the former versus the latter had a significantly larger HR reduction (17 ± 22 versus 4 ± 15 bpm; P value=0.027). Peak oxygen

consumption (VO_{2max}) was significantly higher when resting HR was <70 versus ≥ 70 bpm (17.5 ± 5.5 versus 14.4 ± 3.3 mL/min/kg, respectively; P value=0.038). Similar results were observed after 6 months. Patients in whom resting HR decreased at follow-up compared to baseline had a 2.0 ± 3.2 mL/min/kg increase in VO_{2max} compared to a 1.2 ± 7.7 mL/min/kg increase in patients who did not demonstrate a lower resting HR (P value=0.033).

CONCLUSIONS: In recent onset HFrEF, exercise performance was better when resting HR was controlled <70 bpm with beta-blocker therapy. However, despite aggressive dose uptitration, many patients did not achieve this target as they had little HR reduction with beta-blocker therapy.

Eur J Heart Fail. 2015 Sep;17(9):956-63.

Response and tolerance to oral vasodilator up-titration after intravenous vasodilator therapy in advanced decompensated heart failure.

Verbrugge FH, Dupont M, Finucan M, Gabi A, Hawwa N, Mullens W, Taylor DO³, Young JB, Starling RC, Tang WH.

Abstract

AIMS: The aim of this study was to assess the haemodynamic response and tolerance to aggressive oral hydralazine/isosorbide dinitrate (HYD/ISDN) up-titration after intravenous vasodilator therapy in advanced decompensated heart failure (ADHF).

METHODS AND RESULTS: Medical records of 147 consecutive ADHF patients who underwent placement of a pulmonary artery catheter and received intravenous vasodilator therapy were reviewed. Intravenous sodium nitroprusside and sodium nitroglycerin as first-line agent for those with preserved blood pressures were utilized in 143 and 32 patients, respectively. Sixty-one percent of patients were converted to oral HYD/ISDN combination therapy through a standardized conversion protocol. These patients had a significantly higher admission mean pulmonary arterial wedge pressure compared with patients not converted (28 ± 7 vs. 25 ± 8 mmHg, respectively; P -value 0.024). Beneficial haemodynamic response to decongestive therapy, defined as low cardiac filling pressures and cardiac index ≥ 2.20 L/min/m² without emergent

hypotension, was achieved in 32% and 29% of patients who did or did not receive oral HYD/ISDN, respectively (P -value 0.762). HYD/ISDN dosing was progressively and consistently decreased up to the moment of hospital discharge and during outpatient follow-up, primarily due to incident hypotension.

CONCLUSION: The use of a standardized haemodynamically guided up-titration protocol for conversion from intravenous to oral vasodilators may warrant subsequent dose reductions upon stabilization.

Am Heart J. 2015 Jun;169(6):806-12.

A disproportionate elevation in right ventricular filling pressure, in relation to left ventricular filling pressure, is associated with renal impairment and increased mortality in advanced decompensated heart failure.

Grodin JL, Drazner MH, Dupont M, Mullens W, Taylor DO, Starling RC, Tang WH.

Abstract

BACKGROUND: Discordance between left- and right-sided filling pressures occurs in a subset of patients presenting with acute decompensated heart failure (ADHF). We hypothesized that a disproportionately increased right atrial pressure (RAP) relative to the pulmonary capillary wedge pressure (PCWP) would be associated with both renal dysfunction and mortality in ADHF.

METHODS: A total of 367 patients admitted with ADHF with elevated intracardiac filling pressures were treated with intensive medical therapy guided by invasive hemodynamic monitoring. Baseline characteristics, hemodynamics, and renal function at admission were stratified by RAP/PCWP quartiles. The association of RAP/PCWP quartile with all-cause mortality after a median follow-up of 2.4 years was assessed in univariable and multivariable models, which included adjustment for the RAP.

RESULTS: The median RAP/PCWP was 0.58 (interquartile range 0.43-0.75). Increasing RAP/PCWP was inversely associated with estimated glomerular filtration rate at baseline and with treatment ($P < .0001$) independently of RAP. High RAP/PCWP was associated with increased mortality (quartile 4 vs 1: hazard ratio [95%

CI] 2.1 [1.3-3.5], $P = .002$). The association of RAP/PCWP with mortality persisted after adjustment for age, gender, mean arterial pressure, RAP, cardiac index, pulmonary vascular resistance, and estimated glomerular filtration rate (hazard ratio 2.4 [1.4-3.9], $P = .007$).

CONCLUSION: A disproportionate increase in right to left ventricular filling pressures is associated with renal dysfunction and mortality, independently of the right atrial pressure.

Eur J Heart Fail. 2015 Jul;17(7):689-96.

Prognostic role of cardiac power index in ambulatory patients with advanced heart failure.

Grodin JL, Mullens W, Dupont M, Wu Y, Taylor DO, Starling RC, Tang WH.

Abstract

BACKGROUND: Cardiac pump function is often quantified by left ventricular ejection fraction by various imaging modalities. As the heart is commonly conceptualized as a hydraulic pump, cardiac power describes the hydraulic function of the heart. We aim to describe the prognostic value of resting cardiac power index (CPI) in ambulatory patients with advanced heart failure.

METHODS AND RESULTS: We calculated CPI in 495 sequential ambulatory patients with advanced heart failure who underwent invasive haemodynamic assessment with longitudinal follow-up of adverse outcomes (all-cause mortality, cardiac transplantation, or ventricular assist device placement). The median CPI was 0.44 W/m(2) (interquartile range 0.37, 0.52). Over a median of 3.3 years, there were 117 deaths, 104 transplants, and 20 ventricular assist device placements in our cohort. Diminished CPI (<0.44 W/m(2)) was associated with increased adverse outcomes [hazard ratio (HR) 2.4, 95% confidence interval (CI) 1.8-3.1, $P < 0.0001$]. The prognostic value of CPI remained significant after adjustment for age, gender, pulmonary capillary wedge pressure, cardiac index, pulmonary vascular resistance, left ventricular ejection fraction, and creatinine [HR 1.5, 95% CI 1.03-2.3, $P = 0.04$]. Furthermore, CPI can risk stratify independently of peak oxygen consumption (HR 2.2, 95% CI 1.4-3.4, $P = 0.0003$).

CONCLUSION: Resting cardiac power index provides independent and incremental prediction in adverse outcomes beyond traditional haemodynamic and cardio-renal risk factors.

J Am Coll Cardiol. 2015 Feb 3;65(4):378-88.

The pathophysiological role of interstitial sodium in heart failure.

Nijst P, Verbrugge FH, Grieten L, Dupont M, Steels P, Tang WH, Mullens W.

Abstract

The current understanding of heart failure (HF) does not fully explain the spectrum of HF symptoms. Most HF hospitalizations are related to sodium (Na^+) and fluid retention resulting from neurohumoral up-regulation. Recent insights suggest that Na^+ is not distributed in the body solely as a free cation, but that it is also bound to large interstitial glycosaminoglycan (GAG) networks in different tissues, which have an important regulatory function. In HF, high Na^+ intake and neurohumoral alterations disrupt GAG structure, leading to loss of the interstitial buffer capacity and disproportionate interstitial fluid accumulation. Moreover, a diminished endothelial GAG network (the endothelial glycocalyx) results in increased vascular resistance and disturbed endothelial nitric oxide production. New imaging modalities can help evaluate interstitial Na^+ and endothelial glycocalyx integrity. Furthermore, several therapies have been proven to stabilize interstitial GAG networks. Hence, a better appreciation of this new Na^+ "compartment" might improve current management of HF.

JACC Heart Fail. 2015 Jan;3(1):40-9.

Comparative assessment of short-term adverse events in acute heart failure with cystatin C and other estimates of renal function: results from the ASCEND-HF trial.

Tang WH, Dupont M, Hernandez AF, Voors AA, Hsu AP, Felker GM, Butler J, Metra M, Anker SD, Troughton RW, Gottlieb SS, McMurray JJ, Armstrong PW, Massie BM, Califf RM, O'Connor CM, Starling RC.

Abstract

OBJECTIVES: The purpose of this study

was to investigate the predictive values of baseline and changes in cystatin C (CysC) and its derived equations for short-term adverse outcomes and the effect of nesiritide therapy on CysC in acute decompensated heart failure (ADHF).

BACKGROUND: Newer renal biomarkers or their derived estimates of renal function have demonstrated long-term prognostic value in chronic heart failure.

METHODS: CysC levels were measured in sequential plasma samples from 811 subjects with ADHF who were enrolled in the ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) biomarker sub-study (randomized to nesiritide therapy vs. placebo), and followed for all-cause death (180 days) and recurrent hospital stay (30 days).

RESULTS: Median CysC levels were 1.49 (interquartile range [IQR]: 1.20 to 1.96) mg/l at baseline, 1.56 (IQR: 1.28 to 2.13) mg/l at 48 to 72 h, and 1.58 (IQR: 1.24 to 2.11) mg/l at 30 days. Higher baseline (but not follow-up) CysC levels were associated with increased risk of 30-day adverse events and less improvement in dyspnea after 24 h as well as 180-day mortality, although not incremental to blood urea nitrogen. Worsening renal function (defined as a 0.3 mg/l increase in CysC) occurred in 161 of 701 (23%) patients, but it was not predictive of adverse events. Changes in CysC levels were similar between the nesiritide and placebo groups.

CONCLUSIONS: Our findings confirmed the prognostic value of baseline CysC levels in the setting of ADHF. However, worsening renal function based on CysC rise was not predictive of adverse events. Nesiritide did not worsen renal function compared with placebo.

Anaesthesiol Intensive Ther. 2015;47(2):156-61.

From therapeutic hypothermia towards targeted temperature management: a decade of evolution.

Palmer PJ, Hiltrop N, Ameloot K, Timmermans P, Ferdinande B, Sinnaeve P, Nieuwendijk R, Malbrain ML.

Abstract

More than a decade after the first randomised controlled trials with targeted tem-

perature management (TTM), it remains the only treatment with proven favourable effect on postanoxic brain damage after out-of-hospital cardiac arrest. Other well-known indications include neurotrauma, subarachnoidal haemorrhage, and intracranial hypertension. When possible pitfalls are taken into consideration when implementing TTM, the side effects are manageable. After the recent TTM trials, it seems that classic TTM (32-34°C) is as effective and safe as TTM at 36°C. This supports the belief that fever prevention is one of the pivotal mechanisms that account for the success of TTM. Uncertainty remains concerning cooling method, timing, speed of cooling and rewarming. New data indicates that TTM is safe and feasible in cardiogenic shock, one of its classic contra-indications. Moreover, there are limited indications that TTM might be considered as a therapy for cardiogenic shock per se.

Ann Thorac Surg. 2015 Oct;100(4):1437-9.

Anomalous Origin of the Circumflex Artery: An Underestimated Threat During Mitral Valve Operation.

Pettinari M, Gutermann H, Van Kerrebroeck C, Dion R.

Abstract

Ischemic iatrogenic lesions can complicate surgical procedures on the mitral valve. One of the causative mechanisms is direct injury to or distortion of the circumflex coronary artery. The risk of damaging the circumflex coronary artery depends mainly on the proximity of that vessel to the posterior segment of the mitral annulus, and this varies from patient to patient. Herein, we report the case of an iatrogenic circumflex coronary artery lesion after mitral annuloplasty in a patient with an anomalous origin of the circumflex artery.

J Am Coll Cardiol. 2015 Feb 10;65(5):452-61.

Mitral valve area during exercise after restrictive mitral valve annuloplasty: importance of diastolic anterior leaflet tethering.

Bertrand PB, Verbrugge FH, Verhaert D, Smeets CJ, Grieten L, Mullens W, Gutermann H, Dion RA, Levine RA, Vandervoort PM.

Abstract

BACKGROUND: Restrictive mitral valve annuloplasty (RMA) for secondary mitral regurgitation might cause functional mitral stenosis, yet its clinical impact and underlying pathophysiological mechanisms remain debated.

OBJECTIVES: The purpose of our study was to assess the hemodynamic and clinical impact of effective orifice area (EOA) after RMA and its relationship with diastolic anterior leaflet (AL) tethering at rest and during exercise.

METHODS: Consecutive RMA patients (n = 39) underwent a symptom-limited supine bicycle exercise test with Doppler echocardiography and respiratory gas analysis. EOA, transmitral flow rate, mean transmitral gradient, and systolic pulmonary arterial pressure were assessed at different stages of exercise. AL opening angles were measured at rest and peak exercise. Mortality and heart failure readmission data were collected for at least 20 months after surgery.

RESULTS: EOA and AL opening angle were 1.5 ± 0.4 cm(2) and $68 \pm 10^\circ$, respectively, at rest ($r = 0.4$; $p = 0.014$). EOA increased significantly to 2.0 ± 0.5 cm(2) at peak exercise ($p < 0.001$), showing an improved correlation with AL opening angle ($r = 0.6$; $p < 0.001$). Indexed EOA (EOAi) at peak exercise was an independent predictor of exercise capacity (maximal oxygen uptake, $p = 0.004$) and was independently associated with freedom from all-cause mortality or hospital admission for heart failure ($p = 0.034$). Patients with exercise EOAI < 0.9 cm(2)/m(2) (n = 14) compared with ≥ 0.9 cm(2)/m(2) (n = 25) had a significantly worse outcome ($p = 0.048$). In multivariate analysis, AL opening angle at peak exercise ($p = 0.037$) was the strongest predictor of exercise EOAI.

CONCLUSIONS: In RMA patients, EOA increases during exercise despite fixed annular size. Diastolic AL tethering plays a key role in this dynamic process, with increasing AL opening during exercise being associated with higher exercise EOA. EOAI at peak exercise is a strong and independent predictor of exercise capacity and is associated with clinical outcome. Our findings stress the importance of maximizing AL opening by targeting the subvalvular apparatus in future repair algorithms for secondary mitral regurgitation.

Curr Heart Fail Rep. 2015 Dec;12(6):367-78.

Current Approach to Decongestive Therapy in Acute Heart Failure.

Martens P, Nijst P, Mullens W.

Abstract

Congestion, defined by elevated cardiac filling pressures, is the major driver of hospitalization in acute decompensated heart failure. Careful clinical assessment should allow to determine whether volume overload or volume misdistribution is the predominating mechanism of congestion. Differentiation is imperative because therapy differs. If volume overloads prevails, loop diuretics are considered the mainstay therapy. However, early use of combination therapy with diuretics acting more proximal or distal in the nephron could allow for a more profound natriuresis and diuresis. A stepped guided pharmacological treatment should focus on achieving complete decongestion, because persistent congestion is a major driver of readmission. If diuretic strategies remain unsuccessful, ultrafiltration should be considered. Ultrafiltration should be used with caution in the setting of worsening of renal function. When volume misdistribution and impaired venous capacitance predominate the picture of congestion, unloading-more than diuretics-with arteriolar and venous vasodilators might mitigate the clinical picture of congestion. This review offers a thorough overview and practical insight in the use of current and potential decongestive therapies.

J Am Coll Cardiol. 2015 Feb 10;65(5):480-92.

Hyponatremia in acute decompensated heart failure: depletion versus dilution.

Verbrugge FH, Steels P, Grieten L, Nijst P, Tang WH, Mullens W.

Abstract

Hyponatremia frequently poses a therapeutic challenge in acute decompensated heart failure (ADHF). Treating physicians should differentiate between depletion versus dilutional hyponatremia. The former is caused by diuretic agents, which enhance sodium excretion, often with concomitant potassium/magnesium losses. This can be treated with isotonic

saline, whereas potassium/magnesium administration may be helpful if plasma concentrations are low. In contrast, as impaired water excretion, rather than sodium deficiency, is the culprit in dilutional hyponatremia, isotonic saline administration may further depress the serum sodium concentration. Because free water excretion is achieved by continuous sodium reabsorption in distal nephron segments with low water permeability, diuretic agents that impair this mechanism (e.g., thiazide-type diuretic agents and mineralocorticoid receptor antagonists) should be avoided, and proximally acting agents (e.g., acetazolamide and loop diuretic agents) are preferred. Vasopressin antagonists, which promote low water permeability in the collecting ducts and, hence, free water excretion, remain under investigation for dilutional hyponatremia in ADHF.

JACC Heart Fail. 2015 Feb;3(2):108-11.

Renin-Angiotensin-aldosterone system activation during decongestion in acute heart failure: friend or foe?

Verbrugge FH, Tang WH, Mullens W.

J Geatr Cardiol. 2015 Jan; 12(1):76-82.

The role of extracellular matrix in age-related conduction disorders: a forgotten player?

Spadaccio C, Rainer A, Mozetic P, Trombetta M, Dion Ra, Barbato R, Nappi F, Chello M

Echocardiography. 2015 Mar;32(3):557-64.

The figure-of-eight artifact in the echocardiographic assessment of percutaneous disc occluders: impact of imaging depth and device type.

Bertrand PB, Grieten L, Smeets CJ, Verbrugge FH, Mullens W, Vrolix M, Rivero-Ayerza M, Verhaert D, Vandervoort PM.

Abstract

PURPOSE: Echocardiography is increasingly important in the guidance and follow-up of percutaneous transcatheter device closures. It was recently shown that the Amplatzer left atrial appendage occluder frequently presents as a figure-of-eight artifact due to interaction of device mesh and ultrasound waves. It remains unknown whether this can

be translated to other types of disc occluders. Furthermore, the morphology of this figure-of-eight artifact appears to be different in the transesophageal and transthoracic image of the same device. The aim of this study was to evaluate the echocardiographic appearance of different types of disc occluders, and to clarify differences in morphology of the figure-of-eight artifact.

METHODS: A mathematical model of an epitrochoid curve was used for numerical simulation of disc occluder appearance at various imaging depths. In addition, an in vitro setup was used for echocardiographic analysis of different types of disc occluders at adjustable imaging depth and position.

RESULTS: Mathematically, decreasing the imaging depth resulted in a more asymmetric figure-of-eight, i.e. with small upper part and wide lower part. In vitro results were in close agreement with the mathematical results. In addition, in vitro a figure-of-eight artifact was obtained in all different types of disc occluder devices.

CONCLUSIONS: Different types of percutaneous disc occluders all present as a figure-of-eight artifact on echocardiography when imaged from a coronal imaging position. The morphology of the artifact depends on the imaging depth, with a more asymmetric figure-of-eight morphology at smaller probe-to-device distance. This clarifies the differences observed between transesophageal and transthoracic imaging.

Acta Cardiol. 2015 Dec;70(6):747-9.

Targeted capture sequencing in a large LQTS family reveals a new pathogenic mutation c.2038delG in KCNH2 initially missed due to allelic dropout.

Robyns T, Kuiperi C, Willems R, Corveleyn A, Nuyens D.

Abstract

We present a new mutation in KCNH2 (c.2038delG) resulting in a frameshift and premature truncation of the IKr channel protein in a large LQTS family with several sudden death cases. This mutation was initially missed by mutation scanning with DHPLC due to allelic dropout and only retrieved after repeat genetic testing with targeted capture and massive parallel

sequencing. There was full penetrance of this mutation, only if an individualized QT correction derived from 24-hour Holter data was used. This case again underscores the importance of repeat genetic testing in robust cases of LQTS that remained genotype negative with mutation scanning techniques.

Ann Noninvasive Electrocardiol. 2015 Aug 25.

Evaluation of Index of Cardio-Electrophysiological Balance (iCEB) as a New Biomarker for the Identification of Patients at Increased Arrhythmic Risk.

Robyns T, Lu HR, Gallacher DJ, Garweg C, Ector J, Willems R, Janssens S, Nuyens D.

Abstract

BACKGROUND: Recently a new risk marker for drug-induced arrhythmias called index of cardio-electrophysiological balance (iCEB), measured as QT interval divided by QRS duration, was evaluated in an animal model. It was hypothesized that iCEB is equivalent to the cardiac wavelength λ (λ = effective refractory period (ERP) x conduction velocity) and that an increased or decreased value of iCEB would potentially predict an increased susceptibility to TdP or non-TdP mediated VT/VF, respectively.

METHODS: First, the correlation between QT interval and ERP was evaluated by invasively measuring ERP during a ventricular stimulation protocol in humans (N = 40). Then the effect of administration of sotalol and flecainide on iCEB was measured in 40 patients with supraventricular tachycardias. Finally iCEB was assessed in carriers of a long QT syndrome (LQTS, N = 70) or Brugada syndrome (BrS, N = 57) mutation and compared them with genotype negative family members (N = 65).

RESULTS: The correlation between QT interval and ERP was established (Pearson $R^2 = 0.25$) which suggests that $iCEB \approx ERP \times CV \approx QT / QRS$. Sotalol administration increased iCEB (+ 0.23; $P = 0.01$), while it decreased with the administration of flecainide (-0.21, $P = 0.03$). In the LQTS group iCEB was increased (5.22 ± 0.93 , $P < 0.0001$) compared to genotype negative family members (4.24 ± 0.5), while it was decreased in the BrS group (3.52 ± 0.43 , $P < 0.0001$).

CONCLUSIONS: Our data suggest that iCEB (QT/QRS) is a simple but effective ECG surrogate of cardiac wavelength. iCEB is increased in situations that predispose to TdP and is decreased in situations that predispose to non-TdP mediated VT/VF. Therefore, iCEB might serve as a non-invasive and readily measurable marker to detect increased arrhythmic risk.

Eurpace. 2015 Jan;17(1):152-9.

Left ventricular four-dimensional rotational angiography with low radiation dose through interphase registration.

Wielandts JY, De Buck S, Ector J, Nuyens D, Maes F, Heidbuchel H.

Abstract

AIMS: Ventricular tachycardia ablations could benefit from four-dimensional (4D) (dynamic 3D) visualization of the left ventricle (LV) as roadmap for anatomy-guided procedures. Our aim was to develop an algorithm that combines information of several cardiac phases to improve signal-to-noise ratio in low-dose, noisy rotational angiography [three-dimensional rotational angiography (3DRA)] image datasets, enabling semi-automatic segmentation and generation of 4D rotational angiography (4DRA) LV surface models.

METHODS AND RESULTS: We developed a novel slow pacing protocol for low-dose 4DRA imaging and applied interphase registration (IPR) to improve contrast-to-noise ratio (CNR) such that 4D LV segmentation could be achieved using a single iso-intensity value (ISO). The method was applied to construct four-phase dynamic LV models from five porcine experiments. Optimal choice of IPR and ISO parameters and resulting LV model accuracy were assessed by comparison with 'groundtruth' manual LV delineations using surface distance measures [root mean square distance (RMSD), Hausdorff distance (HD), fraction of surface distances ≤ 3 mm (d3 mm)]. Using IPR with optimized parameters, CNR improved by 88% ($P < 0.0001$) and increased segmentation accuracy was proven irrespective of ISO. Significant improvement was achieved in RMSD [mean at optimal ISO: -28.3% (95% confidence interval (CI) -21.7 to -35.0, $P < 0.0001$), HD [-21.4% (95% CI -18.6 to -24.1, $P < 0.0001$), and

d3 mm [+7.8% (95% CI +4.6 to +10.9, $P < 0.0001$)]. An average d3 mm of $95.6 \pm 2.8\%$ was reached at optimal ISO. Time to generate a 4D model was ± 11.5 min with IPR vs. ± 22 min without.

CONCLUSION: Interphase registration significantly improves 4DRA image quality and facilitates semi-automatic segmentation, resulting in clinically useful accuracy despite low-dose image acquisition protocols, while shortening 4D model generation time. This opens the prospect of 4D imaging in clinical settings.

Eur J Cardiothorac Surg. 2015 Apr;47(4):703-9.

Bilateral internal thoracic artery grafting increases long-term survival in elderly patients.

Pettinari M, Sergeant P, Meuris B.

Abstract

OBJECTIVES: Bilateral internal thoracic artery (BITA) grafting is extensively underused in coronary artery bypass graft surgery and it is mostly preserved for patients under the age of 70. The purpose of the present study was to compare outcomes in propensity score-matched patients aged 70 years or greater using a BITA, with patients using a single internal thoracic artery (SITA) graft.

METHODS: Among 18 761 patients operated on in our unit until December 2006, we selected 3496 patients aged 70 years or greater; of these, 1328 received a BITA (BITA group) and 2168 received a SITA (SITA group). Propensity score matching was used to reduce the preoperative patient variability. The 3-month and 10-year survival, stroke, myocardial infarction and sternal wound complication rate (defined as sternal instability or need for refixation) were compared between the two groups.

RESULTS: After the correction, 892 patients per group were selected. Survival at 3 months was 90.6% in the SITA group and 91.6% in the BITA group ($P = 0.34$) and at 10 years was 38.9 and 57.5% ($P = 0.02$), respectively. The rates of stroke (1.01 vs 1.12%, $P = 1$), myocardial infarction (1.91 vs 2.13%, $P = 0.86$) and sternal wound complications (3.30 vs 5.42%, $P = 0.17$) were all similar between the SITA and BITA groups, respectively.

CONCLUSIONS: The use of BITA grafting in elderly patients improves the 10-year survival rate, with similar postoperative morbidity. Thus, using adequate selection criteria, this technique should be routinely extended also to patients older than 70 years.

Eur Heart J. 2015 Jan 14;36(3):158-69.

EuroEco (European Health Economic Trial on Home Monitoring in ICD Patients): a provider perspective in five European countries on costs and net financial impact of follow-up with or without remote monitoring.

Heidbuchel H, Hindricks G, Broadhurst P, Van Erven L, Fernandez-Lozano I, Rivero-Ayerza M, Malinowski K, Marek A, Romero Garrido RF, Löscher S, Beeton I, Garcia E, Cross S, Vijgen J, Koivisto UM, Peinado R, Smala A, Annemans L.

Abstract

AIM: Remote follow-up (FU) of implantable cardiac defibrillators (ICDs) allows for fewer in-office visits in combination with earlier detection of relevant findings. Its implementation requires investment and reorganization of care. Providers (physicians or hospitals) are unsure about the financial impact. The primary end-point of this randomized prospective multicentre health economic trial was the total FU-related cost for providers, comparing Home Monitoring facilitated FU (HM ON) to regular in-office FU (HM OFF) during the first 2 years after ICD implantation. Also the net financial impact on providers (taking national reimbursement into account) and costs from a healthcare payer perspective were evaluated.

METHODS AND RESULTS: A total of 312 patients with VVI- or DDD-ICD implants from 17 centres in six EU countries were randomised to HM ON or OFF, of which 303 were eligible for data analysis. For all contacts (in-office, calendar- or alert-triggered web-based review, discussions, calls) time-expenditure was tracked. Country-specific cost parameters were used to convert resource use into monetary values. Remote FU equipment itself was not included in the cost calculations. Given only two patients from Finland (one in each group) a monetary valuation analysis was not performed for Finland. Aver-

age age was 62.4 ± 13.1 years, 81% were male, 39% received a DDD system, and 51% had a prophylactic ICD. Resource use with HM ON was clearly different: less FU visits (3.79 ± 1.67 vs. 5.53 ± 2.32 ; $P < 0.001$) despite a small increase of unscheduled visits (0.95 ± 1.50 vs. 0.62 ± 1.25 ; $P < 0.005$), more non-office-based contacts (1.95 ± 3.29 vs. 1.01 ± 2.64 ; $P < 0.001$), more Internet sessions (11.02 ± 15.28 vs. 0.06 ± 0.31 ; $P < 0.001$) and more in-clinic discussions (1.84 ± 4.20 vs. 1.28 ± 2.92 ; $P < 0.03$), but with numerically fewer hospitalizations (0.67 ± 1.18 vs. 0.85 ± 1.43 , $P = 0.23$) and shorter length-of-stay (6.31 ± 15.5 vs. 8.26 ± 18.6 ; $P = 0.27$), although not significant. For the whole study population, the total FU cost for providers was not different for HM ON vs. OFF [mean (95% CI): €204 (169-238) vs. €213 (182-243); range for difference (€-36 to 54), NS]. From a payer perspective, FU-related costs were similar while the total cost per patient (including other physician visits, examinations, and hospitalizations) was numerically (but not significantly) lower. There was no difference in the net financial impact on providers [profit of €408 (327-489) vs. €400 (345-455); range for difference (€-104 to 88), NS], but there was heterogeneity among countries, with less profit for providers in the absence of specific remote FU reimbursement (Belgium, Spain, and the Netherlands) and maintained or increased profit in cases where such reimbursement exists (Germany and UK). Quality of life (SF-36) was not different.

CONCLUSION: For all the patients as a whole, FU-related costs for providers are not different for remote FU vs. purely in-office FU, despite reorganized care. However, disparity in the impact on provider budget among different countries illustrates the need for proper reimbursement to ensure effective remote FU implementation.

J Thorac Oncol. 2015 Oct;10(10):1458-67.

Safety and Immunogenicity of MAGE-A3 Cancer Immunotherapeutic with or without Adjuvant Chemotherapy in Patients with Resected Stage IB to III MAGE-A3-Positive Non-Small-Cell Lung Cancer.

Pujol JL, Vansteenkiste JF, De Pas TM, Atanackovic D, Reck M, Thomeer M, Douil-

lard JY, Fasola G, Potter V, Taylor P, Bosquée L, Scheubel R, Jarnjak S, Debois M, de Sousa Alves P, Louahed J, Brichard VG, Lehmann FF.

Abstract

INTRODUCTION: To assess the safety and immunogenicity of MAGE-A3 immunotherapeutic in patients with stage IB-III MAGE-A3-positive non-small-cell lung cancer (NSCLC) who were or were not undergoing standard cisplatin/vinorelbine chemotherapy.

METHODS: This open, prospective, multicenter, parallel-group phase I study (NCT00455572) enrolled patients with resected (cohorts 1-3) or unresectable (cohort 4) MAGE-A3-positive NSCLC. MAGE-A3 immunotherapeutic (300 µg recombinant MAGE-A3 formulated with AS15) was administered (eight doses, 3 weeks apart) concurrent with (cohort 1), after (cohort 2), or without (cohort 3) standard-adjuvant chemotherapy, or after standard radiotherapy and/or chemotherapy (cohort 4).

RESULTS: Sixty-seven patients received greater than or equal to 1 dose of MAGE-A3 immunotherapeutic. Grade 3/4 adverse events (AEs) were reported for 16 out of 19 (84%), 2 out of 18 (11%), 5 out of 18 (28%), and 1 out of 12 (8%) patients in cohorts 1, 2, 3, and 4, respectively. Many grade 3/4 AEs in cohort 1 (e.g., neutropenia) were typical of chemotherapy. Six patients, including three in cohort 1, reported study treatment-related grade 3/4 AEs (injection-site reactions or musculoskeletal/back pain, which resolved within 5 days). One patient (in cohort 4) died, but this and the other serious adverse events were not study treatment related. MAGE-A3-specific antibody responses to immunotherapy were induced in all patients evaluated in all cohorts. MAGE-A3-specific CD4 T-cell responses to immunotherapy were detected in 4 out of 11 (36%), 4 out of 15 (27%), 2 out of 8 (25%), and 5 out of 6 (83%) evaluated patients in cohorts 1, 2, 3, and 4, respectively; and CD8 T-cell responses were only detected in four patients.

CONCLUSION: In resected and unresectable NSCLC patients and irrespective of whether standard chemotherapy was concurrent or not, MAGE-A3 immunotherapeutic is well tolerated and induces MAGE-A3-specific immune responses.

J Thorac Oncol. 2015 Jun;10(6):e46.

Metabolomics a novel biomarker in lung cancer.

Stinkens K, Vanhove K, Thomeer M.

J Am Soc Echocardiogr. 2015 Nov;28(11):1376-7.

Mirror artifacts in two-dimensional echocardiography: don't forget objects in the third dimension.

Bertrand PB, Verhaert D, Vandervoort PM.

J Med Internet Res. 2015 Jul 23;17(7):e185.

Medium-Term Effectiveness of a Comprehensive Internet-Based and Patient-Specific Telerehabilitation Program With Text Messaging Support for Cardiac Patients: Randomized Controlled Trial.

Frederix I, Hansen D, Coninx K, Vandervoort P, Vandijck D, Hens N, Van Craenenbroeck E, Van Driessche N, Dendale P.

Abstract

BACKGROUND: Cardiac telerehabilitation has been introduced as an adjunct or alternative to conventional center-based cardiac rehabilitation to increase its long-term effectiveness. However, before large-scale implementation and reimbursement in current health care systems is possible, well-designed studies on the effectiveness of this new additional treatment strategy are needed.

OBJECTIVE: The aim of this trial was to assess the medium-term effectiveness of an Internet-based, comprehensive, and patient-tailored telerehabilitation program with short message service (SMS) texting support for cardiac patients.

METHODS: This multicenter randomized controlled trial consisted of 140 cardiac rehabilitation patients randomized (1:1) to a 24-week telerehabilitation program in combination with conventional cardiac rehabilitation (intervention group; n=70) or to conventional cardiac rehabilitation alone (control group; n=70). In the telerehabilitation program, initiated 6 weeks after the start of ambulatory rehabilitation, patients were stimulated to increase physical activity levels. Based on registered activity data, they received semiautomatic telecoaching via email and SMS text message encouraging them to gradu-

ally achieve predefined exercise training goals. Patient-specific dietary and/or smoking cessation advice was also provided as part of the telecoaching. The primary endpoint was peak aerobic capacity (VO₂ peak). Secondary endpoints included accelerometer-recorded daily step counts, self-assessed physical activities by International Physical Activity Questionnaire (IPAQ), and health-related quality of life (HRQL) assessed by the HeartQoL questionnaire at baseline and at 6 and 24 weeks. **RESULTS:** Mean VO₂ peak increased significantly in intervention group patients (n=69) from baseline (mean 22.46, SD 0.78 mL/[min*kg]) to 24 weeks (mean 24.46, SD 1.00 mL/[min*kg], P<.01) versus control group patients (n=70), who did not change significantly (baseline: mean 22.72, SD 0.74 mL/[min*kg]; 24 weeks: mean 22.15, SD 0.77 mL/[min*kg], P=.09). Between-group analysis of aerobic capacity confirmed a significant difference between the intervention group and control group in favor of the intervention group (P<.001). At 24 weeks, self-reported physical activity improved more in the intervention group compared to the control group (P=.01) as did the global HRQL score (P=.01).

CONCLUSIONS: This study showed that an additional 6-month patient-specific, comprehensive telerehabilitation program can lead to a bigger improvement in both physical fitness (VO₂ peak) and associated HRQL compared to center-based cardiac rehabilitation alone. These results are supportive in view of possible future implementation in standard cardiac care.

BMC Cardiovasc Disord. 2015 May 7;15:29.

Telerehab III: a multi-center randomized, controlled trial investigating the long-term effectiveness of a comprehensive cardiac telerehabilitation program--rationale and study design.

Frederix I, Hansen D, Coninx K, Vandervoort P, Van Craenenbroeck EM, Vrints C, Dendale P.

Abstract

BACKGROUND: Telerehabilitation has been proposed as an adjunct/alternative to standard center-based cardiac rehabilitation. Two recent systematic reviews showed non-inferiority and/or superiority of this remote ap-

proach for cardiac rehabilitation. However, these trials focused only on one core component of cardiac rehabilitation and telemonitoring, rather than implementing a more comprehensive approach. The aim of Telerehab III is to investigate the long-term effectiveness of the addition of a patient-tailored, internet-based telerehabilitation program implementing multiple cardiac rehabilitation core components and using both telemonitoring and telecoaching strategies to standard cardiac rehabilitation.

METHODS/DESIGN: In this prospective, multi-center randomized, controlled trial 140 patients with coronary artery disease and/or chronic heart failure patients will be recruited between February 2013 and February 2015. Patients will be randomized 1:1 to an intervention group (receiving an internet-based telerehabilitation program in addition to standard cardiac rehabilitation) or to standard cardiac rehabilitation alone. The mean follow-up is at least 6 months. The primary endpoint is peak oxygen consumption (VO₂ peak). Secondary endpoints include measured and self-reported daily physical activity, cardiovascular risk factor control, health-related quality of life, days lost due to (non)cardiovascular rehospitalizations and time to first (non)cardiovascular rehospitalization. A clinical event committee blinded to treatment allocation assesses causes of rehospitalizations.

DISCUSSION: Telerehab III will be one of the first studies to examine the added value of a more comprehensive cardiac telerehabilitation program, focusing on multiple cardiac rehabilitation core components. It has the potential to augment current standard center-based cardiac rehabilitation practices and to be used as a model for other disease prevention programs.

Eur J Gen Pract. 2015;21(3):156-63.

Heart-type fatty acid binding protein (H-FABP) in patients in an emergency department setting, suspected of acute coronary syndrome: optimal cut-off point, diagnostic value and future opportunities in primary care.

Willemsen RT, van Severen E, Vandervoort PM, Grieten L, Buntinx F, Glatz JF, Dinant GJ.

Abstract

BACKGROUND: Most patients presenting

chest complaints in primary care are referred to secondary care facilities, whereas only a few are diagnosed with acute coronary syndrome (ACS).

OBJECTIVE: The aim is to determine the optimal cut-off value for a point-of-care heart-type fatty acid binding protein (H-FABP) test in patients presenting to the emergency department and to evaluate a possible future role of H-FABP in safely ruling out ACS in primary care.

METHODS: Serial plasma H-FABP (index test) and high sensitivity troponin T (hs-cTnT) (reference test) were determined in patients with any new-onset chest complaint. In a receiver operating characteristic (ROC) curve, the optimal cut-off value of H-FABP for ACS was determined. Predictive values of H-FABP for ACS were calculated.

RESULTS: For 202 consecutive patients (prevalence ACS 59%), the ROC curve based on the results of the first H-FABP was equal to the ROC curve of hs-cTnT (AUC 0.79 versus 0.80). Using a cut-off value of 4.0 ng/ml for H-FABP, sensitivity for ACS of the H-FABP (hs-cTnT) tests was 73.9% (70.6%). Negative predictive value (NPV) of H-FABP for ACS in a population representative for primary care (incidence of ACS 22%) thus could reach 90.8%.

CONCLUSION: In patients presenting chest pain, plasma H-FABP reaches the highest diagnostic value when a cut-off value of 4 ng/ml is used. Diagnostic values of an algorithm combining point-of-care H-FABP measurement and a score of signs and symptoms should be studied in primary care, to learn if such an algorithm could safely reduce referral rate by GPs.

Am J Cardiol. 2015 Apr 1;115(7):918-23.

Comparison of left ventricular torsion and strain with biventricular pacing in patients with underlying right bundle branch block versus those with left bundle branch block.

De S, Popović ZB, Verhaert D, Dresing T, Wilkoff B, Starling R, Tang WH, Thomas JD, Grimm RA.

Abstract

The benefits of biventricular pacing in patients with cardiac resynchronization therapy (CRT) remain poorly understood in those with right bundle branch block

(RBBB). The aim of this study was to examine the differences in several speckle tracking-derived parameters, including left ventricular torsion and longitudinal strain with CRT on and off for patients with underlying left bundle branch block (LBBB) and RBBB. Twelve patients with CRT and RBBB were compared with a similar group of patients with underlying LBBB who were sent for evaluation and atrioventricular optimization. Echocardiographic images were acquired with biventricular pacing on and off. The 2 groups had similar baseline characteristics, including age, the ejection fraction, and QRS duration. During intrinsic conduction (CRT off), patients with LBBB had lower torsion angles than those with RBBB ($2.3 \pm 1.0^\circ$ in those with LBBB vs $6.3 \pm 1.0^\circ$ in those with RBBB, $p = 0.03$) but trended toward improvements in torsional parameters, including torsional angle and peak untwisting velocity with CRT on, whereas these parameters worsened in patients with RBBB. Compared with CRT off, analyses of septal and lateral strain curves showed significant improvements in septal strain during 100% and 200% of systole with CRT on in patients with LBBB, whereas biventricular pacing resulted in a trend toward worsening of septal strain in patients with RBBB. Negligible changes were noted in lateral strain values. In conclusion, CRT favorably improves regional mechanics in patients with LBBB primarily involving the ventricular septum, with a negligible positive impact on cardiac function in patients with underlying RBBB.

Osteoporos Int. 2015 Jul;26(7):2043.

Erratum to: Hypophosphatemic osteomalacia: an unusual clinical presentation of multiple myeloma.

Reyskens M, Sleurs K, Verresen L, Janssen M, van den Bergh J, Geusens P.

Osteoporos Int. 2015 Jul;26(7):2039-42.

Hypophosphatemic osteomalacia: an unusual clinical presentation of multiple myeloma.

Reyskens M, Sleurs K, Verresen L, Janssen M, van den Bergh J, Geusens P.

Acta Cardiol. 2015 Oct;70(5):516-21.

The STIB score: a simple clinical test to predict clopidogrel resistance.

Legrand D, Barbato E, Chenu P, Magne J, Vrolix M, Wijns W, Legrand V; STIB investigators.

Abstract

BACKGROUND: High platelet reactivity (HPR) to clopidogrel is associated with an increased risk of ischaemic complications during and after coronary interventions and concerns up to 50% of patients undergoing PCI.

AIM OF THE STUDY: The aim of the study was to identify patients with HPR to clopidogrel using bedside clinical information obtained in the Stent Thrombosis In Belgium (STIB) trial.

METHODS: Data on platelet reactivity using the VerifyNow® point-of-care assay were obtained in 844 patients undergoing PCI for stable coronary artery disease 12 to 24 hours after a 600-mg loading dose of clopidogrel was given. Demographic, clinical and baseline routine biological tests were obtained and compared with P2Y12 reaction units (PRU). Patients with PRU>230 (HPR) were considered as non-responders to clopidogrel.

RESULTS: HPR was observed in 424/844 pts. Age, weight, body mass index (BMI), HPR to aspirin, diabetes, renal failure (MDRD<60 ml/min), haemoglobin (Hb), haematocrit, fibrinogen, glycaemia and glycated haemoglobin were associated with HPR to clopidogrel. In multivariate analysis, only Hb (OR: 0.77), BMI (OR: 1.06) and diabetes (OR: 1.62) emerged as independent risk factors. Hb<13.9 g/dl, BMI>28 kg/m² and presence of diabetes were equally associated to predict HPR and can be added to derive a simple score to predict clopidogrel resistance. Although 38.5% of patients without a single clinical predictor still have HPR, 2/3 patients with 2 or 3 risk factors are resistant to clopidogrel.

CONCLUSIONS: STIB HPR score allows identification of patients with a high probability of resistance to clopidogrel based on diabetes, Hb<13.9 g/dl and BMI>28 kg/m². This bedside clinical test could be useful for the identification of patients in whom another P2Y12 inhibitor should be recommended before and after PCI.

EuroIntervention. 2015 Dec;11(8):885-94.

Incidence and potential mechanism of resolved, persistent and newly acquired malapposition three days after implantation of self-expanding or

balloon-expandable stents in a STEMI population: insights from optical coherence tomography in the APPPOSITION II study.

Nakatani S, Onuma Y, Ishibashi Y, Karanasos A, Regar E, Garcia-Garcia HM, Tamburino C, Fajadet J, Vrolix M, Witzensbichler B, Eeckhout E, Spaulding C, Reczuch K, La Manna A, Spaargaren R, Capodanno D, Van Langenhove G, Verheye S, Serruys PW, van Geuns RJ.

Abstract

AIMS: The aim of the current study was to investigate the frequency and mechanisms of sequential incomplete stent apposition (ISA) changes such as persistent, resolved or newly acquired ISA during the first three days after primary PCI (pPCI) in a matched segment-level analysis, with the comparison between self-expanding and balloon-expandable stents assessed by optical coherence tomography (OCT).

METHODS AND RESULTS: The current analysis is a substudy of the APPPOSITION II study that included 69 patients (self-expanding: 35, balloon-expandable: 34) using serial optical coherence tomography (OCT) post procedure and three days after pPCI. In order to evaluate a temporal change in ISA, stented regions were segmented using fiducial landmarks. In a total of 228 corresponding segments, persistent and newly acquired ISA were less frequently observed in self-expanding stents than in balloon-expandable stents (11.5% vs. 33.9%, $p<0.01$, 2.7% vs. 14.8%, $p<0.01$, respectively). New appearances of ISA were caused by tissue resorption, vasorelaxation and "early" recoil in balloon-expandable stents, and only tissue resorption in self-expanding stents.

CONCLUSIONS: Three days after pPCI, tissue resorption and vasorelaxation were biological factors associated with new appearance of ISA while "early" recoil of balloon-expandable stents was a mechanical factor. Both persistent ISA and newly acquired ISA occurred less frequently in self-expanding stents, resulting in a low number of ISA segments compared to balloon-expandable stents. Clinical Trials Registration Information: Randomised Comparison Between the STENTYS Self-expanding Coronary Stent and a Balloon-expandable Stent in Acute Myocardial Infarction (APPOSITION II).

N Engl J Med. 2015 Feb 5;372(6):519-27.

Efficacy of a device to narrow the coronary sinus in refractory angina.

Verheye S, Jolicœur EM, Behan MW, Pettersson T, Sainsbury P, Hill J, Vrolix M, Agostoni P, Engstrom T, Labinaz M, de Silva R, Schwartz M, Meyten N, Uren NG, Doucet S, Tanguay JF, Lindsay S, Henry TD, White CJ, Edelman ER, Banai S.

Abstract

BACKGROUND: Many patients with coronary artery disease who are not candidates for revascularization have refractory angina despite standard medical therapy. The balloon-expandable, stainless steel, hourglass-shaped, coronary-sinus reducing device creates a focal narrowing and increases pressure in the coronary sinus, thus redistributing blood into ischemic myocardium.

METHODS: We randomly assigned 104 patients with Canadian Cardiovascular Society (CCS) class III or IV angina (on a scale from I to IV, with higher classes indicating greater limitations on physical activity owing to angina) and myocardial ischemia, who were not candidates for revascularization, to implantation of the device (treatment group) or to a sham procedure (control group). The primary end point was the proportion of patients with an improvement of at least two CCS angina classes at 6 months.

RESULTS: A total of 35% of the patients in the treatment group (18 of 52 patients), as compared with 15% of those in the control group (8 of 52), had an improvement of at least two CCS angina classes at 6 months ($P=0.02$). The device was also associated with improvement of at least one CCS angina class in 71% of the patients in the treatment group (37 of 52 patients), as compared with 42% of those in the control group (22 of 52) ($P=0.003$). Quality of life as assessed with the use of the Seattle Angina Questionnaire was significantly improved in the treatment group, as compared with the control group (improvement on a 100-point scale, 17.6 vs. 7.6 points; $P=0.03$). There were no significant between-group differences in improvement in exercise time or in the mean change in the wall-motion index as assessed by means of dobutamine echocardiography. At 6 months, 1 patient in the treatment group had had a myocardial infarction; in the control group, 1 patient had died and 3 had had a myocardial infarction.

CONCLUSIONS: In this small clinical trial, implantation of the coronary-sinus reducing device was associated with significant improvement in symptoms and quality of life in patients with refractory angina who were not candidates for revascularization.

EuroIntervention. 2015 Sep;11(5):541-8.

A first-in-man clinical evaluation of Ultimaster, a new drug-eluting coronary stent system: CENTURY study.

Barbato E, Salinger-Martinovic S, Sagic D, Beleslin B, Vrolix M, Neskovic AN, Jagic N, Verheye S, Mehmedbegovic Z, Wijns W.

Abstract

AIMS: To report the six-month angiographic and two-year clinical outcome data from the first-in-man study with the Ultimaster DES, a thin-strut cobalt-chromium sirolimus-eluting stent (SES) with an innovative abluminal-gradient-coated bioresorbable polymer.

METHODS AND RESULTS: CENTURY is a multicentre, single-arm, prospective study that enrolled 105 patients (113 lesions) with coronary artery disease. All patients were scheduled to have an angiographic follow-up at six months, while 45 and 20 patients respectively had IVUS and OCT assessments. The primary endpoint was six-month in-stent late lumen loss. Secondary endpoints included clinical, IVUS and OCT outcomes. Clinical follow-up is available up to two years and will continue up to five years. Procedural success was 97.1% and device success was 100%. Angiographic late loss at six months was 0.04 ± 0.35 mm, also reflected in a low binary restenosis rate of 0.9% and confirmed by IVUS-assessed neointimal volume obstruction of $1.02\pm1.62\%$. The mean strut coverage assessed by OCT was 96.2% with 1.66 ± 4.02 malapposed stent struts. There were no deaths in the study, three (2.9%) periprocedural and one (0.9%) spontaneous myocardial infarction, not related to the target vessel. At one and two years, the target lesion failure rate was 3.8% and 5.7%, while the TLR rate was 1.9% and 2.8%, respectively. There was one acute definite stent thrombosis.

CONCLUSIONS: The Ultimaster™ novel bioresorbable polymer sirolimus-eluting stent demonstrated good performance, including high procedural success and strong suppression of neointimal proliferation at six months.

Good safety and effectiveness were shown up to two years in the studied population.

Catheter Cardiovasc Interv. 2015 Dec 1;86(7):1141-50.

Bioabsorbable polymer-coated sirolimus-eluting stent implantation preserves coronary vasomotion: A DESSOLVE II trial sub-study.

Rusinaru D, Vrolix M, Verheye S, Chowdhary S, Schoors D, Di Mario C, Desmet W, Donohoe DJ, Ormiston JA, Knappe C, Bezerra H, Lansky AJ, Wijns W; DESSOLVE II Investigators.

Abstract

OBJECTIVES: We studied coronary vasomotion in patients treated with the Mistent® absorbable polymer sirolimus-eluting stent (APSES) and in patients implanted with the Endeavor® zotarolimus-eluting stent (ZES). **BACKGROUND:** First generation (1st-gen) drug-eluting stents (DES) induce persistent vasomotor dysfunction in the treated coronary artery. It is unknown whether and to what extent the implantation of an absorbable polymer DES impairs coronary vasomotion.

METHODS: This sub-study of the DESSOLVE II trial included 19 APSES Mistent® and 10 ZES Endeavor® patients. Incremental atrial pacing and quantitative coronary angiography were used to assess vasomotion proximal and distal to the stent and in a reference segment at 9 months after implantation. Percent changes in vessel diameter with pacing versus baseline were calculated and compared. Vasomotor response of the APSES group was also compared with changes observed in a historical group of 17 patients implanted with a 1st-gen sirolimus-eluting stent (SES).

RESULTS: Normal vasomotion (vasodilation) was preserved and of comparable magnitude in the APSES and in the ZES group both proximally ($P=0.34$) and distally ($P=0.38$) to the stent. This finding was not observed in the 1st-gen SES group showing marked pacing-induced vasoconstriction at both stent edges ($P<0.05$ vs. APSES). The results were practically unchanged after excluding patients with absolute changes in vessel diameter $<3\%$ between baseline and maximal pacing.

CONCLUSIONS: The implantation of an absorbable polymer sirolimus-eluting stent is associated with preserved coronary vaso-

motion, comparable to that observed after implantation of the Endeavor®) ZES, and distinct from 1st-gen SES which induce coronary vasomotor dysfunction.

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

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

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

Abstract

AIMS: To investigate the optimal periprocedural antithrombotic strategy in patients on long-term oral anticoagulation (OAC) who require percutaneous coronary intervention with stenting.

METHODS AND RESULTS: The WOEST study was a randomised controlled trial which recruited 573 patients on long-term OAC who underwent PCI. The periprocedural treatment strategy was left to the operator's discretion. To assess the safety and feasibility of uninterrupted oral anticoagulation (UAC) and bridging therapy (BT), bleeding complications and MACCE were assessed in patients treated according to UAC (n=241) and BT (n=322) regimen. After 30 days, as well as after one year, there were no significant differences in bleeding complications (HR 1.14, 95% CI: 0.77-1.69, p=0.51, and HR 1.26, 95% CI: 0.94-1.69, p=0.12, respectively) and MACCE. MACCE tended to be less frequent in the UAC group (respectively HR 0.48, 95% CI: 0.15-1.51, p=0.21, and HR 0.72, 95% CI: 0.46-1.14, p=0.16). Additionally, adjustment with a propensity score revealed no significant differences. Periprocedural INR was not associated with bleeding or MACCE.

CONCLUSIONS: In the WOEST study, UAC was not associated with an increase of bleeding or MACCE compared to bridging therapy. This is the largest study up to now to support the current guidelines.

EuroIntervention. 2015 Apr;10(12):1383-90.

Randomised study of a bioabsorbable polymer-coated sirolimus-eluting stent: results of the DESSOLVE II trial.

Wijns W, Vrolix M, Verheye S, Schoors D,

Slagboom T, Gosselink M, Benit E, Donohoe D, Knappe C, Attizzani GF, Lansky AJ, Ormiston J; DESSOLVE II Investigators.

Abstract

AIMS: To compare the efficacy and safety of the MiStent absorbable polymer sirolimus-eluting stent (APSES) with a zotarolimus-eluting stent (ZES).

METHODS AND RESULTS: The trial was a 2:1 randomisation at 26 sites of 184 patients implanted with an APSES (n=123) versus a ZES (n=61). Following stent implantation, all patients underwent quantitative coronary angiography at baseline and at nine months of follow-up, while a select subgroup also underwent optical coherence tomography (OCT). The primary efficacy hypothesis was superiority of in-stent late lumen loss (LLL) of APSES compared to ZES. At nine months, the primary endpoint was met, with a mean in-stent LLL of 0.27±0.46 mm in 103 APSES patients versus 0.58±0.41 mm in 52 ZES patients (p<0.001). The proportion of uncovered stent struts by OCT at nine months was very low in both groups. The mean neointimal thickness of covered struts (p=0.002) and percent net volume obstruction (p≤0.003) were significantly lower in the APSES than in the ZES group. Major adverse cardiac event and stent thrombosis rates were low and comparable between groups.

CONCLUSIONS: The DESSOLVE II trial demonstrated superiority in the primary efficacy endpoint of nine-month mean LLL for APSES compared to ZES. Strut coverage by OCT was high with both stents and the clinical safety endpoints including stent thrombosis were equally low in both groups.

Metabolomics, 11 (1), p. 225-236. 2015

Phenotyping human blood plasma by 1H-NMR: a robust protocol based on metabolite spiking and its evaluation in breast cancer.

Louis, Evelyne; Bervoets, Liene; Reekmans, Gunter; De Jonge, Eric; Mesotten, Liesbet; Thomeer, Michiel & Adriaenssens, Peter.

Journal of thoracic oncology, 10 (10), p. 1458-1467.

Safety and Immunogenicity of MAGE-A3 Cancer Immunotherapeutic

with or without Adjuvant Chemotherapy in Patients with Resected Stage IB to III MAGE-A3-Positive Non-Small-Cell Lung Cancer.

Pujol, Jean-Louis; Vansteenkiste, Johan F.; De Pas, Tommaso Martino; Atanackovic, Djordje; Reck, Martin; Thomeer, Michiel; Douillard, Jean-Yves; Fasola, Gianpiero; Potter, Vanessa; Taylor, Paul; Bosquee, Lionel; Scheubel, Robert; Jarnjak, Silvija; Debois, Muriel; Alves, Pedro de Sousa; Louahed, Jamila; Brichard, Vincent G. & Lehmann, Frederic F.

Metabolomics, 11 (5), p. 1197-1207. (2015)

Influence of preanalytical sampling conditions on the H-1 NMR metabolic profile of human blood plasma and introduction of the Standard PREanalytical Code used in biobanking.

Bervoets, Liene; Louis, Evelyne; Reekmans, Gunter; Mesotten, Liesbet; Thomeer, Michiel; Adriaenssens, Peter & Linsen, Loes

Metabolomics 2015

Influence of preanalytical sampling conditions on the 1H-NMR metabolic profile of human blood plasma and introduction of the standard preanalytical code used in biobanking.

BERVOETS, Liene; LOUIS, Evelyne; REEKMANS, Gunter; MESOTTEN, Liesbet; THOMEER, Michiel; ADRIAENSENS, Peter & LINSEN, Loes (2015)

Journal of Thoracic Oncology, 10 (6), p. e46. (2015)

Metabolomics a novel biomarker in lung cancer.

Stinkens, Kirsten; Vanhove, Karolien & Thomeer, Michiel

Journal of nuclear medicine, 56 (S3). (2015)

Prognostic value of quantitative FDG PET/CT uptake metrics in NSCLC.

Vanhove, Karolien; Liesbet, Mesotten; Louis, Evelyne; Thomeer, Michiel; Adriaenssens, Peter & Boellaard, Ronald

Osteoporosis Int 2015 Jul;26(7): 2039-2042

Hypophosphatemic osteomalacia: an unusual clinical presentation of multiple myeloma.

Reyskens M, Sleurs K, Verresen L, Janssen M, vd Bergh J, Geusens P.

J Endovasc Ther. 2015 Feb;22(1):1-10.

Superiority of stent-grafts for in-stent restenosis in the superficial femoral artery: twelve-month results from a multicenter randomized trial.

Bosiers M, Deloose K, Callaert J, Verbist J, Hendriks J, Lauwers P, Schroë H, Lansink W, Scheinert D, Schmidt A, Zeller T, Beschorner U, Noory E, Torsello G, Austermann M, Peeters P.

Abstract

PURPOSE: To evaluate the short- and mid-term outcomes of the Viabahn endoprosthesis with Propaten Bioactive Surface vs. standard balloon angioplasty for treatment of in-stent restenosis in the superficial femoral artery.

METHODS: Between June 2010 and February 2012, 83 patients with superficial femoral artery in-stent and Rutherford category 2 to 5 ischemia were enrolled at 7 sites participating in this prospective randomized controlled study (RELIN; ClinicalTrials.gov; identifier NCT01108861). The patients were randomized to treatment with either the heparin-bonded Viabahn endoprosthesis (n = 39: 29 men; mean age 67.7 ± 9.8 years) or a standard angioplasty balloon (n = 44: 32 men; mean age 69.0 ± 9.7 years). The primary effectiveness outcome was primary patency at 12 months, defined as no restenosis/occlusion within the target lesion based on duplex ultrasound and no target lesion revascularization. The primary safety endpoint was the incidence of serious device-related adverse events within 30 days of the procedure.

RESULTS: All patients randomized to receive dilation or the Viabahn stent-graft were treated according to their assignment. The technical success was 100% for the Viabahn group and 81.8% for the angioplasty group (p = 0.002) owing to 9 patients requiring a bailout procedure after unsuccessful angioplasty. The 12-month primary patency rates were 74.8% for the Viabahn group and 28.0% for the angioplasty group (p < 0.001). Excluding the 9 angioplasty patients who received bailout stenting, the primary patency for optimal balloon angioplasty was 37.0% (p < 0.001). Three patients experienced device-related adverse events within 30 days: occlusion of the target lesion (Viabahn group), peripheral embolization (angioplasty

group), and reocclusion of the target lesion (angioplasty group).

CONCLUSION: In this study, the treatment of femoropopliteal in-stent restenosis with a Viabahn endoprosthesis showed significantly better results than treatment with a standard balloon at 1 year.

DIVISIE 3 (ABDOMEN - ZINTUIGEN - GASTRO-ENTEROLOGIE - ONCOLOGIE)

MC Geriatr. 2015 Jul 9;15:79.

A cohort study on the evolution of psychosocial problems in older patients with breast or colorectal cancer: comparison with younger cancer patients and older primary care patients without cancer.

Deckx L, van Abbema DL, van den Akker M, van den Broeke C, van Driel M, Bulens P, Tjan-Heijnen VC, Kenis C, de Jonge ET, Houben B, Buntinx F.

Abstract

BACKGROUND: Although older cancer survivors commonly report psychosocial problems, the impact of both cancer and ageing on the occurrence of these problems remains largely unknown. The evolution of depression, cognitive functioning, and fatigue was evaluated in a group of older cancer patients in comparison with a group of younger cancer patients and older persons without cancer.

METHODS: Older (≥ 70 years) and younger cancer patients (50-69 years) with breast or colorectal cancer stage I-III, and older persons without cancer (≥ 70 years) were included. Data were collected at baseline and one year follow-up and were available for 536 persons. Depression was evaluated with the 15-item Geriatric Depression Scale. Cognitive functioning was measured with the cognitive functioning subscale of the European Organization for Research and Treatment of Cancer. Fatigue was measured with a Visual Analogue Scale. Risk factors for depression, cognitive functioning, and fatigue were analysed using multivariate logistic regression analyses. Risk factors included cancer- and ageing-related factors such as functional status, cancer treatment, and comorbidities.

RESULTS: The evolution of psychosocial problems was similar for the group of older ($N = 125$) and younger cancer patients ($N = 196$): an increase in depression ($p < 0.01$), slight worsening in cognitive functioning ($p = 0.01$), and no clear change in fatigue. Also, compared to the group of people without cancer ($N = 215$), the differences were small and after one year of follow-up only depression was more frequent in older cancer patients compared to older persons without cancer (18%

versus 9%, $p = 0.04$). In multivariate analyses the main risk factors for psychosocial problems after one year follow-up were changes in functional status and presence of baseline depression, fatigue, or cognitive impairment.

CONCLUSION: Over the course of one year after a diagnosis of cancer, cancer patients face increasing levels of depression and increasing difficulties in cognitive functioning. The main risk factor for psychosocial problems was presence of the problem at baseline. This calls for regular screening for psychosocial problems and exchange of information on psychosocial functioning between different health care providers and settings during the treatment and follow-up trajectory of cancer patients.

Psychooncology. 2015 Nov;24(11):1521-8.

Loneliness in patients with cancer: the first year after cancer diagnosis.

Deckx L, van den Akker M, van Driel M, Bulens P, van Abbema D, Tjan-Heijnen V, Kenis C, de Jonge ET, Houben B, Buntinx F.

Abstract

OBJECTIVES: We studied the frequency and evolution of social and emotional loneliness in older cancer patients in comparison with younger cancer patients and older people without cancer. We evaluated if changes in common cancer-related and ageing-related problems such as fatigue, cognitive functioning and functional status contributed to the occurrence of loneliness.

METHODS: This study was part of the KLIMOP study (Dutch acronym for project on older cancer patients in Belgium and the Netherlands) and included older (≥ 70 years) and younger cancer patients (50-69 years) and older people without cancer. Data were collected at baseline and 1-year follow-up. Loneliness was measured with the loneliness scale of De Jong-Gierveld. The relationship between loneliness after 1 year and changes in fatigue, cognitive functioning and functional status was tested in multivariate logistic regression analyses.

RESULTS: Data were available for 475 participants. At baseline, older cancer patients were less lonely compared with older people without cancer. After 1 year, the frequency of emotional loneliness had

significantly increased for older cancer patients (26-42%, $p < 0.001$) and had reached levels of older people without cancer. Emotional loneliness also increased for younger cancer patients (25-34%, $p = 0.02$), but not for older people without cancer (40-38%, $p = 0.69$). Frequency of social loneliness did not change significantly. People who were persistently fatigued and people who became or were persistently impaired on cognitive functioning were at increased risk of becoming lonely. **CONCLUSION:** Loneliness, in particular emotional loneliness, is a common problem in cancer patients, and its frequency changes considerably over time.

B-ENT. 2015;11(1):77-80.

Mucocutaneous leishmaniasis of the nose: a case report.

Menten K, Soentjens P, Caenepeel P, Lemkens P.

Abstract

Mucocutaneous leishmaniasis of the nose: a case report. Leishmaniasis is a parasitic infection that is rarely seen in Belgium. The majority of new diagnoses are seen in patients living in or visiting endemic regions, which are mostly developing countries. Here we describe the case of a 60-year-old male patient who was referred to an ENT specialist because of an erythematous swelling of the left side of the nose tip, which had persisted for 3 months. Biopsies showed the presence of leishmaniasis. This case report alerts ENT physicians that leishmaniasis is part of the differential diagnosis in patients who present with an uncommon persistent lesion in the head and neck region and who have travelled to endemic regions or are immunodeficient.

Tongue and cheek metastases as the first clinical sign of a primary cancer.

Menten K, Janssen M, Drieskens O, Lemkens P.

Abstract

Metastases to the oral cavity are rare and are most frequently seen in the jawbones. Soft tissue metastases as the first clinical sign of a metastatic cancer are quite exceptional. In this case report, we des-

cribe the history of a 67-year old patient presenting with painless oral lesions for 4 weeks. Biopsies showed metastases of an adenocarcinoma that was not yet identified. This case report highlights that an ENT physician should consider metastases to the oral cavity as part of the differential diagnosis in every patient with an uncommon, persistent oral lesion with unclear origin.

J Clin Lipidol. 2015 Nov-Dec;9(6):741-50.

Efficacy and safety of rosuvastatin therapy in children and adolescents with familial hypercholesterolemia: Results from the CHARON study.

Braamskamp MJ, Langslet G, McCrindle BW, Cassiman D, Francis GA, Gagné C, Gaudet D, Morrison KM, Wiegman A, Turner T, Kusters DM, Miller E, Raichlen JS, Wissmar J, Martin PD, Stein EA, Kastelein JJ.

Abstract

OBJECTIVE: Heterozygous familial hypercholesterolemia (HeFH) is an autosomal dominant disorder leading to premature atherosclerosis. Guidelines recommend initiating statins early to reduce low-density lipoprotein cholesterol (LDL-C). Studies have evaluated rosuvastatin in children aged ≥ 10 years, but its efficacy and safety in younger children is unknown.

METHODS: Children with HeFH and fasting LDL-C > 4.92 mmol/L (190 mg/dL) or > 4.10 mmol/L (> 158 mg/dL) with other cardiovascular risk factors received rosuvastatin 5 mg daily. Based on LDL-C targets (< 2.85 mmol/L [< 110 mg/dL]), rosuvastatin could be uptitrated to 10 mg (aged 6-9 years) or 20 mg (aged 10-17 years). Treatment lasted 2 years. Changes in lipid values, growth, sexual maturation, and adverse events (AEs) were assessed.

RESULTS: The intention-to-treat analysis included 197 patients. At 24 months, LDL-C was reduced by 43, 45, and 35% vs baseline in patients aged 6-9, 10-13, and 14-17 years, respectively ($P < .001$ for all groups). Most AEs were mild. Intermittent myalgia was reported in 11 (6%) patients and did not lead to discontinuation of rosuvastatin treatment. Serious AEs were reported by 9 (5%) patients, all considered unrelated to treatment by the investigators. No clinically important changes in hepatic biochemistry

were reported. Rosuvastatin treatment did not appear to adversely affect height, weight, or sexual maturation.

CONCLUSIONS: In HeFH patients aged 6-17 years, rosuvastatin 5-20 mg over 2 years significantly reduced LDL-C compared with baseline. Treatment was well tolerated, with no adverse effects on growth or sexual maturation

Acta Gastroenterol Belg. 2015 Jul-Sep;78(3):299-305.

Budd-Chiari syndrome: reassessment of a step-wise treatment strategy.

Martens P, Maleux GA, Devos T, Monbaliu D, Heye S, Verslype C, Laleman W, Cassiman D, Van der Merwe SW, Van Steenberghe W, Jochmans I, Aerts R, Pi-
renne J, Nevens F.

Abstract

BACKGROUND AND STUDY AIMS: The Budd-Chiari syndrome is a rare disorder characterized by hepatic venous outflow obstruction. A step-wise management was recently proposed. The aim of this study is to reassess our treatment approach and long-term outcome.

PATIENTS AND METHODS: The data of 37 Budd-Chiari patients, seen in our unit, were critically analyzed and compared with the ENVIE (European Network For Vascular Disorders of the Liver) data.

RESULTS: Most patients had multiple prothrombotic conditions (41%), of which an underlying myeloproliferative neoplasm was the most frequent (59%). The JAK-2V617F mutation was associated with more complete occlusion of all hepatic veins (JAK2 mutation +: 70% vs JAK2 mutation -: 23% and a higher severity score. The step-wise treatment algorithm used in our unit, in function of the severity of the liver impairment and the number and the extension of hepatic veins occluded, resulted in the following treatments: only anticoagulation ($n = 7.21\%$), recanalization procedure ($n = 4.21\%$), portosystemic shunts ($n = 9.26\%$) and liver transplantation ($n = 14.44\%$). This resulted in a 10 year survival rate of 90%. Treatment of the underlying hemostatic disorder offered a low recurrence rate. None of the 21 patients with a myeloproliferative neoplasm died in relation to the hematologic disorder.

CONCLUSIONS: An individualized treatment regimen consisting of anticoagulation and interventional radiology and/or transplantation when necessary and strict follow-up of the underlying hematologic disorder, provided an excellent long-term survival, which confirm the data of the ENVIE study.

PLoS One. 2015 Aug 6;10(8):e0132701.

Synergistic Activity of the Plant Defensin HsAFP1 and Caspofungin against Candida albicans Biofilms and Planktonic Cultures.

Vriens K, Cools TL, Harvey PJ, Craik DJ, Spincemaille P, Cassiman D, Braem A, Vleugels J, Nibbering PH, Drijfhout JW, De Coninck B, Cammue BP, Thevissen K.

Abstract

Plant defensins are small, cysteine-rich peptides with antifungal activity against a broad range of yeast and fungi. In this study we investigated the antibiofilm activity of a plant defensin from coral bells (*Heuchera sanguinea*), i.e. HsAFP1. To this end, HsAFP1 was heterologously produced using *Pichia pastoris* as a host. The recombinant peptide rHsAFP1 showed a similar antifungal activity against the plant pathogen *Fusarium culmorum* as native HsAFP1 purified from seeds. NMR analysis revealed that rHsAFP1 consists of an α -helix and a triple-stranded antiparallel β -sheet stabilised by four intramolecular disulfide bonds. We found that rHsAFP1 can inhibit growth of the human pathogen *Candida albicans* as well as prevent *C. albicans* biofilm formation with a BIC50 (i.e. the minimum rHsAFP1 concentration required to inhibit biofilm formation by 50% as compared to control treatment) of 11.00 ± 1.70 μM . As such, this is the first report of a plant defensin exhibiting inhibitory activity against fungal biofilms. We further analysed the potential of rHsAFP1 to increase the activity of the conventional antimycotics caspofungin and amphotericin B towards *C. albicans*. Synergistic effects were observed between rHsAFP1 and these compounds against both planktonic *C. albicans* cells and biofilms. Most notably, concentrations of rHsAFP1 as low as 0.53 μM resulted in a synergistic activity with caspofungin against pre-grown

C. albicans biofilms. rHsAFP1 was found non-toxic towards human HepG2 cells up to 40 μ M, thereby supporting the lack of a general cytotoxic activity as previously reported for HsAFP1. A structure-function study with 24-mer synthetic peptides spanning the entire HsAFP1 sequence revealed the importance of the γ -core and its adjacent regions for HsAFP1 antibiofilm activity. These findings point towards broad applications of rHsAFP1 and its derivatives in the field of antifungal and antibiofilm drug development.

JIMD Rep. 2015 Jun 21.

Liver Fibrosis Associated with Iron Accumulation Due to Long-Term Heme-Arginate Treatment in Acute Intermittent Porphyrria: A Case Series.

Willandt B, Langendonk JG, Biermann K, Meersseman W, D'Heygere F, George C, Verslype C, Monbaliu D, [Cassiman D](#).

Abstract

Acute intermittent porphyria (AIP) is an autosomal dominant disorder of heme biosynthesis due to a mutation in the δ -aminolevulinic acid dehydratase gene. The mutation causes a deficiency in the δ -aminolevulinic acid dehydratase enzyme, thereby causing an accumulation of heme precursors (δ -aminolevulinic acid and δ -ALA). These neurotoxic heme precursors elicit acute neurovisceral attacks, which can be treated with heme-arginate infusions. Some patients require heme-arginate infusions on a regular basis for many years, which ultimately leads to an iron accumulation (increased serum ferritin and iron accumulation in the liver, spleen, and bone marrow on MRI). We report three AIP patients, who developed iron accumulation (with serum ferritin up to 7,850 microgram/liter) due to multiple heme-arginate infusions. We report for the first time that the iron accumulation in these patients was associated with fibrosis on liver histology.

CONCLUSION: Regular heme-arginate treatment in AIP does not only lead to increased serum ferritin but may also induce liver fibrosis. This should be taken into account, when weighing the risks and benefits of repeated heme-arginate treatment against the risk and benefits of treating refractory AIP by liver transplantation.

Gastroenterology. 2015 Sep;149(3):635-48.e14.

Association of Adipose Tissue Inflammation With Histologic Severity of Nonalcoholic Fatty Liver Disease.

du Plessis J, van Pelt J, Korf H, Mathieu C, van der Schueren B, Lannoo M, Oyen T, Topal B, Fetter G, Nayler S, van der Merwe T, Windmolders P, Van Gaal L, Verrijken A, Hubens G, Gericke M, [Cassiman D](#), Francque S, Nevens F, van der Merwe S.

Abstract

BACKGROUND & AIMS: The prevalence of nonalcoholic fatty liver disease (NAFLD) has increased with the obesity pandemic. We analyzed the transcriptional profiles of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT), and phenotypes and functional characteristics of adipocyte tissue macrophages (ATMs), in obese patients undergoing bariatric surgery.

METHODS: We collected anthropometric data; plasma samples; and SAT, VAT, and liver tissues from 113 obese patients undergoing bariatric surgery at academic hospitals in Europe (Antwerp and Leuven) and South Africa. Based on clinical and histologic features, patients were assigned to the following groups: obese, NAFLD, nonalcoholic steatohepatitis (NASH), or NASH with fibrosis. Microarray analyses were performed to identify genes expressed differentially among groups. We measured levels of cytokines and chemokines in plasma samples and levels of RNAs in adipose tissues by quantitative reverse-transcription polymerase chain reaction. ATMs were isolated from patients and 13 lean individuals undergoing cholecystectomy (controls), analyzed by flow cytometry, and cultured; immunophenotypes and levels of cytokines and chemokines in supernatants were determined.

RESULTS: We observed increased expression of genes that regulate inflammation in adipose tissues from patients with NAFLD and NASH; expression of these genes increased as disease progressed from NAFLD to NASH. We found 111 genes associated with inflammation that were expressed differentially between VAT and SAT. Serum levels of interleukin 8, chemokine (C-C motif) ligand 3, and tumor

necrosis factor- α correlated with liver inflammation and NAFLD activity score. We developed 2 models that could be used to determine patients' liver histology based on gene expression in VAT and SAT. Flow cytometry showed increased proportions of CD11c+CD206+ and CCR2+ macrophages in VAT from patients with NASH, and supernatants of cultured macrophages had increased levels of cytokines and chemokines compared with controls.

CONCLUSIONS: VAT and SAT from patients with NAFLD and NASH have an increased expression of genes that regulate inflammation, and ATMs produce increased levels of inflammatory cytokines, compared with adipose tissues from controls. We identified an expression profile of 5 genes in SAT that accurately predict liver histology in these patients. Transcript profiling: accession numbers: GSE58979 and GSE59045.

Clin Res Hepatol Gastroenterol. 2015 Apr;39(2):205-14.

The quality of hereditary haemochromatosis guidelines: a comparative analysis.

Vanclouster A, [Cassiman D](#), Van Steenberghe W, Swinkels DW, Janssen MC, Drenth JP, Aertgeerts B, Wollersheim H.

Abstract

BACKGROUND AND OBJECTIVES: Hereditary haemochromatosis (HH) is the most prevalent genetic liver disease, with an incidence of 1/200 to 1/400 in the Caucasian population. HH patients are treated by family physicians as well as different specialists. When left untreated or insufficiently treated, the complications can become life threatening. To support and evaluate qualitative care for HH, we evaluated and compared the available structured guidelines on screening, diagnosis and management of HH patients.

METHODS: Seven appraisers systematically reviewed the retrieved guidelines. The Appraisal of Guidelines Research and Evaluation II (AGREE II) was used to score and discuss the quality and reach consensus. The content of recommendations and the evidence behind them, were evaluated.

RESULTS: Three guidelines, developed by the American Association for the Study of Liver Diseases (AASLD), the European As-

sociation for the Study of the Liver (EASL) and a DUTCH guideline were found. Fifty-seven percent of the recommendations were not shared between the guidelines, pointing to inconsistency of their content. Only two references supporting the recommendations were shared between all three guidelines. The AASLD guideline contains no information about management and follow-up. Moreover, the methodological quality of the AASLD guideline was rated insufficient, except for 'clarity and presentation' (77%). Applicability of the guidelines was scored very low in all three (AASLD: 31%, EASL: 23%, DUTCH: 35%). The DUTCH guideline was judged best.

CONCLUSIONS: Very poor consistency between available guidelines for HH hampers qualitative care and its evaluation. An updated high-quality and evidence-based guideline that covers follow-up and management of patients with HH is needed.

JIMD Rep. 2015;18:51-62.

Clinical, Biochemical, and Molecular Characterization of Novel Mutations in ABCA1 in Families with Tangier Disease.

Brunham LR, Kang MH, Van Karnebeek C, Sadananda SN, Collins JA, Zhang LH, Sayson B, Miao F, Stockler S, Frohlich J, Cassiman D, Rabkin SW, Hayden MR.

Abstract

Tangier disease is a rare, autosomal recessive disorder caused by mutations in the ABCA1 gene and is characterized by near absence of plasma high-density lipoprotein cholesterol, accumulation of cholesterol in multiple tissues, peripheral neuropathy, and accelerated atherosclerosis. Here we report three new kindreds with Tangier disease harboring both known and novel mutations in ABCA1. One patient was identified to be homozygous for a nonsense mutation, p.Gln1038*. In a remarkably large Tangier disease pedigree with four affected siblings, we identified compound heterozygosity for previously reported missense variants, p.Arg937Val and p.Thr940Met, and show that both of these mutations result in significantly impaired cholesterol efflux in transfected cells. In a third pedigree, the proband was identified to be compound heterozygous

for two novel mutations, a frameshift (p.Ile1200Hisfs*4) and an intronic variant (c.4176-11T>G), that lead to the creation of a cryptic splice site acceptor and premature truncation, p.Ser1392Argfs*6. We demonstrate that this mutation arose de novo, the first demonstration of a pathogenic de novo mutation in ABCA1 associated with Tangier disease. We also report results of glucose tolerance testing in a Tangier disease kindred for the first time, showing a gene-dose relationship between ABCA1 activity and glucose tolerance and suggesting that Tangier disease patients may have substantially impaired islet function. Our findings provide insight into the diverse phenotypic manifestations of this rare disorder, expand the list of pathogenic mutations in ABCA1, and increase our understanding of how specific mutations in this gene lead to abnormal cellular and physiological phenotypes.

J Oral Maxillofac Res. 2015 Jun 30;6(2):e1.

Coronectomy of Deeply Impacted Lower Third Molar: Incidence of Outcomes and Complications after One Year Follow-Up.

Agbaje JO, Heijsters G, Salem AS, Van Slycke S, Schepers S, Politis C, Vrielinck L.

Abstract

OBJECTIVES: The purpose of present study was to assess the surgical management of impacted third molar with proximity to the inferior alveolar nerve and complications associated with coronectomy in a series of patients undergoing third molar surgery.

MATERIAL AND METHODS: The position of the mandibular canal in relation to the mandibular third molar region and mandibular foramen in the front part of the mandible (i.e., third molar in close proximity to the inferior alveolar nerve [IAN] or not) was identified on panoramic radiographs of patients scheduled for third molar extraction.

RESULTS: Close proximity to the IAN was observed in 64 patients (35 females, 29 males) with an impacted mandibular third molar. Coronectomy was performed in these patients. The most common complication was tooth migration away from the mandibular canal (n = 14), followed

by root exposure (n = 5). Re-operation to remove the root was performed in cases with periapical infection and root exposure.

CONCLUSIONS: The results indicate that coronectomy can be considered a reasonable and safe treatment alternative for patients who demonstrate elevated risk for injury to the inferior alveolar nerve with removal of the third molars. Coronectomy did not increase the incidence of damage to the inferior alveolar nerve and would be safer than complete extraction in situations in which the root of the mandibular third molar overlaps or is in close proximity to the mandibular canal.

J Immunol. 2015 Aug 1;195(3):832-40.

Circulating Follicular Regulatory T Cells Are Defective in Multiple Sclerosis.

Dhaeze T, Peelen E, Hombrouck A, Peeters L, Van Wijmeersch B, Lemkens N, Lemkens P, Somers V, Lucas S, Broux B, Stinissen P, Hellings N.

Abstract

Follicular regulatory T cells (TFR) have been extensively characterized in mice and participate in germinal center responses by regulating the maturation of B cells and production of (auto)antibodies. We report that circulating TFR are phenotypically distinct from tonsil-derived TFR in humans. They have a lower expression of follicular markers, and display a memory phenotype and lack of high expression of B cell lymphoma 6 and ICOS. However, the suppressive function, expression of regulatory markers, and FOXP3 methylation status of blood TFR is comparable with tonsil-derived TFR. Moreover, we show that circulating TFR frequencies increase after influenza vaccination and correlate with anti-flu Ab responses, indicating a fully functional population. Multiple sclerosis (MS) was used as a model for autoimmune disease to investigate alterations in circulating TFR. MS patients had a significantly lower frequency of circulating TFR compared with healthy control subjects. Furthermore, the circulating TFR compartment of MS patients displayed an increased proportion of Th17-like TFR. Finally, TFR of MS patients had a strongly reduced suppressive function compared with healthy control subjects. We conclu-

de that circulating TFR are a circulating memory population derived from lymphoid resident TFR, making them a valid alternative to investigate alterations in germinal center responses in the context of autoimmune diseases, and TFR impairment is prominent in MS.

Acta Gastroenterol Belg. 2015 Jan-Mar;78(1):18-25.

Quality assessment of colonoscopy in Flanders: a voluntary survey among Flemish gastroenterologist.

Macken E, Vannoote J, Moreels T, Peeters M, Wouters K.

Abstract

Colonoscopy is an important endoscopic examination for the diagnosis and treatment of pathological conditions of the colon, like polyps and colorectal cancer. However, several factors determine the quality of colonoscopy and thus the quality of polyp and colorectal cancer detection. The Flemish Society of Gastroenterology (VUGE) performed a voluntary on-line registry among its members to identify quality of colonoscopy in Flanders, Belgium. 64 gastroenterologists voluntarily registered 4276 consecutive colonoscopies performed during a 3 month study period. Colonoscopy quality indicators were prospectively collected and analysed. Results showed a low voluntary participation rate (17%), acceptable overall adenoma detection rate of 20,5% and colorectal cancer interval rate of 5,4%. Complications were low (perforation 0,1% and major bleeding 1,5%). The current study showed that in Flanders, Belgium on-line registration of colonoscopy quality indicators is feasible and that quality of colonoscopy in daily practice meets the expectations of (inter) national guidelines. However, further improvement of the registry and an open debate on the quality control of colonoscopy in Flanders is warranted (Belgian Registry B30020096548).

B-ENT. 2015;11(1):73-6.

Secondary non-Hodgkin lymphoma of the ethmoid sinus after temozolomide.

Broes K, Van Ginderachter L, Joosens E, Maes A, Theunissen K, Schepers S, Deben K, Claes J, Mebis J, Cox T.

Abstract

The paranasal sinuses are rarely the site of malignancy, especially non-Hodgkin lymphoma. In such cases, the ethmoid sinus is the second most frequently involved paranasal sinus. Diagnosis of these malignancies is difficult because the early symptoms often mimic benign sinus pathology. Thus, most cases are diagnosed at an advanced stage, and their prognosis is poor. Here we describe the case of a 58-year-old man with a secondary high-grade B-cell non-Hodgkin lymphoma of the ethmoid sinus. This malignancy was diagnosed two years after the patient had received treatment with temozolomide for a glioblastoma multiforme. This case highlights that malignant tumours of the paranasal sinuses should always be included in the differential diagnosis of sinus disease. Additionally, patients treated with temozolomide should receive regular follow-up care including vigilant evaluation for secondary tumours, such as non-Hodgkin lymphoma.

J Craniomaxillofac Surg. 2015 Oct;43(8):1670-7.

Elevation of the maxillary sinus membrane for de-novo bone formation: First results of a prospective study in humans.

Lie N, Merten HA, Meyns J, Lethaus B, Wiltfang J, Kessler P.

Abstract

PURPOSE: Sinus floor elevation via the lateral window approach represents a reliable technique for bone augmentation in the atrophic posterior maxilla. It is known that sinus membrane elevation leads to new bone formation. This prospective clinical study compared a specific technique in sinus membrane elevation with a conventional sinus floor augmentation (xenogenous/autogenous bone) in a human split mouth model.

METHODS: Five edentulous patients with highly atrophic posterior maxillae were included in this study. On one maxillary side a degradable PDLA-membrane was placed to create a space underneath the sinus membrane. Contralateral a mixture of autogenous and xenogenous bone was used for sinus floor augmentation. A two-stage procedure was carried out.

The following variables were assessed: bone regeneration on cone-beam computed tomography (cone-beam CT), implant success, prosthetic comfort and patient satisfaction. Bone biopsies were taken with simultaneous implant placement. The samples were histologically analyzed. **RESULTS:** Cone-beam CTs revealed new bone formation on both sides. Thirty implants were placed, 15 in the augmented region and 15 in the non-augmented side. Thirty bone biopsies were taken and evaluated. Vital new bone was detected on the experimental side (osteinductivity). On the conventional side a mixture of autogenous and residual bone substitute material was seen (osteoconductivity). Implant survival was 100% so far. Patient's satisfaction was high and prosthetic complications were not encountered.

CONCLUSION: As it provides the highest rate of bone formation, autogenous bone in combination with bone substitute material can be considered as a very reliable standard procedure in sinus floor augmentation. The specific sinus membrane elevation technique as presented here showed satisfying results and might be a suitable alternative for maxillary sinus augmentation.

Plast Reconstr Surg Glob Open. 2015 Jan 8;2(12):e271.

The modifications of the sagittal ramus split osteotomy: a literature review.

Böckmann R, Meyns J, Dik E, Kessler P.

Abstract

BACKGROUND: In 1953, the sagittal ramus split osteotomy was introduced by Obwegeser. For many years, and in some countries still, this technique has defined the term oral and maxillofacial surgery.

METHODS: The basic design of the sagittal ramus split surgical procedure evolved very quickly. The original operation technique by Obwegeser was shortly after improved by Dal Pont's modification. The second major improvement of the basic technique was added by Hunsuck in 1967. Since then, the technical and biological procedure has been well defined. Resolution of the problems many surgeons encountered has, however, taken longer. Some of these problems, such as the un-

favorable split or the damage of the inferior alveolar nerve, have not been satisfactorily resolved.

RESULTS: Further modifications, with or without the application of new instruments, have been introduced by Epker and Wolford, whose modification was recently elaborated by Böckmann. The addition of a fourth osteotomy at the inferior mandibular border in an in vitro experiment led to a significant reduction of the torque forces required for the mandibular split.

CONCLUSIONS: The literature was reviewed, and the last modifications of the successful traditional splitting procedure are presented narrowly. It indicates the better the split is preformatted by osteotomies, the less torque force is needed while splitting, giving more control, a better predictability of the lingual fracture and maybe less neurosensory disturbances of the inferior alveolar nerve.

J Oral Maxillofac Surg. 2015 Feb;73(2):316-23.

In vitro comparison of the sagittal split osteotomy with and without inferior border osteotomy.

Böckmann R, Schön P, Neuking K, Meyns J, Kessler P, Eggeler G.

Abstract

PURPOSE: By adding an osteotomy of the inferior border of the mandibular body to the classic sagittal split osteotomy, the authors expected to prevent unfavorable splits and damage to the inferior alveolar nerve.

MATERIALS AND METHODS: Thirty-five human mandibles were used to perform 70 sagittal split osteotomies as an in vitro study. Conducted as a split-mouth model, each mandible was split at the midline. One side of the mandible was split using the traditional Obwegeser-Dal Pont technique, and the other side was split in the same manner with an additional osteotomy of the inferior mandible border. The torque used to split the mandible was measured, and the fracture line of the mandible was recorded.

RESULTS: The average torque associated with the original technique was 1.38 Nm (standard deviation, 0.60 Nm), with a fracture line along the mandibular canal. The average torque required to split the hemimandible with the modified technique was 1.02 Nm

(standard deviation, 0.50 Nm), a significant ($P < .001$) difference, with a fracture line parallel to the posterior ramus of the mandible. The fracture pattern depended significantly on the technique used ($P < .001$), but not on the applied torque force.

CONCLUSION: By adding an osteotomy of the inferior mandibular border to the sagittal split osteotomy, less torque was needed to split the mandible. The fracture line was more predictable, even when all the surgical manipulations were performed at a safe distance from the inferior alveolar nerve.

Retin Cases Brief Rep. 2015 Spring;9(2):106-8.

Bilateral diffuse uveal melanocytic proliferation with good clinical response to plasmapheresis and treatment of the primary tumor.

Schelvergem KV, Wirix M, Nijs I, Leys A.

Abstract

PURPOSE: To report successful treatment of bilateral diffuse uveal melanocytic proliferation.

METHODS: Case report of a patient with clinical diagnosis of bilateral diffuse uveal melanocytic proliferation, imaged with fluorescein angiography and spectral domain optical coherence tomography, and with follow-up data after treatment with plasmapheresis, radiation, and chemotherapy.

RESULTS: A 67-year-old white man presented with a history of bilateral rapidly declining vision. The ophthalmoscopic examination, fluorescein angiography, and optical coherence tomography showed in both eyes an exudative retinal detachment and subretinal lesions highly suggestive for bilateral diffuse uveal melanocytic proliferation. Further investigation demonstrated a large cell lung carcinoma. Subsequently, the patient was treated with plasmapheresis, radiation, and chemotherapy. In a few weeks, the exudative retinal detachments resolved with gain of vision, and the retina remained flat during the 5-month follow-up.

CONCLUSION: Plasmapheresis and treatment of the primary tumor are valuable treatment options for visually impaired patients with bilateral diffuse uveal melanocytic proliferation.

Int J Drug Policy. 2015 Nov 28. pii: S0955-3959(15)00351-5.

Recommandations pour la prise en charge de l'infection par le virus de l'hépatite C chez les usagers de drogues par injection.

Grebely J, Robaey G, Bruggmann P, Ag-hemo A, Backmund M, Bruneau J, Byrne J, Dalgard O, Feld JJ, Hellard M, Hickman M, Kautz A, Litwin A, Lloyd AR, Mauss S, Prins M, Swan T, Schaefer M, Taylor LE, Dore GJ; l'International Network on Hepatitis among Substance Users (Réseau international sur l'hépatite chez les consommateurs de drogues).

Int J Drug Policy. 2015 Nov 28

Empfehlungen zur Hepatitis Versorgung bei Drogenkonsumierenden.

Grebely J, Robaey G, Bruggmann P, Ag-hemo A, Backmund M, Bruneau J, Byrne J, Dalgard O, Feld JJ, Hellard M, Hickman M, Kautz A, Litwin A, Lloyd AR, Mauss S, Prins M, Swan T, Schaefer M, Taylor LE, Dore GJ; im Namen vom International Network on Hepatitis care in Substance Users.

Int J Drug Policy. 2015 Oct;26(10):1028-38.

Recommendations for the management of hepatitis C virus infection among people who inject drugs.

Grebely J, Robaey G, Bruggmann P, Ag-hemo A, Backmund M, Bruneau J, Byrne J, Dalgard O, Feld JJ, Hellard M, Hickman M, Kautz A, Litwin A, Lloyd AR, Mauss S, Prins M, Swan T, Schaefer M, Taylor LE, Dore GJ; International Network for Hepatitis in Substance Users.

Abstract

In high income countries, the majority of new and existing hepatitis C virus (HCV) infections occur among people who inject drugs (PWID). In many low and middle income countries large HCV epidemics have also emerged among PWID populations. The burden of HCV-related liver disease among PWID is increasing, but treatment uptake remains extremely low. There are a number of barriers to care which should be considered and systematically addressed, but should not exclude PWID from HCV treatment. The rapid development of interferon-free direct-acting

antiviral (DAA) therapy for HCV infection has brought considerable optimism to the HCV sector, with the realistic hope that therapeutic intervention will soon provide near optimal efficacy with well-tolerated, short duration, all oral regimens. Further, it has been clearly demonstrated that HCV treatment is safe and effective across a broad range of multidisciplinary healthcare settings. Given the burden of HCV-related disease among PWID, strategies to enhance HCV assessment and treatment in this group are urgently needed. These recommendations demonstrate that treatment among PWID is feasible and provide a framework for HCV assessment and care. Further research is needed to evaluate strategies to enhance testing, linkage to care, treatment, adherence, viral cure, and prevent HCV reinfection among PWID, particularly as new interferon-free DAA treatments for HCV infection become available.

J Oral Maxillofac Res. 2015 Jun 30;6(2):e1.
Coronectomy of Deeply Impacted Lower Third Molar: Incidence of Outcomes and Complications after One Year Follow-Up.

Agbaje JO, Heijsters G, Salem AS, Van Slycke S, Schepers S, Politis C, Vrielinck L.

Abstract

OBJECTIVES: The purpose of present study was to assess the surgical management of impacted third molar with proximity to the inferior alveolar nerve and complications associated with coronectomy in a series of patients undergoing third molar surgery.

MATERIAL AND METHODS: The position of the mandibular canal in relation to the mandibular third molar region and mandibular foramen in the front part of the mandible (i.e., third molar in close proximity to the inferior alveolar nerve [IAN] or not) was identified on panoramic radiographs of patients scheduled for third molar extraction.

RESULTS: Close proximity to the IAN was observed in 64 patients (35 females, 29 males) with an impacted mandibular third molar. Coronectomy was performed in these patients. The most common complication was tooth migration away from the mandibular canal (n = 14), followed by root

exposure (n = 5). Re-operation to remove the root was performed in cases with periapical infection and root exposure.

CONCLUSIONS: The results indicate that coronectomy can be considered a reasonable and safe treatment alternative for patients who demonstrate elevated risk for injury to the inferior alveolar nerve with removal of the third molars. Coronectomy did not increase the incidence of damage to the inferior alveolar nerve and would be safer than complete extraction in situations in which the root of the mandibular third molar overlaps or is in close proximity to the mandibular canal.

Radiother Oncol. 2015 May;115(2):186-90.
Prostate tumor delineation using multiparametric magnetic resonance imaging: Inter-observer variability and pathology validation.

Steenbergen P, Haustermans K, Lerut E, Oyen R, De Wever L, Van den Bergh L, Kerkmeijer LG, Pameijer FA, Veldhuis WB, van der Voort van Zyp JR, Pos FJ, Heijmink SW, Kalisvaart R, Teertstra HJ, Dinh CV, Ghobadi G, van der Heide UA.

Abstract

BACKGROUND AND PURPOSE: Boosting the dose to the largest (dominant) lesion in radiotherapy of prostate cancer may improve treatment outcome. The success of this approach relies on the detection and delineation of tumors. The agreement among teams of radiation oncologists and radiologists delineating lesions on multiparametric magnetic resonance imaging (mp-MRI) was assessed by measuring the distances between observer contours. The accuracy of detection and delineation was determined using whole-mount histopathology specimens as reference.

MATERIAL AND METHODS: Six observer teams delineated tumors on mp-MRI of 20 prostate cancer patients who underwent a prostatectomy. To assess the inter-observer agreement, the inter-observer standard deviation (SD) of the contours was calculated for tumor sites which were identified by all teams.

RESULTS: Eighteen of 89 lesions were identified by all teams, all were dominant lesions. The median histological volume of these was 2.4cm(3). The median inter-observer

SD of the delineations was 0.23cm. Sixty-six of 69 satellites were missed by all teams.

CONCLUSION: Since all teams identify most dominant lesions, dose escalation to the dominant lesion is feasible. Sufficient dose to the whole prostate may need to be maintained to prevent under treatment of smaller lesions and undetected parts of larger lesions.

Urol Oncol. 2015 Mar;33(3):109.e23-31.

Final analysis of a prospective trial on functional imaging for nodal staging in patients with prostate cancer at high risk for lymph node involvement.

Van den Bergh L, Lerut E, Haustermans K, Deroose CM, Oyen R, Isebaert S, Budiharto T, Ameye F, Mottaghy FM, Bogaerts K, Van Poppel H, Joniau S.

Abstract

PURPOSE: Accurate staging modalities to diagnose lymph node involvement in patients with prostate cancer (PCa) are lacking. We wanted to prospectively assess sensitivity, specificity, and positive predictive value (PPV) and negative predictive value of (11)C-choline positron emission tomography (PET)-computed tomography (CT) and diffusion-weighted (DW) magnetic resonance imaging (MRI) for nodal staging in patients with PCa at high risk for lymph node involvement.

MATERIAL AND METHODS: In total, 75 patients with a risk $\geq 10\%$ but $< 35\%$ for lymph node (LN) metastases (Partin tables) who had NO lesions based on the findings of contrast-enhanced CT scans were included. Patients underwent (11)C-choline PET-CT and DW MRI before surgery, which consisted of a superextended lymph node dissection followed by radical prostatectomy. LNs were serially sectioned and histopathologically examined after pankeratin staining. These results were used as the gold standard to compare with the imaging results.

RESULTS: Of 1,665 resected LNs (median = 21, range: 7-49), 106 affected LNs (median = 2, range: 1-10) were found in 37 of 75 patients (49%). On a region-based analysis, we found a low sensitivity of 8.2% and 9.5% and a PPV of 50.0% and 40.0% for (11)C-choline PET-CT and DW MRI, respectively. The patient-based ana-

lysis showed a sensitivity of 18.9% and 36.1% for and a PPV of 63.6% and 86.7% (11)C-choline PET-CT and DW MRI, respectively. Even when both imaging modalities were combined, sensitivity values remained too low to be clinically useful.

CONCLUSIONS: Because of the low sensitivity, there is no indication for routine clinical use of either (11)C-choline PET-CT or DW MRI for LN staging in patients with PCa, in whom CT scan findings were normal.

Acta Oncol. 2015 Jun;54(6):896-902.

Reliability of sentinel node procedure for lymph node staging in prostate cancer patients at high risk for lymph node involvement.

Van den Bergh L, Joniau S, Haustermans K, Deroose CM, Isebaert S, Oyen R, Motlaghy FM, Ameye F, Berkens J, Van Poppel H, Lerut E.

Abstract

AIM: To investigate the reliability of a sentinel node (SN) procedure for nodal staging in prostate cancer (PCa) patients at high risk for lymph node (LN) involvement.

MATERIAL AND METHODS: Seventy-four patients with localized prostate adenocarcinoma, who were clinically node-negative and had a risk of LN involvement of $\geq 10\%$ (Partin tables), were prospectively enrolled. Upon intraprostatic 99mTc-nanocolloid injection, they underwent planar scintigraphy and SPECT imaging. Surgical removal of the SN, located by means of a gamma probe, was completed with a superextended LN dissection (seLND) as a reference and followed by radical prostatectomy.

RESULTS: In total, 470 SN (median 6, IQR 3-9) were scintigraphically detected of which 371 (median 4, IQR 2-6) were located by gamma probe and selectively removed during surgery (79%). Histopathology confirmed LN metastases in 37 patients (50%) having 106 affected LN in total (median number per patient 2, IQR 1-4). Twenty-eight patients were node positive (N+) based on the analysis of the resected SN. However, the seLND that was performed as a reference revealed nine additional N+ patients resulting in a sensitivity of 76% (28/37). In total, 15 of 37 patients (41%) had metastases in SN only and could have been spared seLND to remove all affected nodes.

CONCLUSION: We found a relatively low sensitivity when addressing the SN procedure for nodal staging in PCa patients at high risk for LN involvement. Importantly, only less than half of the N+ patients could have been spared a seLND to remove all affected lymphoid tissue.

BMC Cancer. 2015 Dec 16;15:980.

BEV-IP: Perioperative chemotherapy with bevacizumab in patients undergoing cytoreduction and intraperitoneal chemoperfusion for colorectal carcinomatosis.

Willaert W, Van Der Speeten K, Liberale G, Ceelen W.

Abstract

BACKGROUND: Selected patients with peritoneal carcinomatosis (PC) from colorectal cancer (CRC) benefit from cytoreductive surgery (CRS) combined with intraperitoneal chemoperfusion (IPC). However, even after optimal cytoreduction, systemic and locoregional recurrence are common. Perioperative chemotherapy with bevacizumab (BEV) may improve the outcome of these patients.

METHODS/DESIGN: The BEV-IP study is a phase II, single-arm, open-label study aimed at patients with colorectal or appendiceal adenocarcinoma with synchronous or metachronous PC. This study evaluates whether perioperative chemotherapy including BEV in combination with CRS and oxaliplatin-based IPC results in acceptable morbidity and mortality (primary composite endpoint). Secondary endpoints are treatment completion rate, chemotherapy-related toxicity, pathological response, progression free survival, and overall survival.

DISCUSSION: The BEV-IP trial is the first prospective assessment of the safety and efficacy of perioperative chemotherapy combined with anti-angiogenic treatment in patients undergoing CRS and IPC for colorectal peritoneal metastases.

Colorectal Dis. 2015 Jun;17(6):522-9.

COMPRES: a prospective postmarketing evaluation of the compression anastomosis ring CAR 27™ / ColonRing™.

D'Hoore A, Albert MR, Cohen SM, Herbst F, Matter I, Van Der Speeten K, Domin-

quez J, Rutten H, Muldoon JP, Bardakcioglu O, Senagore AJ, Ruppert R, Mills S, Stamos MJ, Pahlman L, Choman E, Wexner SD; COMPRES collaborative study group.

Abstract

AIM: Preclinical studies have suggested that nitinol-based compression anastomosis might be a viable solution to anastomotic leak following low anterior resection. A prospective multicentre open label study was therefore designed to evaluate the performance of the ColonRing™ in (low) colorectal anastomosis.

METHOD: The primary outcome measure was anastomotic leakage. Patients were recruited at 13 different colorectal surgical units in Europe, the United States and Israel. Institutional review board approval was obtained.

RESULTS: Between 21 March 2010 and 3 August 2011, 266 patients completed the study protocol. The overall anastomotic leakage rate was 5.3% for all anastomoses, including a rate of 3.1% for low anastomoses. Septic anastomotic complications occurred in 8.3% of all anastomoses and 8.2% of low anastomoses.

CONCLUSION: Nitinol compression anastomosis is safe, effective and easy to use and may offer an advantage for low colorectal anastomosis. A prospective randomized trial comparing ColonRing™ with conventional stapling is needed.

J Healthc Eng. 2015;6(4):779-89.

Accuracy of a Dedicated Bone-Supported Surgical Template for Dental Implant Placement with Direct Visual Control.

Sun Y, Luebbbers HT, Agbaje JO, Kong L, Schepers S, Daems L, Legrand P, Jacobs R, Politis C, Vrielinck L.

Abstract

The aim of this study is to evaluate feasibility and accuracy of dental implant placement utilizing a dedicated bone-supported surgical template. Thirty-eight implants (sixteen in maxilla, twenty-two in mandible) were placed in seven fully edentulous jaws (three maxillae, four mandibles) guided by the designed bone-supported surgical template. A voxel-based registration technique was applied to match pre- and

post-operative CBCT scans. The mean angular deviation and mean linear deviation at the implant hex and apex were $6.4 \pm 3.7^\circ$ (0.7° - 14.8°), 1.47 ± 0.64 mm (0.5 - 2.56 mm) and 1.70 ± 1.01 mm (0.71 - 4.39 mm), respectively. The presented bone-supported surgical template showed acceptable accuracy for clinical use. In return for reduced accuracy, clinicians gain accessibility when using this type of surgical template for both the maxilla and the mandible. This is particularly important in patients with reduced mouth opening.

Clin Implant Dent Relat Res. 2015 Oct;17(5):862-70.

Accuracy of Dental Implant Placement Using CBCT-Derived Mucosa-Supported Stereolithographic Template.

Sun Y, Luebbbers HT, Agbaje JO, Schepers S, Politis C, Van Slycke S, Vrielinck L.

Abstract

PURPOSE: The aim of the present in vivo study was to evaluate whether a difference exists between the maxilla and the mandible regarding the precision of implant placement utilizing a cone beam computed tomography (CBCT)-derived mucosa-supported stereolithographic (SLA) template.

MATERIALS AND METHODS: Eighty implants (44 maxilla, 36 mandible) were placed in 18 fully edentulous jaws (10 maxillas, eight mandibles) using a mucosa-supported SLA surgical template. A voxel-based registration technique was applied to match the postoperative and preoperative CBCT scans.

RESULTS: Vertical deviation ($p = .026$) at the implant hex and angular deviation ($p = .0188$) were significantly lower in the maxilla than in the mandible. The global linear deviation and lateral deviation at the implant hex were not significantly different. At the implant apex, the average maximum vertical deviation was within 1 mm (0.1 - 4.6 mm). The average maximum lateral deviation was 1.8 mm (0.9 - 5.5 mm) in the maxilla and 2.3 mm (0.5 - 5.5 mm) in the mandible when a 15-mm-long implant was placed.

CONCLUSIONS: When using CBCT-derived mucosa-supported SLA templates, clinicians should be aware of differences in the angular deviation of the implants in the

mandible and maxilla. The average maximum linear deviation should be considered as a safety margin at the implant apex.

J Neurol (2015) 262:742-751

Patient outcome in the Belgian medical need program on bevacizumab for recurrent glioblastoma

Johnny Duerinck, Paul M. Clement, Frank Bouttens, Chantal Andre, Bart Neyns, Yves Staelens, Frank Van Fraeyenhove, Jean-Francois Baurain, Sylvie Luce, Lionel D'hondt, Eric Joosens, Pol Specenier, Vincent Verschaeve, Bertrand Filleul, Philippe Vroman, Barbara Stragier, Anne Rogiers

Abstract

Bevacizumab (BEV) has demonstrated anti-tumor activity in patients with recurrent glioblastoma (rGB). Given the unmet need for active therapeutic options in rGB patients, a medical need program was initiated by the Belgian competent authorities. Between November 2010 and February 2013, a total of 313 patients with rGB initiated treatment with BEV administered at a dose of 10 mg/kg every 2 weeks. All patients had failed prior treatment with at least radiation therapy and temozolomide and the majority of patients (70 %) were treated with corticosteroids at baseline. Patients received a median of 6 BEV administrations (range 1-53). Overall, BEV was well tolerated. During BEV treatment the WHO-Performance Score (WHO-PS) improved in 59 patients (19 %) and stabilized for at least 6 weeks in an additional 139 (44 %) patients. Corticosteroid treatment could be stopped in 16 % or reduced in dose in 32 % of patients. The best objective tumor response rate using RANO criteria (investigator's assessment) was 3.5 % CR, 22 % PR, 38 % SD and 37 % PD. The median and 6-month PFS were 13 weeks (95 % CI 12.7-14) and 27.3 % (95 % CI 22.3-32.5), median and 6-month OS rates were 26 weeks (23-29) and 52 % (46.4-58.6), respectively. WHO-PS (0-1 vs. 2-3) and baseline steroid use were significantly correlated with PFS and OS. Our observations support the use of BEV as a monotherapy for patients with rGB who have no alternative treatment options. Optimal benefit from BEV treatment is likely to be obtained when treatment is initiated before the performance status deteriorates to two or less.

DIVISIE 4 (NEUROLOGIE - ORTHOPEDIE - REVALIDATIE - MULTIDISCIPLINAIR PIJNCENTRUM)

Orthop Surg. 2013 Aug;5(3):229-32.

Upper arm compartment syndrome: a case report and review of the literature.

Maeckelbergh L, Colen S, Anné L.

Acta Orthop Belg. 2015 Sep;81(3):471-7.

Current opinions about coronal plane alignment in total knee arthroplasty: A survey article.

Thienpont E, Cornu O, Bellemans J, Victor J.

Abstract

PURPOSE: To survey an audience of international knee surgeons about their current opinions on the analysis of coronal knee alignment and their objectives for postoperative alignment in total knee arthroplasty.

METHODS: Survey of 300 surgeons from 32 different countries with an audience response system allowing three possible answers being either a positive or negative answer or an abstention.

RESULTS: Surveyed surgeons perform rarely preoperative and postoperative full leg radiographs and evaluate radiological outcomes more with short films. The main trend in this survey was towards neutral mechanical alignment, however varus alignment is acceptable in constitutional varus patients. This residual varus should be obtained through a femoral varus cut rather than a tibial varus cut. The valgus knee can remain in slight valgus but most of the correction will be performed at the femoral level. The main objective of postoperative alignment in TKA is a joint line parallel to the floor and a central load-bearing axis through the middle of the arthroplasty. Surgeons prefer unicompartmental arthroplasty more for themselves than for their patients in case of medial bone on bone arthritis.

CONCLUSIONS: Neutral mechanical axis with a joint line parallel to the floor and a centrally running load bearing axis remains the central scope of the surveyed surgeons. Because of the literature on residual varus it becomes more acceptable for the orthopaedic community to accept this type of outlier before aiming at a surgical correction.

Hum Mov Sci. 2015 Dec;44:234-45.

Lower extremity muscle activation onset times during the transition from double-leg stance to single-leg

stance in anterior cruciate ligament injured subjects.

Dingenen B, Janssens L, Luyckx T, Claes S, Bellemans J, Staes FF.

Abstract

The goal of this study was to evaluate muscle activation onset times (MAOT) of both legs during a transition task from double-leg stance (DLS) to single-leg stance (SLS) in anterior cruciate ligament injured (ACLI) (n=15) and non-injured control subjects (n=15) with eyes open and eyes closed. Significantly delayed MAOT were found in the ACLI group compared to the control group for vastus lateralis, vastus medialis obliquus, hamstrings medial, hamstrings lateral, tibialis anterior, peroneus longus and gastrocnemius in both vision conditions, for gluteus maximus and gluteus medius with eyes open and for tensor fascia latae with eyes closed. Within the ACLI group, delayed MAOT of tibialis anterior with eyes open and gastrocnemius with eyes closed were found in the injured leg compared to the non-injured leg. All other muscles were not significantly different between legs. In conclusion, the ACLI group showed delayed MAOT not only around the knee, but also at the hip and ankle muscles compared to the non-injured control group. No differences between both legs of the ACLI group were found, except for tibialis anterior and gastrocnemius. These findings indirectly support including central nervous system re-education training to target the underlying mechanisms of these altered MAOT after ACL injury.

Acta Orthop Belg. 2015 Jun;81(2):289-95.

Injuries in male versus female soccer players: epidemiology of a nationwide study.

Muftu S, Bollars P, Vanlommel L, Van Crombrugge K, Corten K, Bellemans J.

Abstract

The aim of this study is to analyse soccer injuries on a national scale over one decade and to compare injury rates by gender. Detailed injury data obtained from the Royal Belgian Football Association from seasons 1999-2000 and 2009-2010 were recorded and gender differences in inci-

dences of injuries, type of injury, affected body part and timing of injury were compared. A significant decrease in injuries from 7.56 to 5.96 injuries per 100 players was seen ($p < 0.0001$). Overall male players sustained more contusions, fractures, joint dislocations and musculotendinous injuries than female players. Proportionally, females sustained more severe injuries than men ($p < 0.0001$). Significantly more injuries were sustained during competition in both males and females. The number of injuries in male and female soccer players has decreased over the past decade. A higher injury rate was seen in men but proportionally, females sustained more severe injuries.

J Arthroplasty. 2015 Dec;30(12):2315-9.

Anteroposterior Laxity After Bicruciate-Retaining Total Knee Arthroplasty Is Closer to the Native Knee Than ACL-Resecting TKA: A Biomechanical Cadaver Study.

Halewood C, Traynor A, Bellemans J, Victor J, Amis AA.

Abstract

The purpose of this study was to examine whether a bicruciate retaining (BCR) TKA would yield anteroposterior (AP) laxity closer to the native knee than a posterior cruciate ligament retaining (CR) TKA. A BCR TKA was designed and compared to CR TKA and the native knee using cadaver specimens. AP laxity with the CR TKA was greater than the native knee ($P = 0.006$) and BCR TKA ($P = 0.039$), but no difference was found between the BCR TKA and the native knee. No significant differences were found in rotations between the prostheses and the native knee. BCR TKA was shown to be surgically feasible, reduced AP laxity versus CR TKA, and may improve knee stability without using conforming geometry in the implant design.

Arch Med Sci. 2015 Apr 25;11(2):311-8.

Does joint line elevation after revision knee arthroplasty affect tibio-femoral kinematics, contact pressure or collateral ligament lengths? An in vitro analysis.

Kowalczewski JB, Labey L, Chevalier Y, Okon T, Innocenti B, Bellemans J.

Abstract

INTRODUCTION: Correct restoration of the joint line is generally considered as crucial when performing total knee arthroplasty (TKA). During revision knee arthroplasty however, elevation of the joint line occurs frequently. The general belief is that this negatively affects the clinical outcome, but the reasons are still not well understood.

MATERIAL AND METHODS: In this cadaveric in vitro study the biomechanical consequences of joint line elevation were investigated using a previously validated cadaver model simulating active deep knee squats and passive flexion-extension cycles. Knee specimens were sequentially tested after total knee arthroplasty with joint line restoration and after 4 mm joint line elevation.

RESULTS: The tibia rotated internally with increasing knee flexion during both passive and squatting motion (range: 17° and 7° respectively). Joint line elevation of 4 mm did not make a statistically significant difference. During passive motion, the tibia tended to become slightly more adducted with increasing knee flexion (range: 2°), while it went into slightly less adduction during squatting (range: -2°). Neither of both trends was influenced by joint line elevation. Also anteroposterior translation of the femoral condyle centres was not affected by joint line elevation, although there was a tendency for a small posterior shift (of about 3 mm) during squatting after joint line elevation. In terms of kinetics, ligaments lengths and length changes, tibiofemoral contact pressures and quadriceps forces all showed the same patterns before and joint line elevation. No statistically significant changes could be detected.

CONCLUSIONS: Our study suggests that joint line elevation by 4 mm in revision total knee arthroplasty does not cause significant kinematic and kinetic differences during passive flexion/extension movement and squatting in the tibio-femoral joint, nor does it affect the elongation patterns of collateral ligaments. Therefore, clinical problems after joint line elevation are probably situated in the patello-femoral joint or caused by joint line elevation of more than 4 mm.

Hum Mov Sci. 2015 Jun;41:46-58.

Postural stability deficits during the transition from double-leg stance to single-leg stance in anterior cruciate ligament reconstructed subjects.

Dingenen B, Janssens L, Claes S, Bellemans J, Staes FF.

Abstract

The goal of this study was to evaluate postural stability during the transition from double-leg stance (DLS) to single-leg stance (SLS) in anterior cruciate ligament reconstructed (ACLR) (n=20) and non-injured control subjects (n=20). All ACLR subjects had fully returned to their pre-injury sport participation. Both groups were similar for age, gender, height, weight, body mass index and activity level. Spatiotemporal center of pressure outcomes of both legs of each subject were measured during the transition from DLS to SLS in eyes open and eyes closed conditions. Movement speed was standardized. The center of pressure displacement after a new stability point was reached during the SLS phase was significantly increased in the ACLR group compared to the control group in the eyes closed condition (P=.001). No significant different postural stability outcomes were found between the operated and non-operated legs. In conclusion, the ACLR group showed postural stability deficits, indicating that these persons may have a decreased ability to stabilize their body after the internal postural perturbation created by the transition from DLS to SLS. The non-operated leg may not be the best reference when evaluating postural stability of the operated leg after ACLR, as no differences were found between legs.

Clin Biomech (Bristol, Avon). 2015 Mar;30(3):283-9.

Postural stability during the transition from double-leg stance to single-leg stance in anterior cruciate ligament injured subjects.

Dingenen B, Janssens L, Luyckx T, Claes S, Bellemans J, Staes FF.

Erratum in: Clin Biomech (Bristol, Avon). 2015 Aug;30(7):765-7.

Abstract

BACKGROUND: An anterior cruciate ligament injury may lead to deteriorations in postural stability. The goal of this study was to evaluate postural stability during the transition from double-leg stance to single-leg stance of both legs in anterior cruciate ligament injured subjects and non-injured control subjects with a standardized methodology.

METHODS: Fifteen control subjects and 15 anterior cruciate ligament injured subjects (time after injury: mean (SD)=1.4 (0.7) months) participated in the study. Both groups were similar for age, gender, height, weight and body mass index. Spatiotemporal center of pressure outcomes of both legs of each subject were measured during the transition from double-leg stance to single-leg stance in eyes open and eyes closed conditions. Movement speed was standardized.

FINDINGS: The center of pressure displacement after a new stability point was reached during the single-leg stance phase was significantly increased in the anterior cruciate ligament injured group compared to the control group in the eyes closed condition (P<.001). No significant different postural stability outcomes were found between both legs within both groups (P>.05). No significant differences were found during the transition itself (P>.05).

INTERPRETATION: The anterior cruciate ligament injured group showed postural stability deficits during the single-leg stance phase compared to the non-injured control group in the eyes closed condition. Using the non-injured leg as a normal reference when evaluating postural stability of the injured leg may lead to misinterpretations, as no significant differences were found between the injured and non-injured leg of the anterior cruciate ligament injured group.

Knee Surg Sports Traumatol Arthrosc. 2015 Jun;23(6):1706-12.

Should we aim at undercorrection when doing a total knee arthroplasty?

Luyckx T, Vanhoorebeeck F, Bellemans J.

Abstract

PURPOSE: Restoration of neutral mechanical alignment is traditionally considered as one of the prerequisites for successful

total knee replacement. The purpose of this study was to investigate whether a certain bias towards undercorrection exists with conventional total knee arthroplasty (TKA) instruments.

METHODS: A cohort of 456 consecutive patients, who underwent the same standardized TKA with restoration of neutral mechanical alignment as target, was studied. Based on the preoperative alignment, patients were stratified into three categories: valgus, neutral and varus. Component and limb alignment were compared between these groups.

RESULTS: The mean post-operative hip-knee-ankle angle was -0.7° (SD 2.5) in valgus knees, 0.2° (SD 1.9) in neutral knees and 2.4° (SD 3.9) in varus knees ($p < 0.001$). About 39.8% of the varus knees remained in $>3^\circ$ of varus post-operative and 20.2% of the valgus knees remained in $<-3^\circ$ of valgus. A systematic unintentional undercorrection was noted in varus knees, which was proportional to the preoperative varus deformity and which was caused by varus positioning of both the femoral and tibial components. In valgus knees, the undercorrection was caused almost exclusively by valgus bias of the femoral component's position.

CONCLUSION: This study showed that conventional TKA instruments are associated with a systematic unintentional bias towards undercorrection of the pre-existing deformity. The clinical relevance of this study is that intentionally aiming at slight undercorrection of the deformity may lead to excessive undercorrection in reality in case the surgeon does not recognise the automatic bias that already exists with standard instruments.

LEVEL OF EVIDENCE: Therapeutic study, Level III.

Knee Surg Sports Traumatol Arthrosc. 2015 Nov;23(11):3343-53.

Post-cam mechanics and tibiofemoral kinematics: a dynamic in vitro analysis of eight posterior-stabilized total knee designs.

Arnout N, Vanlommel L, Vanlommel J, Luyckx JP, Labey L, Innocenti B, Victor J, Bellemans J.

Abstract

PURPOSE: Posterior cruciate ligament (PCL)-substituting total knee arthroplasty (TKA) designs were introduced to avoid

paradoxical roll forward of the femur and to optimize knee kinematics. The aim of this in vitro study was to investigate post-cam function and contact mechanics and relate it to knee kinematics during squatting in eight contemporary posterior-stabilized TKA designs.

METHODS: All prostheses were fixed on custom-designed metal fixtures and mounted in a knee rig and five sequential-loaded squats were performed between 30° and 130° of flexion. Contact pressure and contact area were measured using pressure-sensitive Tekscan sensors on the posterior face of the post. Kinematics was recorded with reflective markers and infrared light-capturing cameras.

RESULTS: The post-cam mechanisms analyzed in this study are very variable in terms of design features. This leads to large variations in terms of the flexion angle at which the post and cam engage maximal contact force, contact pressure and contact area. We found that more functional post-cam mechanisms, which engage at lower flexion angle and have a similar behavior as normal PCL function, generally show more normal rollback and tibial rotation at the expense of higher contact forces and pressures. All designs show high contact forces. A positive correlation was found between contact force and initial contact angle.

CONCLUSION: Post-cam contact mechanics and kinematics were documented in a standardized setting. Post-cam contact mechanics are correlated with post-cam function. Outcomes of this study can help to develop more functional designs in future. Nevertheless, a compromise will always be made between functional requirements and risk of failure. We assume that more normal knee kinematics leads to more patient satisfaction because of better mobility. Understanding of the post-cam mechanism, and knowing how this system really works, is maybe the clue in further development of new total knee designs.

Knee Surg Sports Traumatol Arthrosc. 2015 Oct;23(10):3101-7.

The role of the deep medial collateral ligament in controlling rotational stability of the knee.

Cavaignac E, Carpentier K, Pailhé R, Luyckx T, Bellemans J.

Abstract

PURPOSE: The tibial insertion of the deep medial collateral ligament (dMCL) is frequently sacrificed when the proximal tibial cut is performed during total knee arthroplasty. The role of the dMCL in controlling the knee's rotational stability is still controversial. The aim of this study was to quantify the rotational laxity induced by an isolated lesion of the dMCL as it occurs during tibial preparation for knee arthroplasty.

METHODS: An isolated resection of the deep MCL was performed in 10 fresh-frozen cadaver knees. Rotational laxity was measured during application of a standard 5.0 N.m rotational torque. Maximal tibial rotation was measured at different knee flexion angles using an image-guided navigation system (Medivision Surgetics system, Praxim, Grenoble, France) before and after dMCL resection.

RESULTS: In all cases, internal and external tibial rotation increased after dMCL resection. Total rotational laxity increased significantly for all knee flexion angles, with an average difference of $+7.8^\circ$ (SD 5.7) with the knee in extension, $+8.9^\circ$ (SD 1.9) in 30° flexion, $+7^\circ$ (SD 2.9) in 60° flexion and $+5.3^\circ$ (SD 2.8) in 90° flexion.

CONCLUSIONS: Sacrificing the tibial insertion of the deep MCL increases rotational laxity of the knee by 5° - 9° , depending on the knee flexion angle. Based on our findings, new surgical techniques and implants that preserve the dMCL insertion such as tibial inlay components should be developed. Further clinical evaluations are necessary.

Knee Surg Sports Traumatol Arthrosc. 2015 Aug;23(8):2159-69.

Restoration of constitutional alignment in TKA leads to more physiological strains in the collateral ligaments.

Delpont H, Labey L, Innocenti B, De Corte R, Vander Sloten J, Bellemans J.

Abstract

PURPOSE: Currently, controversy exists whether restoration of neutral mechanical alignment should be attempted in all patients undergoing TKA. Our hypothesis was that restoration of constitutional rather than neutral mechanical alignment may in theory lead to a more physiological strain pattern in the collateral ligaments;

therefore, it could potentially be beneficial to patients. Thus, the aim of this study was to measure collateral ligament strains during three motor tasks in the native knee and compare them with the strains noted after TKA in different post-operative alignment conditions.

METHODS: Six cadaver specimens (approval number ML4190 from the Research Ethics Committee of University of Leuven, Belgium) were examined using a validated knee kinematics rig under physiological loading conditions. The effect of coronal malalignment was evaluated by using custom-made tibial implant inserts that induced different alignment conditions. The study of six specimens allows us to show that a difference in the mean strains in MCL and LCL of 3.6 and 5.8 %, respectively, was statistically significant with a probability (power) of 0.8.

RESULTS: The results indicated that after TKA insertion, the strains in the collateral ligaments closely resembled the pre-operative pattern of the native knee specimens when constitutional alignment was restored. Restoration to neutral mechanical alignment was associated with greater collateral strain deviations from the native knee.

CONCLUSION: Based upon this study, it was concluded that restoration of constitutional alignment within a "safe zone" of $\pm 2^\circ$ during TKA leads to more physiological peri-articular soft tissue strains during loaded as well as unloaded motor tasks.

J Orthop Res. 2015 Dec 3.

Gait alterations can reduce the risk of edge loading.

Wesseling M, Meyer C, de Groote F, Corten K, Simon JP, Desloovere K, Jonkers I.

Abstract

Following metal-on-metal hip arthroplasty, edge loading (i.e. loading near the edge of a prosthesis cup) can increase wear and lead to early revision. The position and coverage angle of the prosthesis cup influence the risk of edge loading. This study investigates the effect of altered gait patterns, more specific hip and pelvis kinematics, on the orientation of hip contact force and the consequent risk of antero-superior edge loading using muscle driven simulations of gait. With a cup

orientation of 25° anteversion and 50° inclination and a coverage angle of 168° , many gait patterns presented risk of edge loading. Specifically at terminal double support, 189 out of 405 gait patterns indicated a risk of edge loading. At this time instant, the high hip contact forces and the proximity of the hip contact force to the edge of the cup indicated the likelihood of the occurrence of edge loading. Although the cup position contributed most to edge loading, altering kinematics considerably influenced the risk of edge loading. Increased hip abduction, resulting in decreasing hip contact force magnitude, and decreased hip extension, resulting in decreased risk on edge loading, are gait strategies that could prevent edge loading.

Knee Surg Sports Traumatol Arthrosc. 2015 Jan;23(1):59-64.

What is the best way to fix a polyurethane meniscal scaffold? A biomechanical evaluation of different fixation modes.

Hardeman F, Corten K, Mylle M, Van Herck B, Verdonk R, Verdonk P, Bellemans J.

J Orthop Res. 2015 Oct;33(10):1498-507.

Biomechanical gait features associated with hip osteoarthritis: Towards a better definition of clinical hallmarks.

Meyer CA, Corten K, Fieuws S, Deschamps K, Monari D, Wesseling M, Simon JP, Desloovere K.

Abstract

Critical appraisal of the literature highlights that the discriminative power of gait-related features in patients with hip osteoarthritis (OA) has not been fully explored. We aimed to reduce the number of gait-related features and define the most discriminative ones comparing the three-dimensional gait analysis of 20 patients with hip osteoarthritis (OA) with those of 17 healthy peers. First, principal component analysis was used to reduce the high-dimensional gait data into a reduced set of interpretable variables for further analysis, including tests for group differences. These differences were indicative for the selection of the top 10 variables to be included into linear discriminant

analysis models (LDA). Our findings demonstrated the successful data reduction of hip osteoarthritic-related gait features with a high discriminatory power. The combination of the top variables into LDA models clearly separated groups, with a maximum misclassification error rate of 19%, estimated by cross-validation. Decreased hip/knee extension, hip flexion and internal rotation moment were gait features with the highest discriminatory power. This study listed the most clinically relevant gait features characteristics of hip OA. Moreover, it will help clinicians and physiotherapists understand the movement pathomechanics related to hip OA useful in the management and design of rehabilitation intervention.

J Orthop Res. 2015 Jul;33(7):1094-102.

Gait alterations to effectively reduce hip contact forces.

Wesseling M, de Groote F, Meyer C, Corten K, Simon JP, Desloovere K, Jonkers I.

Abstract

Patients with hip pathology present alterations in gait which have an effect on joint moments and loading. In knee osteoarthritic patients, the relation between medial knee contact forces and the knee adduction moment are currently being exploited to define gait retraining strategies to effectively reduce pain and disease progression. However, the relation between hip contact forces and joint moments has not been clearly established. Therefore, this study aims to investigate the effect of changes in hip and pelvis kinematics during gait on internal hip moments and contact forces which is calculated using muscle driven simulations. The results showed that frontal plane kinetics have the largest effect on hip contact forces. Given the high correlation between the change in hip adduction moment and contact force at initial stance ($R(2) = 0.87$), this parameter can be used to alter kinematics and predict changes in contact force. At terminal stance the hip adduction and flexion moment can be used to predict changes in contact force ($R(2) = 0.76$). Therefore, gait training that focuses on decreasing hip adduction moments, a wide base gait pattern, has the largest potential to reduce hip contact forces.

Tech Hand Up Extrem Surg. 2015 Mar;19(1):18-22.

The follow-up of trapeziometacarpal arthrodesis using V-shaped osteotomy for osteoarthritis of the first carpometacarpal joint.

Harston A, Manon-Matos Y, McGill S, Jones R, Duerinckx J, Wolff TW.

Abstract

INTRODUCTION: Osteoarthritis of the trapeziometacarpal joint, also known as the thumb carpometacarpal joint, is one of the most common anatomic sites of arthritis in the human body. Many surgical techniques to address this problem have been developed; including, trapeziectomy with or without ligament reconstruction tendon interposition, implant arthroplasty, and arthrodesis. No methods have yet proven superior to the others, and each has associated limitations and complications. The primary complication found in the literature after arthrodesis of the trapeziometacarpal joint is nonunion; with a reported incidence in the literature as 13% (8% to 39%).

METHODS: In 2010, a new surgical technique for this procedure was published by Wolff and Duerinckx in Techniques in Hand Surgery. In summary, a V-shaped osteotomy is made at the base of the first metacarpal and, together with a matching osteotomy of the trapezium, creates a more stable fusion site. Our current research looks at a minimum of 2-year follow-up of patients treated with this technique between 2004 and 2012.

RESULTS: Twenty-one patients, including 3 who had bilateral procedures, have participated in the study. The average age is 62.6 years (range, 51 to 76 y) with an average follow-up of 4.6 years (range, 2 to 8 y). Sixteen are female and 5 are male, with a variety of occupations. In these patients, the Quick DASH score improved 51% (49.8 to 24.2; $P=0.0006$), and the Quick DASH Work score improved 56% (52.8 to 23.2; $P=0.0035$). Nineteen of 21 patients said that they would have the procedure again. Range of motion and strength of the operated versus nonoperated thumbs were compared and showed very similar capabilities. Seventy-five percent (18 of 24) were able to lay their

hand flat. There were 4 fibrous unions, resulting in an 83% complete fusion rate. There were no infections or reoperations for nonunion.

CONCLUSION: The data suggest that this procedure is a highly successful, pain-relieving, strength-preserving, reproducible arthrodesis with a nonunion rate similar to that of the published literature.

Eur Spine J. 2015 Sep 28.

Cone-beam CT to assess bony fusion following anterior cervical interbody fusion.

Vandevenne JE, Peuskens D, Wijnen L, Wuyts J.

Abstract

PURPOSE: Assessment of bony fusion following anterior cervical interbody fusion (ACIF) is usually done by plain film or CT. We present the first clinical application of Cone-Beam CT (CBCT) to evaluate bony fusion after ACIF.

METHODS: A 56-year-old man with disc herniation at C6-C7 underwent ACIF surgery using a compressed nanocrystalline hydroxyapatite interbody device (nanOss-C, Pioneer Surgical Marquette, MI, USA) and a nanocrystalline hydroxyapatite bone graft filler (nanOss Bioactive, Pioneer Surgical Marquette, MI, USA). Imaging follow-up was performed by CBCT (NewTom 5G, QR Srl, Verona, Italy) at 1 day, 6 weeks, 3 and 9 months post-operatively. Two independent assessors quantitatively measured the greyscale changes of the bone graft filler and qualitatively evaluated the bony fusion process.

RESULTS: Quantitative analysis of the images showed a steadily increasing matrix density of the bone graft filler over the 9 months follow-up, suggesting increasing calcification. Qualitative evaluation demonstrated different stages of the bone fusion process within the disc space around the cage, at the interface between cage and endplates, and at the interface between bone graft filler and the endplates.

CONCLUSIONS: CBCT provides high-resolution cross-sectional imaging of the cervical spine after ACIF. For the first time, in vivo evaluation of the bone graft filler

within the centre of the circumferentially radiodense cage and detailed cross-sectional evaluation of bone fusion was achieved. Confirmation of these promising outlooks of CBCT in a large cohort of ACIF patients is needed with regard to routine clinical application and evaluation of different interbody devices.

DIVISIE 5 (GERIATRIE - ENDOCRINOLOGIE - PSYCHIATRIE)

Disabil Rehabil. 2015 Jul 2:1-7.

"How to conquer a mountain with multiple sclerosis". How a climbing expedition to Machu Picchu affects the way people with multiple sclerosis experience their body and identity: a phenomenological analysis.

Calsius J, Courtois I, Feys P, Van Asch P, De Bie J, D'hooghe M.

Abstract

BACKGROUND: People with multiple sclerosis (MS) frequently complain of chronic or fluctuating fatigue, sometimes accompanied by pain. From a phenomenological point of view, both fatigue and pain are seen as aspects of suffering which adversely affect the physical, psychological, social and even existential dimensions of the individual life.

OBJECTIVE: The present study discusses changes in identity and body awareness in people with MS who completed a 5-d trekking to Machu Picchu in Peru in 2012, after having completed a physical training schedule for several months.

METHOD AND DESIGN: All nine participants took part in a focus group organized after the trip. The Interpretative Phenomenological Analysis (IPA) was used to gain insight in their experiences and to refine pre-existing theoretical understanding of body awareness and identity.

RESULTS: Our phenomenological analysis clarified how aspects of the participants' identity and body experience before, during and after the journey influenced major daily themes as "body", "lived body", "behaviour" and "relationship" and how this contributed to a meaningful experience. When participants describe how they started looking at their own identity more consciously after being watched through the others' eyes, this resulted in a joyful transcending of their bodily power and endurance. In general, our data suggest that the more extreme, positive lived body experiences during the expedition were necessary for optimizing daily "routine" functioning.

CONCLUSION: Participating in Machu Picchu expedition appeared to have a deep and profound effect on body awareness and identity. Participants experienced their body once again as theirs, owning it and above all, allowing it to be a source

of strength, joy and meaningfulness. While MS determined their lives prior to the journey, they now could look at MS as a part of what they are, without totally being absorbed in it. So being a patient with MS before, resulted in merely having MS after the climb. Implications for Rehabilitation Patients experience illness as a disruption of their previous life. A phenomenological approach deals with the lived experience and the concept of body awareness, the meaningful experience of living in the world through the body. This approach complements biomedical viewpoints as providing different. Suffering from a chronic and unpredictable disease like multiple sclerosis (MS) can disturb the implicit and harmonious relation between the body, the mind and the world, already at an early stage. Factors including physical training, professional guidance, social support, becoming a role model and completing a unique expedition outside of national and natural comfort borders may contribute to changes in body and identity experience.

J Hepatol. 2015 Mar;62(3):734-8.

Biallelic inactivation of protoporphyrinogen oxidase and hydroxymethylbilane synthase is associated with liver cancer in acute porphyrias.

Schneider-Yin X, van Tuyl van Serooskerken AM, Siegesmund M, Went P⁴, Barman-Aksözen J, Bladergroen RS, Komminoth P, Cloots RH, Winnepenninckx VJ, zur Hausen A, Weber M, Driessen A, Poblete-Gutiérrez P, Bauer P, Schroeder C, van Geel M, Minder EI, Frank J.

Abstract

Variegate porphyria (VP) and acute intermittent porphyria (AIP), the two most common types of acute porphyrias (AHPs), result from a partial deficiency of protoporphyrinogen oxidase (PPOX) and hydroxymethylbilane synthase (HMBS), respectively. A rare but serious complication in the AHPs is hepatocellular carcinoma (HCC). However, the underlying pathomechanisms are yet unknown. We performed DNA sequence analysis in cancerous and non-cancerous liver tissue of a VP and an AIP patient, both with HCC. In samples of both cancerous and non-cancerous liver tissues from the patients, we identified

the underlying PPOX and HMBS germline mutations, c.1082dupC and p.G111R, respectively. Additionally, we detected a second somatic mutation, only in the cancer tissue i.e., p.L416X in the PPOX gene of the VP patient and p.L220X in the HMBS gene of the AIP patient, both located in trans to the respective germline mutations. Both somatic mutations were not detected in 10 non-porphyria-associated HCCs. Our data demonstrate that in the hepatic cancer tissue of AHP patients, somatic second-hit mutations result in nearly complete inactivation of the enzymes catalyzing major steps in the heme biosynthetic pathway. Both PPOX and HMBS, which might act as tumor suppressors, play a crucial role in the development of HCC in these individuals.

Arthritis Res Ther. 2015 Apr 9;17:97.

Patients lacking classical poor prognostic markers might also benefit from a step-down glucocorticoid bridging scheme in early rheumatoid arthritis: week 16 results from the randomized multicenter CareRA trial.

Verschuere P, De Cock D, Corluy L, Joos R, Langenaken C, Taelman V, Raeman F, Ravelingien I, Vandevyvere K, Lenaerts J, Geens E, Geusens P, Vanhoof J, Durnez A, Remans J, Vander Cruyssen B, Van Essche E, Sileghem A, De Brabanter G, Joly J, Van der Elst K, Meyfroidt S, Westhovens R; CareRA study group.

Abstract

INTRODUCTION: Considering a lack of efficacy data in patients with early rheumatoid arthritis (eRA) presenting without classical markers of poor prognosis, we compared methotrexate (MTX) with or without step-down glucocorticoids in the CareRA trial.

METHODS: Disease-modifying antirheumatic drug-naïve patients with eRA were stratified into a low-risk group based on prognostic markers that included non-erosiveness, anti-citrullinated protein antibodies and rheumatoid factor negativity and low disease activity (Disease Activity Score in 28 joints based on C-reactive protein (DAS28(CRP)) ≤3.2). Patients were randomized to 15 mg of MTX weekly (MTX with tight step-up (MTX-TSU)) or 15 mg of MTX weekly with prednisone brid-

ging, starting at 30 mg and tapered to 5 mg daily from week 6 (Combinatie therapie bij Reumatoïde Artritis (COBRA Slim)). A TSU approach was applied. Outcomes assessed were DAS28(CRP)-determined remission, cumulative disease activity, Health Assessment Questionnaire (HAQ) scores and adverse events (AEs) after 16 treatment weeks.

RESULTS: We analyzed 43 COBRA Slim and 47 MTX-TSU patients and found that 65.1% in the COBRA Slim group and 46.8% in the MTX-TSU group reached remission ($P=0.081$). Mean $\pm$ standard deviation area under the curve values of DAS28(CRP) were 13.84 ± 4.58 and 11.18 ± 4.25 for the MTX-TSU and COBRA Slim patients, respectively ($P=0.006$). More COBRA Slim patients had an HAQ score of 0 (51.2% versus 23.4%, $P=0.006$) at week 16. Therapy-related AEs between groups did not differ.

CONCLUSION: In patients with low-risk eRA, MTX with step-down glucocorticoid bridging seems more efficacious than MTX step-up monotherapy, with a comparable number of AEs observed over the first 16 treatment weeks.

Ann Rheum Dis. 2015 Jan;74(1):27-34.

Methotrexate in combination with other DMARDs is not superior to methotrexate alone for remission induction with moderate-to-high-dose glucocorticoid bridging in early rheumatoid arthritis after 16 weeks of treatment: the CareRA trial.

Verschueren P, De Cock D, Corluy L, Joos R, Langenaken C, Taelman V, Raeman F, Ravelingien I, Vandevyvere K, Lenaerts J, Geens E, Geusens P, Vanhoof J, Durnez A, Remans J, Vander Cruyssen B, Van Essche E, Sileghem A, De Brabanter G, Joly J, Meyfroidt S, Van der Elst K, Westhovens R.

Abstract

OBJECTIVES: To compare the efficacy and safety of intensive combination strategies with glucocorticoids (GCs) in the first 16 weeks (W) of early rheumatoid arthritis (eRA) treatment, focusing on high-risk patients, in the Care in early RA trial.

METHODS: 400 disease-modifying antirheumatic drugs (DMARD)-naïve patients with eRA were recruited and stratified into high risk or low risk according to

classical prognostic markers. High-risk patients ($n=290$) were randomised to 1/3 treatment strategies: combination therapy for early rheumatoid arthritis (COBRA) Classic (methotrexate (MTX)+ sulfasalazine+60 mg prednisone tapered to 7.5 mg daily from W7), COBRA Slim (MTX+30 mg prednisone tapered to 5 mg from W6) and COBRA Avant-Garde (MTX+leflunomide+30 mg prednisone tapered to 5 mg from W6). Treatment modifications to target low-disease activity were mandatory from W8, if desirable and feasible according to the rheumatologist. The primary outcome was remission (28 joint disease activity score calculated with C-reactive protein <2.6) at W16 (intention-to-treat analysis). Secondary endpoints were good European League Against Rheumatism response, clinically meaningful health assessment questionnaire (HAQ) response and HAQ equal to zero. Adverse events (AEs) were registered.

RESULTS: Data from 98 Classic, 98 Slim and 94 Avant-Garde patients were analysed. At W16, remission was reached in 70.4% Classic, 73.6% Slim and 68.1% Avant-Garde patients ($p=0.713$). Likewise, no significant differences were shown in other secondary endpoints. However, therapy-related AEs were reported in 61.2% of Classic, in 46.9% of Slim and in 69.1% of Avant-Garde patients ($p=0.006$).

CONCLUSIONS: For high-risk eRA, MTX associated with a moderate step-down dose of GCs was as effective in inducing remission at W16 as DMARD combination therapies with moderate or high step-down GC doses and it showed a more favourable short-term safety profile.

Gait Posture. 2015 Mar;41(3):852-6.

A color-code based method for the interpretation of plantar pressure measurements in clinical gait analysis.

Deschamps K, Staes F, Desmet D, Roosen P, Matricali GA, Keijsers N, Nobels F, Tits J, Bruyninckx H.

Abstract

Comparing plantar pressure measurements (PPM) of a patient following an intervention or between a reference group and a patient-group is common practice in clinical gait analysis. However, this pro-

cess is often time consuming and complex, and commercially available software often lacks powerful visualization and interpretation tools. In this paper, we propose a simple method for displaying pixel-level PPM deviations relative to a so-called reference PPM pattern. The novel method contains 3 distinct stages: (1) a normalization of pedobarographic fields (for foot length and width), (2) a pixel-level z-score based calculation and, (3) color coding of the normalized pedobarographic fields. The methodological steps associated to this novel method are precisely described and clinical output illustrated. We believe that the advantages of the novel method cover several domains. The strongest advantage of the novel method is that it provides a straightforward visual interpretation of PPM without decreasing the resolution perspective. A second advantage is that it may guide the selection of a local mapping technique (data reduction technique). Finally, it may be easily used as education tool during the therapist-patient interaction.

Infect Dis (Lond). 2015 Sep;47(9):611-7.

Characteristics, causes, and outcome of 54 episodes of bloodstream infections in a cohort of HIV patients.

Declercq S, De Munter P, Derdelinckx I, Verhaegen J, Peetermans WE, Vander-schueren S, Van Wijngaerden E.

Abstract

BACKGROUND: Patients infected with human immunodeficiency virus (HIV) have an increased risk for bloodstream infections (BSIs). Published recent data on characteristics, etiology, and outcome of BSIs in HIV patients in high income countries are scarce.

METHODS: Blood cultures from 2001 to 2011 from adult HIV patients were retrieved. Blood cultures considered to be contamination based on isolates and clinical context were excluded. Clinical and microbiological characteristics of BSIs and patients were described, those of community-acquired and nosocomial episodes were compared, and risk factors for 6-month mortality were analyzed.

RESULTS: We found 54 episodes of true BSI in 46 patients. Demographics were

similar to those of the source cohort of all patients followed between 2001 and 2011. In 63% there was prior AIDS, in 91% a CD4 nadir below 200/mm³, and in 72% a latest CD4 count < 200/mm³. In 13% of patients BSI preceded a new HIV diagnosis within 1 week. Main causative microorganisms were coagulase-negative staphylococci (26%), *Streptococcus pneumoniae* (20%), and *Enterococcus* spp. (13%). The most frequent diagnoses were pneumonia (28%) and catheter-related BSI (CRBSI) (28%); 56% of episodes were nosocomial. The 1-month mortality rate was 17%, with a cause of death apparently unrelated to the BSI in five of nine episodes. The 6-month mortality was 28%. Factors of co-morbidity or immunodeficiency other than HIV were significantly associated with 6-month mortality. **CONCLUSIONS:** BSIs in HIV-infected patients occur predominantly in patients with advanced HIV infection. Community-acquired bacteremic pneumococcal pneumonia and nosocomial staphylococcal CRBSIs are the main causes. Mortality following BSI is high, and seems to be driven by underlying complicated HIV infection.

patients (odds ratio [OR], 2.345 [95% confidence interval {CI}, 1.084-5.071]). For early-onset infection (ie, occurred during the first 3 months after transplant), a longer duration of renal replacement therapy pretransplant and the occurrence of leukopenia were risk factors (OR per year, 1.192 [95% CI, 1.006-1.413] and OR, 3.346 [95% CI, 1.063-10.527], respectively), whereas donor cytomegalovirus seropositivity increased the risk for late-onset IA (ie, occurred >3 months after transplant) (OR, 3.677 [95% CI, 1.388-9.743]). Twelve-week mortality rate was 39%. Disseminated infection, leukopenia, and the height of the serum galactomannan index were associated with an increased risk of death (hazard ratio [HR], 5.080 [95% CI, 1.740-14.830]; HR, 3.198 [95% CI, 1.183-8.649]; and HR, 1.371 [95% CI, 1.123-1.674], respectively). **CONCLUSIONS:** Prolonged renal replacement therapy before kidney transplant increases the risk of IA early after transplant. The height of the serum galactomannan index predicts mortality.

Clin Infect Dis. 2015 May 15;60(10):1505-11.

Invasive aspergillosis after kidney transplant: case-control study.

Heylen L, Maertens J, Naesens M, Van Wijngaerden E, Lagrou K, Bammens B, Claes K, Evenepoel P, Meijers B, Kuypers D, Sprangers B.

Abstract

BACKGROUND: Transplant recipients are at risk for invasive aspergillosis (IA), associated with a significant mortality rate. Renal transplant-specific risk factors have not been established.

METHODS: Forty-one adult kidney transplant recipients diagnosed with proven or probable IA from 1995 through 2013 were identified by search of the computerized patient files in the University Hospitals Leuven. The control population in this 1:2 case-control study consisted of the 2 patients who received a kidney transplant immediately before and after each identified patient and did not develop IA (n = 82).

RESULTS: Leukopenia after kidney transplant increased the risk of IA among all

DIVISIE 6 (KRITIEKE DIENSTEN)

Ann Intensive Care. 2015 Dec;5(1):51.

Prevention and treatment of sepsis-induced acute kidney injury: an update.

Honore PM, Jacobs R, Hendrickx I, Bagshaw SM, Joannes-Boyau O, Boer W, De Waele E, Van Gorp V, Spapen HD.

Abstract

Sepsis-induced acute kidney injury (SAKI) remains an important challenge in critical care medicine. We reviewed current available evidence on prevention and treatment of SAKI with focus on some recent advances and developments. Prevention of SAKI starts with early and ample fluid resuscitation preferentially with crystalloid solutions. Balanced crystalloids have no proven superior benefit. Renal function can be evaluated by measuring lactate clearance rate, renal Doppler, or central venous oxygenation monitoring. Assuring sufficiently high central venous oxygenation most optimally prevents SAKI, especially in the post-operative setting, whereas lactate clearance better assesses mortality risk when SAKI is present. Although the adverse effects of an excessive "kidney afterload" are increasingly recognized, there is actually no consensus regarding an optimal central venous pressure. Noradrenaline is the vasopressor of choice for preventing SAKI. Intra-abdominal hypertension, a potent trigger of AKI in post-operative and trauma patients, should not be neglected in sepsis. Early renal replacement therapy (RRT) is recommended in fluid-overloaded patients' refractory to diuretics but compelling evidence about its usefulness is still lacking. Continuous RRT (CRRT) is advocated, though not sustained by convincing data, as the preferred modality in hemodynamically unstable SAKI. Diuretics should be avoided in the absence of hypervolemia. Antimicrobial dosing during CRRT needs to be thoroughly reconsidered to assure adequate infection control.

Eur J Emerg Med. 2015 Dec 11.

Impact of in or out of office hours at admission time on outcome in out-of-hospital cardiac arrest patients.

Genbrugge C, Viaene E, Meex I, De Vadder K, Eertmans W, Boer W, Jans F, De Deyne C, Dens J, Ferdinande B.

Abstract

BACKGROUND: In out-of-hospital cardiac arrest (OHCA), neurological outcome is determined by the severity of neurological injury, early percutaneous coronary intervention, and application of neuroprotective temperature management. As this is a very time-intensive and manpower-intensive protocol, we hypothesized that there would be a difference in outcome between OHCA patients admitted during and out of office hours.

METHODS: We prospectively collected demographic data of OHCA patients in two hospitals. All patients included were treated at 33°C for 24h, followed by a re-warming phase until 36.6°C. During office hours were defined as arriving between 8:00 a.m. and 5:00 p.m. on weekdays. Neurological outcome at 180 days was assessed following the Cerebral Performance Category scale.

RESULTS: Forty-seven (31%) patients were admitted during office hours and 105 (69%) out of office hours ($P=0.199$). Patients admitted during office hours were significantly older, respectively, 66 ± 14 and 59 ± 15 years ($P=0.014$). There was no significant difference between both groups in the number of patients who underwent coronary angiography, door to angiography time, and number of affected vessels. The median time spent in the target range of PaO₂, PaCO₂, and lactate was also not significantly different. We found no significant difference in survival until 180 days between both groups ($P=0.599$), even after adjustment for age (95% confidence interval: 0.44-1.90, hazard ratio: 0.912).

CONCLUSION: Survival until 180 days between OHCA patients admitted during office hours or out of office hours was not significantly different in two hospitals with a fixed protocol for neuroprotection and 24/7 streamlined access to coronary angiography.

Resuscitation. 2015 Nov;96:280-6.

Low hemoglobin levels are associated with lower cerebral saturations and poor outcome after cardiac arrest.

Ameloot K, Genbrugge C, Meex I, Janssens S, Boer W, Mullens W, Ferdinande B, Dupont M, Dens J, De Deyne C.

Abstract

PURPOSE: Post-cardiac arrest (CA) patients have a large cerebral penumbra at risk for secondary ischemic damage in case of suboptimal brain oxygenation during ICU stay. The aims of this study were to investigate the association between hemoglobin, cerebral oxygenation (SctO₂) and outcome in post-CA patients.

METHODS: Prospective observational study in 82 post-CA patients. Hemoglobin, a corresponding SctO₂ measured by NIRS and SVO₂ in patients with a pulmonary artery catheter ($n=62$) were determined hourly during hypothermia in the first 24h of ICU stay.

RESULTS: We found a strong linear relationship between hemoglobin and mean SctO₂ ($SctO_2=0.70\times\text{hemoglobin}+56$ ($R(2) 0.84$, $p=10(-6)$)). Hemoglobin levels below 10g/dl generally resulted in lower brain oxygenation. There was a significant association between good neurological outcome (43/82 patients in CPC 1-2 at 180 days post-CA) and admission hemoglobin above 13g/dl (OR 2.76, 95% CI 1.09:7.00, $p=0.03$) or mean hemoglobin above 12.3g/dl (OR 2.88, 95%CI 1.02:8.16, $p=0.04$). This association was entirely driven by results obtained in patients with a mean SVO₂ below 70% (OR 6.25, 95%CI 1.33:29.43, $p=0.01$) and a mean SctO₂ below 62.5% (OR 5.87, 95%CI 1.08:32.00, $p=0.03$).

CONCLUSION: Hemoglobin levels below 10g/dl generally resulted in lower cerebral oxygenation. Average hemoglobin levels below 12.3g/dl were associated with worse outcome in patients with suboptimal SVO₂ or SctO₂. The safety of a universal restrictive transfusion threshold of 7g/dl can be questioned in post-CA patients.

Crit Care. 2015 Mar 24;19:112.

Increase in cerebral oxygenation during advanced life support in out-of-hospital patients is associated with return of spontaneous circulation.

Genbrugge C, Meex I, Boer W, Jans F, Heylen R, Ferdinande B, Dens J, De Deyne C.

Abstract

INTRODUCTION: By maintaining sufficient cerebral blood flow and oxygenation, the goal of cardiopulmonary resuscitation (CPR) is to preserve the pre-arrest neuro-

logical state. To date, cerebral monitoring abilities during CPR have been limited. Therefore, we investigated the time-course of cerebral oxygen saturation values (rSO_2) during advanced life support in out-of-hospital cardiac arrest. Our primary aim was to compare rSO_2 values during advanced life support from patients with return of spontaneous circulation (ROSC) to patients who did not achieve ROSC.

METHODS: We performed an observational study to measure rSO_2 using Equanox (Nomin, Plymouth, MI) from the start of advanced life support in the pre-hospital setting.

RESULTS: rSO_2 of 49 consecutive out-of-hospital cardiac arrest patients were analyzed. The total increase from initial rSO_2 value until two minutes before ROSC or end of advanced life support efforts was significantly larger in the group with ROSC 16% (9 to 36) compared to the patients without ROSC 10% (4 to 15) ($P=0.02$). Mean rSO_2 from the start of measurement until two minutes before ROSC or until termination of advanced life support was higher in patients with ROSC than in those without, namely $39\% \pm 7$ and $31\% \pm 4$ ($P=0.05$) respectively.

CONCLUSIONS: During pre-hospital advanced life support, higher increases in rSO_2 are observed in patients attaining ROSC, even before ROSC was clinically determined. Our findings suggest that rSO_2 could be used in the future to guide patient tailored treatment during cardiac arrest and could therefore be a surrogate marker of the systemic oxygenation state of the patient.

COMMENT IN: CEREBRAL OXYGENATION. A new cardiac arrest correlation lacks implication.

Resuscitation. 2015 Jun;91:56-62.

Hemodynamic targets during therapeutic hypothermia after cardiac arrest: A prospective observational study.

Ameloot K, Meex I, Genbrugge C, Jans F, Boer W, Verhaert D, Mullens W, Ferdinande B, Dupont M, De Deyne C, Dens J.

Abstract

AIM: In analogy with sepsis, current post-cardiac arrest (CA) guidelines recommend to target mean arterial pres-

sure (MAP) above 65 mmHg and SVO₂ above 70%. This is unsupported by mortality or cerebral perfusion data. The aim of this study was to explore the associations between MAP, SVO₂, cerebral oxygenation and survival.

METHODS: Prospective, observational study during therapeutic hypothermia (24h - 33 °C) in 82 post-CA patients monitored with near-infrared spectroscopy.

RESULTS: Forty-three patients (52%) survived in CPC 1-2 until 180 days post-CA. The mean MAP range associated with maximal survival was 76-86 mmHg (OR 2.63, 95%CI [1.01; 6.88], $p = 0.04$). The mean SVO₂ range associated with maximal survival was 67-72% (OR 8.23, 95%CI [2.07; 32.68], $p = 0.001$). In two separate multivariate models, a mean MAP (OR 3.72, 95% CI [1.11; 12.50], $p=0.03$) and a mean SVO₂ (OR 10.32, 95% CI [2.03; 52.60], $p = 0.001$) in the optimal range persisted as independently associated with increased survival. Based on more than 1625000 data points, we found a strong linear relation between SVO₂ (range 40-90%) and average cerebral saturation ($R(2) 0.86$) and between MAP and average cerebral saturation for MAP's between 45 and 101 mmHg ($R(2) 0.83$). Based on our hemodynamic model, the MAP and SVO₂ ranges associated with optimal cerebral oxygenation were determined to be 87-101 mmHg and 70-75%.

CONCLUSION: we showed that a MAP range between 76-86 mmHg and SVO₂ range between 67% and 72% were associated with maximal survival. Optimal cerebral saturation was achieved with a MAP between 87-101 mmHg and a SVO₂ between 70% and 75%. Prospective interventional studies are needed to investigate whether forcing MAP and SVO₂ in the suggested range with additional pharmacological support would improve outcome.

Int J Nephrol Renovasc Dis. 2015 Mar 13;8:25-8.

A fresh look into the pathophysiology of ischemia-induced complications in patients with chronic kidney disease undergoing hemodialysis.

Honore PM, Jacobs R, De Waele E, Van

Gorp V, De Regt J, Joannes-Boyau O, Boer W, Spapen HD.

Abstract

Recent case reports of acute esophageal necrosis in patients with chronic kidney disease (CKD) undergoing hemodialysis encouraged us to look beyond hypoperfusion/ischemia as a sole explanation for this dramatic complication. At least three intriguing pathways, ie, accumulation of protein-bound toxins, endotoxin translocation, and altered mucosal defense mechanisms, have been proposed to explain the inherent susceptibility of CKD patients to developing ischemia-related and cardiovascular events. Interestingly, all the proposed pathways can be potentially antagonized or attenuated. At present, however, it is not known whether one pathway predominates or if any interaction exists between these pathways. More solid experimental and clinical data are warranted to acquire a better insight into the complex pathogenesis of CKD-associated ischemia.

Resuscitation. 2015 May;90:121-6.

An observational near-infrared spectroscopy study on cerebral autoregulation in post-cardiac arrest patients: time to drop 'one-size-fits-all' hemodynamic targets?

Ameloot K, Genbrugge C, Meex I, Jans F, Boer W, Vander Laenen M, Ferdinande B, Mullens W, Dupont M, Dens J, DeDeyne C.

Abstract

AIMS: A subgroup of patients with ROSC after cardiac arrest (CA) with disturbed cerebral autoregulation might benefit from higher mean arterial pressures (MAP). We aimed to (1) phenotype patients with disturbed autoregulation, (2) investigate whether these patients have a worse prognosis, (3) define an individual optimal MAP per patient and (4) investigate whether time under this individual optimal MAP is associated with outcome.

METHODS: Prospective observational study in 51 post-CA patients monitored with near infrared spectroscopy.

RESULTS: (1) 18/51 patients (35%) had disturbed autoregulation. Phenotypically, a higher proportion of patients with disturbed autoregulation had pre-CA hy-

pertension (31±47 vs. 65±49%, $p=0.02$) suggesting that right shifting of autoregulation is caused by chronic adaptation of cerebral blood flow to higher blood pressures. (2) In multivariate analysis, patients with preserved autoregulation ($n=33$, 65%) had a significant higher 180-days survival rate (OR 4.62, 95% CI [1.06:20.06], $p=0.04$). Based on an index of autoregulation (COX), the average COX-predicted optimal MAP was 85 mmHg in patients with preserved and 100 mmHg in patients with disturbed autoregulation. (3) An individual optimal MAP could be determined in 33/51 patients. (4) The time under the individual optimal MAP was negatively associated with survival (OR 0.97, 95% CI [0.96:0.99], $p=0.02$). The time under previously proposed fixed targets (65, 70, 75, 80 mmHg) was not associated with a differential survival rate.

CONCLUSION: Cerebral autoregulation showed to be disturbed in 35% of post-CA patients of which a majority had pre-CA hypertension. Disturbed cerebral autoregulation within the first 24h after CA is associated with a worse outcome. In contrast to uniform MAP goals, the time spent under a patient tailored optimal MAP, based on an index of autoregulation, was negatively associated with survival.

Trials. 2015 Mar 4;16:74.

Safety and feasibility of xenon as an adjuvant to sevoflurane anaesthesia in children undergoing interventional or diagnostic cardiac catheterization: study protocol for a randomised controlled trial.

Devroe S, Lemiere J, Van de Velde M, Ge-willig M, Boshoff D, Rex S.

Abstract

BACKGROUND: Xenon has minimal haemodynamic side effects when compared to volatile or intravenous anaesthetics. Moreover, in in vitro and in animal experiments, xenon has been demonstrated to convey cardio- and neuroprotective effects. Neuroprotection could be advantageous in paediatric anaesthesia as there is growing concern, based on both laboratory studies and retrospective human clinical studies, that anaesthetics may trigger an injury in the developing brain, resulting

in long-lasting neurodevelopmental consequences. Furthermore, xenon-mediated neuroprotection could help to prevent emergence delirium/agitation. Altogether, the beneficial haemodynamic profile combined with its putative organ-protective properties could render xenon an attractive option for anaesthesia of children undergoing cardiac catheterization.

METHODS/DESIGN: In a phase-II, mono-centre, prospective, single-blind, randomised, controlled study, we will test the hypothesis that the administration of 50% xenon as an adjuvant to general anaesthesia with sevoflurane in children undergoing elective cardiac catheterization is safe and feasible. Secondary aims include the evaluation of haemodynamic parameters during and after the procedure, emergence characteristics, and the analysis of peri-operative neuro-cognitive function. A total of 40 children ages 4 to 12 years will be recruited and randomised into two study groups, receiving either a combination of sevoflurane and xenon or sevoflurane alone.

DISCUSSION: Children undergoing diagnostic or interventional cardiac catheterization are a vulnerable patient population, one particularly at risk for intra-procedural haemodynamic instability. Xenon provides remarkable haemodynamic stability and potentially has cardio- and neuroprotective properties. Unfortunately, evidence is scarce on the use of xenon in the paediatric population. Our pilot study will therefore deliver important data required for prospective future clinical trials.

Anesthesiology. 2015 Feb;122(2):399-406.
Effect of minocycline on lumbar radicular neuropathic pain: a randomized, placebo-controlled, double-blind clinical trial with amitriptyline as a comparator.

Vanelderden P, Van Zundert J, Kozicz T, Puylaert M, De Vooght P, Mestrum R, Heylen R, Roubos E, Vissers K.

Abstract

BACKGROUND: Less than 50% of patients experience sufficient pain relief with current drug therapy for neuropathic pain. Minocycline shows promising results in rodent models of neuropathic pain but was

not studied in humans with regard to the treatment of neuropathic pain.

METHODS: In this randomized, double-blind, placebo-controlled clinical trial, patients with subacute lumbar radicular pain received placebo, amitriptyline 25 mg, or minocycline 100 mg once a day ($n = 20$ per group) for 14 days. Primary outcome measure was the pain intensity in the leg as measured by a numeric rating scale ranging from 0 to 10 on days 7 and 14. Secondary outcome measures were the reduction of neuropathic pain symptoms in the leg as determined with a neuropathic pain questionnaire, consumption of rescue medication, and adverse events on days 7 and 14.

RESULTS: Sixty patients were randomized and included in an intention-to-treat analysis. After 14 days, patients in the minocycline and amitriptyline groups reported a reduction of 1.47 (95% confidence interval, 0.16-2.83; $P = 0.035$) and 1.41 (95% confidence interval, 0.05-2.78; $P = 0.043$), respectively, in the numeric rating scale compared to the placebo group. No differences were seen in the neuropathic pain questionnaire values at any time point during treatment between the three groups. The rate of adverse events in the amitriptyline group was 10% versus none in the minocycline and placebo groups. No differences were noted in the consumption of rescue medication.

CONCLUSIONS: Although both groups differed from placebo, their effect size was small and therefore not likely to be clinically meaningful.

Local Reg Anesth. 2015 Dec 7;8:105-11.

Impact of volume expansion on the efficacy and pharmacokinetics of liposome bupivacaine.

Hadzic A, Abikhalel JA, Harmon WJ.

Abstract

Liposome bupivacaine is a prolonged-release liposomal formulation of bupivacaine indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia of longer duration than traditional local anesthetics. This review summarizes the available data on how volume expansion may impact the analgesic efficacy of liposome bupivacaine. The

Phase II and III clinical studies that involved surgical site administration of liposome bupivacaine at various concentrations in different surgical settings revealed no apparent concentration-efficacy relationship. A single-center, prospective study comparing the efficacy of transversus abdominis plane infiltration with liposome bupivacaine administered in a lower (266 mg/40 mL) vs a higher (266 mg/20 mL) dose concentration in subjects undergoing robotic-assisted laparoscopic prostatectomy also reported similar postsurgical pain intensity scores and opioid usage in both treatment groups. The pharmacokinetic profile of liposome bupivacaine following subcutaneous injections in rats was unaltered by differences in drug concentration, dose, or injection volume within the ranges tested. Volume expansion of liposome bupivacaine to a total volume of 300 mL or less does not appear to impact its clinical efficacy or pharmacokinetic profile, thus allowing flexibility to administer the formulation across a wide range of diluent volumes.

Anaesthesia. 2015 Dec;70(12):1418-26.

Neurotoxicity of perineural vs intraneural-extr fascicular injection of liposomal bupivacaine in the porcine model of sciatic nerve block.

Damjanovska M, Cvetko E, [Hadzic A](#), Seliskar A, Plavec T, Mis K, Vuckovic Hasanbegovic I, Stopar Pintaric T.

Abstract

Liposomal bupivacaine is a prolonged-release local anaesthetic, the neurotoxicity of which has not yet been determined. We used quantitative histomorphometric and immunohistochemical analyses to evaluate the neurotoxic effect of liposomal bupivacaine after perineural and intraneural (extr fascicular) injection of the sciatic nerve in pigs. In this double-blind prospective randomised trial, 4 ml liposomal bupivacaine 1.3% was injected either perineurally ($n = 5$) or intraneurally extr fascicularly ($n = 5$). Intraneural-extr fascicular injection of saline ($n = 5$) was used as a control. After emergence from anaesthesia, neurological examinations were conducted over two weeks. After harvesting the sciatic nerves, no changes

in nerve fibre density or myelin width indicative of nerve injury were observed in any of the groups. Intraneural injections resulted in longer sensory blockade than perineural ($p < 0.003$) without persistent motor or sensory deficit. Sciatic nerve block with liposomal bupivacaine in pigs did not result in histological evidence of nerve injury.

Reg Anesth Pain Med. 2015 Sep-Oct;40(5):401-30.

The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine: Executive Summary 2015.

Neal JM, Barrington MJ, Brull R, [Hadzic A](#), Hebl JR, Horlocker TT, Huntoon MA, Kopp SL, Rathmell JP, Watson JC.

Abstract

Neurologic injury associated with regional anesthetic or pain medicine procedures is extremely rare. The Second American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine focuses on those complications associated with mechanical, ischemic, or neurotoxic injury of the neuraxis or peripheral nervous system. As with the first advisory, this iteration does not focus on hemorrhagic or infectious complications or local anesthetic systemic toxicity, all of which are the subjects of separate practice advisories. The current advisory offers recommendations to aid in the understanding and potential limitation of rare neurologic complications that may arise during the practice of regional anesthesia and/or interventional pain medicine.

WHAT'S NEW: The Second American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine updates information that was originally presented at the Society's first open forum on this subject (2005) and published in 2008. Portions of the second advisory were presented in an open forum (2012) and are herein updated, with attention to those topics subject to evolving know-

ledge since the first and second advisory conferences. The second advisory briefly summarizes recommendations that have not changed substantially. New to this iteration of the advisory is information related to the risk of nerve injury inherent to common orthopedic surgical procedures. Recommendations are expanded regarding the preventive role of various monitoring technologies such as ultrasound guidance and injection pressure monitoring. New clinical recommendations focus on emerging concerns including spinal stenosis and vertebral canal pathologies, blood pressure management during neuraxial anesthesia, administering blocks in anesthetized or deeply sedated patients, patients with preexisting neurologic disease, and inflammatory neuropathies. An updated diagnostic and treatment algorithm is presented.

Reg Anesth Pain Med. 2015 Sep-Oct;40(5):572-82.

Safety and Side Effect Profile of Liposome Bupivacaine (Exparel) in Peripheral Nerve Blocks.

Ilfeld BM, Viscusi ER, [Hadzic A](#), Minkowitz HS, Morren MD, Lookabaugh J, Joshi GP.

Abstract

BACKGROUND: Liposome bupivacaine (Exparel) is a multivesicular liposomal formulation of bupivacaine currently approved in the United States for single-dose administration into the surgical site to provide postsurgical analgesia. This retrospective analysis examined safety data from clinical trials involving the off-label use of this formulation in peripheral nerve blocks.

METHODS: Data from 6 controlled (phases I-III) studies were compiled involving single-injection ankle, femoral nerve, and intercostal nerve blocks (2 each). Adverse events (AEs) were monitored for 1 to 30 days after study drug administration.

RESULTS: Of 575 subjects, 335 received liposome bupivacaine (2-310 mg), 33 received bupivacaine HCl (75-125 mg), and 207 received normal saline (placebo). Overall, 76% of subjects receiving liposome bupivacaine experienced 1 or more AEs compared with 61% receiving bupivacaine HCl and 76% receiving placebo.

The most frequently reported AEs among subjects receiving liposome bupivacaine were nausea, pyrexia, pruritus, constipation, and vomiting. The most common treatment-related AE was hypesthesia among subjects treated with liposome bupivacaine or bupivacaine HCl. Incidence of nervous system AEs for liposome bupivacaine, bupivacaine HCl, and placebo was 21%, 27%, and 21%, respectively. Similarly, incidence of cardiac AEs was 9%, 0%, and 12%, respectively. At least 1 serious AE occurred in 8% of subjects receiving liposome bupivacaine compared with 10% of those receiving placebo (none assessed by investigators as related to study medication).

CONCLUSIONS: Liposome bupivacaine has a similar safety and side effect profile to bupivacaine HCl and normal saline, suggesting that most of the more common AEs are related to either opioid rescue or the surgical procedure itself.

Reg Anesth Pain Med. 2015 Sep-Oct;40(5):479-90.

Pathophysiology and Etiology of Nerve Injury Following Peripheral Nerve Blockade.

Brull R, [Hadzic A](#), Reina MA, Barrington MJ.

Abstract

This review synthesizes anatomical, anesthetic, surgical, and patient factors that may contribute to neurologic complications associated with peripheral nerve blockade. Peripheral nerves have anatomical features unique to a given location that may influence risk of injury. Peripheral nerve blockade-related peripheral nerve injury (PNI) is most severe with intrafascicular injection. Surgery and its associated requirements such as positioning and tourniquet have specific risks. Patients with preexisting neuropathy may be at an increased risk of postoperative neurologic dysfunction. Distinguishing potential causes of PNI require clinical assessment and investigation; a definitive diagnosis, however, is not always possible. Fortunately, most postoperative neurologic dysfunction appears to resolve with time, and the incidence of serious long-term nerve injury directly

attributable to peripheral nerve blockade is relatively uncommon. Nonetheless, despite the use of ultrasound guidance, the risk of block-related PNI remains unchanged.

WHAT'S NEW: Since the 2008 Practice Advisory, new information has been published, furthering our understanding of the microanatomy of peripheral nerves, mechanisms of peripheral nerve injection injury, toxicity of local anesthetics, the etiology of and monitoring methods, and technologies that may decrease the risk of nerve block-related peripheral nerve injury.

Crit Care. 2015 Apr 2;19:171.

2015, big data in healthcare: for whom the bell tolls?

[Van Poucke S](#), [Thomeer M](#), [Hadzic A](#).

Anesthesiology. 2015 Apr;122(4):952-3.

When the statistics steal the show.

Levine M, Halaszynski T, Capdevila X, Ahmad I, Ivani G, [Vandepitte C](#), [Hadzic A](#).

Anesth Analg. 2015 May;120(5):1138-41.

The Disposition of Radiocontrast in the Interscalene Space in Healthy Volunteers.

Gautier P, [Vandepitte C](#), Schaub I, Fourneau K, Kuroda MM, De Merlier Y, [Hadzic A](#).

Abstract

BACKGROUND: We measured the spread of radiocontrast in the interscalene space after injection under low (<15 psi) and high (>20 psi) pressures.

METHODS: Nine healthy volunteers received ultrasound-guided injections of 10 mL radio-opaque NaCl 0.9% in both interscalene spaces. Spread of injectate as assessed by computed tomography scan and discomfort on injection were recorded.

RESULTS: Under both opening pressure conditions, injectate contacted 3 brachial plexus roots and spilled over the surface of the anterior and/or middle scalene muscles underneath the cervical fascia.

CONCLUSIONS: Regardless of injection pressure, the interscalene space was filled with 10 mL of radiocontrast injectate.

Reg Anesth Pain Med. 2015 Jan-Feb;40(1):75-81.

Ultrasound-guided lumbar plexus block using a transverse scan through the lumbar intertransverse space: a prospective case series.

[Karmakar MK](#), [Li JW](#), [Kwok WH](#), [Hadzic A](#).

Abstract

BACKGROUND AND OBJECTIVES: A paramedian transverse scan (PMTS) can be used to delineate the anatomy relevant for ultrasound-guided lumbar plexus block (LPB) through the lumbar intertransverse space. This case series evaluated the feasibility of using the PMTS to guide LPBs for anesthesia.

METHODS: After research ethics committee approval and written informed consent, 15 American Society of Anesthesiologists physical status 1 to III patients with body mass index of less than 35 kg/m scheduled for lower-extremity surgery received an ultrasound-guided LPB and a sciatic nerve block for anesthesia. The blocks were performed using the PMTS and in-plane needle insertion. Localization of the lumbar plexus was confirmed by obtaining quadriceps muscle twitch. Successful blocks were defined as adequate anesthesia for lower-extremity surgery in the sensory territory of the lumbar plexus.

RESULTS: The articular process and psoas muscle were visualized on ultrasound in all 15 patients (mean age, 46.3 ± 20.4 years; body mass index, 22.2 ± 2.4 kg/m), but the lumbar plexus was identified in two-thirds of the patients. Blocks were successfully performed in 14 (93%) of the 15 patients. Poor visibility in 1 patient (7%) precluded the use of ultrasound guidance. The needle was visualized in the psoas muscle in 14 patients (93%), whereas proper needle location was confirmed in all patients by nerve stimulation. Needle to lumbar plexus contact was delineated on ultrasound in 8 (53%) and 14 patients (93%), before and after injection of local anesthetic, respectively. Adequate anesthesia was accomplished in all patients within 30 minutes of injection.

CONCLUSION: Ultrasound-guided LPBs can be reliably accomplished using the PMTS.

Acta Anaesthesiol Belg. 2015;66(1):11-7.
Cerebral tissue oxygen saturation during arthroscopic shoulder surgery in the beach chair and lateral decubitus position.

Meex I, Genbrugge C, De Deyne C, Jans F.

Abstract

Arthroscopic shoulder surgery is a common procedure and can be performed with the patient in the lateral decubitus position (LDP) or beach chair position (BCP). Although the BCP is associated with better visualization and less bleeding, it has also been associated with hemodynamic changes and consequently cerebral hypoperfusion. Devastating events reported after surgery in the BCP were attributed to a combination of the upright position and hypotension. Besides position and blood pressure, ventilator management and type of anesthesia should be taken into account. Near infrared spectroscopy might be able to provide an early warning sign of cerebral hypoperfusion during shoulder surgery in the BCP. It was therefore recommended to continuously monitor cerebral oxygenation in patients undergoing shoulder surgery in the BCP, to potentially prevent devastating outcomes. However, more clinical research on the safe lower limits of cerebral tissue oxygen saturation is needed for this recommendation to gain broad acceptance.

Pain Med. 2015 Dec 15.

Reply to Remarks on the Six-Month Cohort Study on PRF for Chronic Intractable Radicular Pain Pain Medicine 2015.

Van Boxem K, de Meij N, Kessels A, Van Kleef M, Van Zundert J.

Pain Med. 2015 Jun;16(6):1155-62.

Pulsed radiofrequency for chronic intractable lumbosacral radicular pain: a six-month cohort study.

Van Boxem K, de Meij N, Kessels A, Van Kleef M, Van Zundert J.

Abstract

BACKGROUND AND OBJECTIVES: There is little evidence concerning the medical management of lumbosacral radicular

pain. The prognosis for patients suffering pain for more than 3 months is poor. Pulsed radiofrequency (PRF) treatment of the dorsal root ganglion (DRG) has been suggested as a minimally invasive treatment. We studied the effect on pain and quality of life of PRF treatment of the DRG in patients with chronic, severe lumbosacral radicular pain.

METHODS: Patients with lumbosacral radicular pain were screened to select a homogeneous population. PRF treatment of the DRG was performed at L5 or S1. Evaluation was carried out at 6 weeks, 3 months, and 6 months. Pain reduction and "fully recovered" or "much improvement," in terms of the global perceived effect, were the primary outcomes. Quality of life (RAND-36), disability (Oswestry Disability Index), and the neuropathic pain scales leads assessment of neuropathic symptoms and signs (LANSS) and DN4 were registered at each time point. Medication use was scored with the Medication Quantification Scale.

RESULTS: Out of 461 screened patients, 65 were included. According to the intention to treat analysis, clinical success was achieved in 56.9%, 52.3%, and 55.4% of the patients at respectively 6 weeks, 3 months, and 6 months. DN4, Oswestry Disability Index and physical component for the RAND-36 quality of life improved significantly while the mental component remained unchanged. The number of patients on opioids was reduced.

CONCLUSIONS: PRF treatment of the DRG may be considered for patients with chronic, severe lumbosacral radicular pain refractory to conventional medical management.

Reg Anesth Pain Med. 2015 Jan-Feb;40(1):85-9.

Impairment of sciatic nerve function during adductor canal block.

Gautier PE, Lecoq JP, Vandepitte C, Harstein G, Brichant JF.

Rev Esp Anestesiol Reanim. 2015 Feb;62(2):116-7.

Safety algorithms for ultrasound-guided blocks: the next challenge.

Sala-Blanch X, Lopez AM, Vandepitte C.

Thrombosis Research. Apr; 135(4):679-83.

Response of platelet concentrates to pressure and temperature changes without impairment of the in vitro function.

Kicken C, Van Poucke S, Marcus AE, Lancé MD, Henskens Y.

BACKGROUND: Rapid platelet concentrate (PC) transfusion is crucial for hemostatic resuscitation. Pressure-aided and warmed transfusion combined with pneumatic tube system (PTS) transport from the laboratory to the operating theatre offers a potentially rapid delivery technique. The aim of this study is a quantitative assessment of in vitro platelet function after PTS transport followed by warmed and/or pressure-aided mock transfusions.

METHODS: Ten PC samples entered a single PTS run and were subsequently aliquoted for testing. PCs were warmed in a blood warmer and/or subjected to pressure-aided mock transfusion at 300 mm Hg on day 2 or day 7 after collection. Platelet function was assessed using light-transmission aggregometry and multiple-electrode aggregometry to measure the response to ADP, arachidonic acid, collagen, and thrombin-receptor activating peptide. Data were analyzed with non-parametric testing; $P < 0.05$ was considered statistically significant.

RESULTS: Single PTS transport markedly reduced ADP response in fresh PCs. Seven-day storage had a pronounced effect on both ADP and collagen response. All other tested platelet agonists revealed preserved function. Subsequent warming and/or application of pressure did not significantly compromise platelet function.

CONCLUSIONS: Pressure-aided plus warmed transfusion and PTS transport was not found to be detrimental to the PC. Further clinical studies are required to determine safety and efficacy of the product.

Acta Clin Belg. 2015 Dec;70(6):447-50.

Late onset of Strongyloides stercoralis meningitis in a retired Belgian miner.

Pypen Y, Oris E, Meeuwissen J, Vander Laenen M, Van Gompel F, Coppens G.

Abstract

We report a rare case of Strongyloides stercoralis meningitis in an immuno-compromised patient treated for a lung carcinoma. Despite his Belgian origin, he was infected with S. stercoralis due to his former work as a miner. Although mostly prevalent in (sub)tropical areas, there are temperate regions where this nematode can occur.

DIVISIE 7 (MEDISCH-DIAGNOSTISCHE DIENSTEN)

J Neurooncol. 2015 Sep;124(2):317-23.

Complications related to the use of an intraventricular access device for the treatment of leptomeningeal metastases from solid tumor: a single centre experience in 112 patients.

Zairi F, Le Rhun E, Bertrand N, Boulangier T, Taillibert S, Aboukais R, Assaker R, Chamberlain MC.

Abstract

Ventricular access devices (VAD) offer several advantages compared to intralumbar injections for the administration of intra-CSF agents in the treatment of leptomeningeal metastases (LM). However, there are few prospective studies reporting on complications with the use of VADs. All complications were prospectively collected that pertained to the implantation and use of a VAD in consecutive patients with solid tumor-related LM from June 2006 to December 2013. Clinical follow-up was every 2 weeks during the initial 2 months of treatment and then once monthly. Complete neuraxis MRI was performed at baseline and then every 2-3 months. A total of 112 patients (88 women) with a mean age of 51.1 years (range 26-73) were included. Primary cancers included breast (79 patients), lung (12) and melanoma (6). All patients were treated with intra-CSF liposomal cytarabine. 72 % of the patients received concomitant systemic and intra-CSF chemotherapy. The placement of the VAD was performed under local anesthesia in all cases. The mean operative time was 15 min and no perioperative complications were reported. The mean number of intraventricular injections per patient was 9.34 (range 1-47). A total of 11 complications in 11 patients were seen including 7 infections, 1 intracranial hemorrhage, 2 instances of symptomatic leukoencephalopathy and 1 catheter malpositioning. 8 complications required an operation and 1 complication was fatal. The use of a VAD is safe and may improve patients' comfort and compliance with LM-directed therapy.

N Engl J Med. 2015 Apr 30;372 (18):1771.

Surgical treatment of moderate

ischemic mitral regurgitation.

Bertrand Pb, Vandervoort Pm, Dion Ra
JTCVS 2015 Nov; 150(5):1040-3

Is the air in Toronto, Rochester, and Cleveland different from that in London, Monaco, Leiden, Genk, Milan, and New York?

Dion R. Expert Opinion

J Hosp Infect. 2015 Oct;91(2):123-8.

A hospital-level cost-effectiveness analysis model for toxigenic Clostridium difficile detection algorithms.

Verhoye E, Vandecandelaere P, De Beenhouwer H, Coppens G, Cartuyvels R, Van den Abeele A, Frans J, Laffut W; Bilulu Study Group.

Abstract

BACKGROUND: Despite thorough analyses of the analytical performance of Clostridium difficile tests and test algorithms, the financial impact at hospital level has not been well described. Such a model should take institution-specific variables into account, such as incidence, request behaviour and infection control policies.

AIM: To calculate the total hospital costs of different test algorithms, accounting for days on which infected patients with toxigenic strains were not isolated and therefore posed an infectious risk for new/secondary nosocomial infections.

METHODS: A mathematical algorithm was developed to gather the above parameters using data from seven Flemish hospital laboratories (Bilulu Microbiology Study Group) (number of tests, local prevalence and hospital hygiene measures). Measures of sensitivity and specificity for the evaluated tests were taken from the literature. List prices and costs of assays were provided by the manufacturer or the institutions. The calculated cost included reagent costs, personnel costs and the financial burden following due and undue isolations and antibiotic therapies. Five different test algorithms were compared.

FINDINGS AND CONCLUSION: A dynamic calculation model was constructed to evaluate the cost:benefit ratio of each algorithm for a set of institution- and time-dependent inputted variables (prevalence, cost fluctuations and test per-

formances), making it possible to choose the most advantageous algorithm for its setting. A two-step test algorithm with concomitant glutamate dehydrogenase and toxin testing, followed by a rapid molecular assay was found to be the most cost-effective algorithm. This enabled resolution of almost all cases on the day of arrival, minimizing the number of unnecessary or missing isolations.

Transpl Infect Dis. 2015 Apr;17(2):303-7.

Resolution of diffuse skin and systemic Kaposi's sarcoma in a renal transplant recipient after introduction of everolimus: a case report.

Detroyer D, Deraedt K, Schöffski P, Hauben E, Lagrou K, Naesens M, Delforge ML, Kuypers D.

Abstract

We present a case report of a patient with diffuse skin and systemic Kaposi's sarcoma (KS), 1 year after renal transplantation. A concomitant Pyrenochaeta romeroi granuloma of the right hallux was diagnosed and illustrated an important immunodysfunction in our patient. Four months after reduction in immunosuppression and switch to everolimus, a total regression of the KS was observed. Reduction in the immunosuppression and treatment with terbinafine cleared the P. romeroi infection, while lowering immunosuppression and changing the type of immunosuppressive therapy were important steps in the successful management of the KS. In recent years, evidence of the antitumor effects of everolimus is increasing: total regression of KS in combination with renal function preservation in renal graft recipients is possible with mammalian target of rapamycin (mTOR) inhibitor-based regimens. In addition, with increasing numbers of human immunodeficiency virus-positive transplant recipients, mTOR inhibitors may play a more crucial role in the management of KS.

Gut. 2015 Apr;64(4):673-83.

Roux-en-y gastric bypass attenuates hepatic mitochondrial dysfunction in mice with non-alcoholic steatohepatitis.

Verbeek J, Lannoo M, Pirinen E, Ryu D, Spincemaille P, Vander Elst I, Windmolders P, Thevissen K, Cammue BP, van Pelt J, Fransis S, Van Eyken P, Ceuterick-De Groote C, Van Veldhoven PP, Bedossa P, Nevens F, Auwerx J, Cassiman D.

Abstract

OBJECTIVE: No therapy for non-alcoholic steatohepatitis (NASH) has been approved so far. Roux-en-y gastric bypass (RYGB) is emerging as a therapeutic option, although its effect on NASH and related hepatic molecular pathways is unclear from human studies. We studied the effect of RYGB on pre-existent NASH and hepatic mitochondrial dysfunction-a key player in NASH pathogenesis-in a novel diet-induced mouse model nicely mimicking human disease.

DESIGN: C57BL/6J mice were fed a high-fat high-sucrose diet (HF-HSD).

RESULTS: HF-HSD led to early obesity, insulin resistance and hypercholesterolaemia. HF-HSD consistently induced NASH (steatosis, hepatocyte ballooning and inflammation) with fibrosis already after 12-week feeding. NASH was accompanied by hepatic mitochondrial dysfunction, characterised by decreased mitochondrial respiratory chain (MRC) complex I and IV activity, ATP depletion, ultrastructural abnormalities, together with higher 4-hydroxynonenal (HNE) levels, increased uncoupling protein 2 (UCP2) and tumour necrosis factor- α (TNF- α) mRNA and free cholesterol accumulation. In our model of NASH and acquired mitochondrial dysfunction, RYGB induced sustained weight loss, improved insulin resistance and inhibited progression of NASH, with a marked reversal of fibrosis. In parallel, RYGB preserved hepatic MRC complex I activity, restored ATP levels, limited HNE production and decreased TNF- α mRNA.

CONCLUSIONS: Progression of NASH and NASH-related hepatic mitochondrial dysfunction can be prevented by RYGB. RYGB preserves respiratory chain complex activity, thereby restoring energy output, probably by limiting the amount of oxidative stress and TNF- α . These data suggest that modulation of hepatic mitochondrial function contributes to

the favourable effect of RYGB on established NASH.

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Environ Int. 2015 Feb;75:81-6.

Blood pressure changes in association with black carbon exposure in a panel of healthy adults are independent of retinal microcirculation.

Louwies T, Nawrot T, Cox B, Dons E, Penders J, Provost E, Panis LI, De Boever P.

Abstract

Exposure to ambient particulate matter and elevated blood pressure are risk factors for cardiovascular morbidity and mortality. Microvascular changes might be an important pathway in explaining the association between air pollution and blood pressure. The objective of the study was to evaluate the role of the retinal microcirculation in the association between black carbon (BC) exposure and blood pressure. We estimated subchronic BC exposure based on 1-week personal measurements (μ -Aethalometer, AethLabs) in 55 healthy nurses. Blood pressure and retinal microvasculature were measured on four different days (range: 2-4) during this week. Subchronic BC exposure averaged ($\pm$ SD) $1334 \pm 631 \text{ ng/m}^3$ and ranged from 338 ng/m^3 to 3889 ng/m^3 . An increased exposure of 631 ng/m^3 BC was associated with a 2.77 mmHg (95% CI: 0.39 to 5.15, $p=0.027$) increase in systolic blood pressure, a 2.35 mmHg (95% CI: 0.52 to 4.19, $p=0.016$) increase in diastolic blood pressure and with $5.65 \mu\text{m}$ (95% CI: 1.33 to 9.96, $p=0.014$) increase in central retinal venular equivalent. Mediation analysis failed to reveal an effect of retinal microvasculature in the association between blood pressure and subchronic BC exposure. In conclusion, we found a positive association between blood pressure and subchronic black carbon exposure in healthy adults. This finding adds evidence to the association between black carbon exposure and cardiovascular health effects, with elevated

blood pressure as a plausible intermediate effector. Our results suggest that the changes in a person's blood pressure as a result of subchronic black carbon exposure operate independently of the retinal microcirculation.

NMR Biomed. 2015 Dec;28(12):1599-624.

Hierarchical non-negative matrix factorization to characterize brain tumor heterogeneity using multi-parametric MRI.

Sauwen N, Sima DM, Van Cauter S, Veraart J, Leemans A, Maes F, Himmelfreich U, Van Huffel S.

Abstract

Tissue characterization in brain tumors and, in particular, in high-grade gliomas is challenging as a result of the co-existence of several intra-tumoral tissue types within the same region and the high spatial heterogeneity. This study presents a method for the detection of the relevant tumor substructures (i.e. viable tumor, necrosis and edema), which could be of added value for the diagnosis, treatment planning and follow-up of individual patients. Twenty-four patients with glioma [10 low-grade gliomas (LGGs), 14 high-grade gliomas (HGGs)] underwent a multi-parametric MRI (MP-MRI) scheme, including conventional MRI (cMRI), perfusion-weighted imaging (PWI), diffusion kurtosis imaging (DKI) and short-TE (1) H MRSI. MP-MRI parameters were derived: T2, T1 + contrast, fluid-attenuated inversion recovery (FLAIR), relative cerebral blood volume (rCBV), mean diffusivity (MD), fractional anisotropy (FA), mean kurtosis (MK) and the principal metabolites lipids (Lip), lactate (Lac), N-acetyl-aspartate (NAA), total choline (Cho), etc. Hierarchical non-negative matrix factorization (hNMF) was applied to the MP-MRI parameters, providing tissue characterization on a patient-by-patient and voxel-by-voxel basis. Tissue-specific patterns were obtained and the spatial distribution of each tissue type was visualized by means of abundance maps. Dice scores were calculated by comparing tissue segmentation derived from hNMF with the manual segmentation by a radiologist. Correlation coefficients were calculated

between each pathologic tissue source and the average feature vector within the corresponding tissue region. For the patients with HGG, mean Dice scores of 78%, 85% and 83% were obtained for viable tumor, the tumor core and the complete tumor region. The mean correlation coefficients were 0.91 for tumor, 0.97 for necrosis and 0.96 for edema. For the patients with LGG, a mean Dice score of 85% and mean correlation coefficient of 0.95 were found for the tumor region. hNMF was also applied to reduced MRI datasets, showing the added value of individual MRI modalities. Copyright © 2015 John Wiley & Sons, Ltd.

NMR Biomed. 2015 Dec;28(12):1599-624.

Hierarchical non-negative matrix factorization to characterize brain tumor heterogeneity using multi-parametric MRI.

Sauwen N, Sima DM, Van Cauter S, Veraart J, Leemans A, Maes F, Himmelreich U, Van Huffel S.

Abstract

Tissue characterization in brain tumors and, in particular, in high-grade gliomas is challenging as a result of the co-existence of several intra-tumoral tissue types within the same region and the high spatial heterogeneity. This study presents a method for the detection of the relevant tumor substructures (i.e. viable tumor, necrosis and edema), which could be of added value for the diagnosis, treatment planning and follow-up of individual patients. Twenty-four patients with glioma [10 low-grade gliomas (LGGs), 14 high-grade gliomas (HGGs)] underwent a multi-parametric MRI (MP-MRI) scheme, including conventional MRI (cMRI), perfusion-weighted imaging (PWI), diffusion kurtosis imaging (DKI) and short-TE (1) H MRSI. MP-MRI parameters were derived: T2, T1 + contrast, fluid-attenuated inversion recovery (FLAIR), relative cerebral blood volume (rCBV), mean diffusivity (MD), fractional anisotropy (FA), mean kurtosis (MK) and the principal metabolites lipids (Lip), lactate (Lac), N-acetyl-aspartate (NAA), total choline (Cho), etc. Hierarchical non-negative matrix factorization (hNMF) was applied to the MP-MRI

parameters, providing tissue characterization on a patient-by-patient and voxel-by-voxel basis. Tissue-specific patterns were obtained and the spatial distribution of each tissue type was visualized by means of abundance maps. Dice scores were calculated by comparing tissue segmentation derived from hNMF with the manual segmentation by a radiologist. Correlation coefficients were calculated between each pathologic tissue source and the average feature vector within the corresponding tissue region. For the patients with HGG, mean Dice scores of 78%, 85% and 83% were obtained for viable tumor, the tumor core and the complete tumor region. The mean correlation coefficients were 0.91 for tumor, 0.97 for necrosis and 0.96 for edema. For the patients with LGG, a mean Dice score of 85% and mean correlation coefficient of 0.95 were found for the tumor region. hNMF was also applied to reduced MRI datasets, showing the added value of individual MRI modalities.

Biomed Res Int. 2015;2015:842923.

Tumour Relapse Prediction Using Multiparametric MR Data Recorded during Follow-Up of GBM Patients.

Ion-Margineanu A, Van Cauter S, Sima DM, Maes F, Van Gool SW, Sunaert S, Himmelreich U, Van Huffel S.

Abstract

PURPOSE: We have focused on finding a classifier that best discriminates between tumour progression and regression based on multiparametric MR data retrieved from follow-up GBM patients.

MATERIALS AND METHODS: Multiparametric MR data consisting of conventional and advanced MRI (perfusion, diffusion, and spectroscopy) were acquired from 29GBM patients treated with adjuvant therapy after surgery over a period of several months. A 27-feature vector was built for each time point, although not all features could be obtained at all time points due to missing data or quality issues. We tested classifiers using LOPO method on complete and imputed data. We measure the performance by computing BER for each time point and wBER for all time points.

RESULTS: If we train random forests, LogitBoost, or RobustBoost on data with complete features, we can differentiate between tumour progression and regression with 100% accuracy, one time point (i.e., about 1 month) earlier than the date when doctors had put a label (progressive or responsive) according to established radiological criteria. We obtain the same result when training the same classifiers solely on complete perfusion data.

CONCLUSIONS: Our findings suggest that ensemble classifiers (i.e., random forests and boost classifiers) show promising results in predicting tumour progression earlier than established radiological criteria and should be further investigated.

Cancer Inform. 2015 Aug 12;14(Suppl 4):41-51.

Assessing Treatment Response Through Generalized Pharmacokinetic Modeling of DCE-MRI Data.

Kontopodis E, Kanli G, Manikis GC, Van Cauter S, Marias K.

Abstract

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) enables the quantification of contrast leakage from the vascular tissue by using pharmacokinetic (PK) models. Such quantitative analysis of DCE-MRI data provides physiological parameters that are able to provide information of tumor pathophysiology and therapeutic outcome. Several assumptive PK models have been proposed to characterize microcirculation in the tumoral tissue. In this paper, we present a comparative study between the well-known extended Tofts model (ETM) and the more recent gamma capillary transit time (GCTT) model, with the latter showing initial promising results in the literature. To enhance the GCTT imaging biomarkers, we introduce a novel method for segmenting the tumor area into subregions according to their vascular heterogeneity characteristics. A cohort of 11 patients diagnosed with glioblastoma multiforme with known therapeutic outcome was used to assess the predictive value of both models in terms of correctly classifying responders and nonresponders based on only one

DCE-MRI examination. The results indicate that GCTT model's PK parameters perform better than those of ETM, while the segmentation of the tumor regions of interest based on vascular heterogeneity further enhances the discriminatory power of the GCTT model.

Cancer Inform. 2015 Jun 10;14(Suppl 4):7-18.

A Proposed Paradigm Shift in Initializing Cancer Predictive Models with DCE-MRI Based PK Parameters: A Feasibility Study.

Roniotis A, Oraiopoulou ME, Tzamali E, Kontopodis E, Van Cauter S, Sakkalis V, Marias K.

Abstract

Glioblastoma multiforme is the most aggressive type of glioma and the most common malignant primary intra-axial brain tumor. In an effort to predict the evolution of the disease and optimize therapeutical decisions, several models have been proposed for simulating the growth pattern of glioma. One of the latest models incorporates cell proliferation and invasion, angiogenic net rates, oxygen consumption, and vasculature. These factors, particularly oxygenation levels, are considered fundamental factors of tumor heterogeneity and compartmentalization. This paper focuses on the initialization of the cancer cell populations and vasculature based on imaging examinations of the patient and presents a feasibility study on vasculature prediction over time. To this end, pharmacokinetic parameters derived from dynamic contrast-enhanced magnetic resonance imaging using Toft's model are used in order to feed the model. K (trans) is used as a metric of the density of endothelial cells (vasculature); at the same time, it also helps to discriminate distinct image areas of interest, under a set of assumptions. Feasibility results of applying the model to a real clinical case are presented, including a study on the effect of certain parameters on the pattern of the simulated tumor.

ANDERE

Crit Care Med. 2015 May;43(5):1053-61.

One fourth of unplanned transfers to a higher level of care are associated with a highly preventable adverse event: a patient record review in six Belgian hospitals.

Marquet K, Claes N, De Troy E, Kox G, Droogmans M, Schrooten W, Weekers F, Vlayen A, Vandersteen M, Vleugels A.

Abstract

OBJECTIVE: The objectives of this study are to determine the prevalence and preventability of adverse events requiring an unplanned higher level of care, defined as an unplanned transfer to the ICU or an in-hospital medical emergency team intervention, and to assess the type and the level of harm of each adverse event.

DESIGN: A three-stage retrospective review process of screening, record review, and consensus judgment was performed.

SETTING: Six Belgian acute hospitals.

PATIENTS: During a 6-month period, all patients with an unplanned need for a higher level of care were selected.

INTERVENTIONS: The records 6-month period, the records of all patients with an unplanned need for a higher level of care were assessed by a trained clinical team consisting of a research nurse, a physician, and a clinical pharmacist.

MEASUREMENTS AND MAIN RESULTS:

Adverse events were found in 465 of the 830 reviewed patient records (56%). Of these, 215 (46%) were highly preventable. The overall incidence rate of patients being transferred to a higher level of care involving an adverse event was 117.6 (95% CI, 106.9-128.3) per 100,000 patient days at risk, of which 54.4 (95% CI, 47.15-61.65) per 100,000 patient days at risk involving a highly preventable adverse event. This means that 25.9% of all unplanned transfers to a higher level of care were associated with a highly preventable adverse event. The adverse events were mainly associated with drug therapy (25.6%), surgery (23.7%), diagnosis (12.4%), and system issues (12.4%). The level of harm varied from temporary harm (55.7%) to long-term or permanent impairment (19.1%) and death (25.2%). Although the direct causality is often hard to prove, it is reasonable

to consider these adverse events as a contributing factor.

CONCLUSION: Adverse events were found in 56% of the reviewed records, of which almost half were considered highly preventable. This means that one fourth of all unplanned transfers to a higher level of care were associated with a highly preventable adverse event.

Psychooncology. 2015 Dec;24(12):1639-45.

Resilience as a predictor for emotional response to the diagnosis and surgery in breast cancer patients.

Markovitz SE, Schrooten W, Arntz A, Peters ML.

Abstract

OBJECTIVE: The purposes of the present study were to investigate the role of resilience in the prediction of emotional response in breast cancer patients and to examine whether this association is specific for women undergoing this emotionally taxing condition or whether resilience is more generally associated with higher levels of emotional well-being.

METHODS: Two hundred fifty-three breast cancer patients and 211 healthy female controls completed four psychological questionnaires. Measures comprised the Connor-Davidson Resilience Scale, the Hospital Anxiety and Depression Scale, Positive and Negative Affect Schedule, and two happiness items. Cancer patients were assessed after diagnosis and surgery.

RESULTS: Cancer patients reported higher levels of anxiety, depression, and negative affect and lower levels of positive affect and current happiness compared with control women. There was no difference between the two groups in level of resilience. Higher levels of resilience were related to better emotional adjustment both in women with breast cancer and in control women, but this association was stronger within the sample of cancer patients. In fact, patients scoring high on resilience seemed to experience similar levels of anxiety, depression, and current happiness as healthy women.

CONCLUSION: Our results confirm that

resilience may at least partially protect against emotional distress in cancer patients. Our findings suggest that resilience may be a relatively stable trait that is not affected by adversity.

J Psychiatr Pract. 2015 Mar;21(2):124-39.

Measuring safety culture in Belgian psychiatric hospitals: validation of the Dutch and French translations of the hospital survey on patient safety culture.

Vlayen A, Hellings J, Claes N, Abdou EA, Schrooten W.

Abstract

OBJECTIVES: To measure safety culture in Belgian psychiatric hospitals on 12 dimensions and to examine the psychometric properties of the Dutch and French translations of the Hospital Survey on Patient Safety Culture (HSPSC) for use in psychiatric hospitals.

METHODS: The authors analyzed 6,658 completed questionnaires (70.5% response rate) from a baseline measurement (2007-2009) in 44 psychiatric hospitals and 8,353 questionnaires (71.5% response rate) from a follow-up measurement (2011) in 46 psychiatric hospitals. Psychometric properties of the questionnaire were evaluated using item analysis, exploratory factor analysis (EFA), confirmatory factor analysis (CFA), reliability analysis (Cronbach's alpha), and analysis of composite scores and inter-correlations.

RESULTS: For both translations, CFA showed an acceptable fit with the original 12-dimensional model. For the Dutch and French translations, EFA showed a 10-factor and a 9-factor optimal measurement model, respectively. Cronbach's alpha indicated an acceptable level of reliability (≥ 0.70) for 7 of 12 dimensions. Most pair-wise correlations were significant and <0.5 , implying good construct validity.

CONCLUSION: The Dutch and French translations of the HSPSC were found to be valid and reliable for measuring patient safety culture in psychiatric hospitals. Our results also suggest the use of combinations of specific dimensions as recommended in previous research.

J Patient Saf. 2015 Jun;11(2):110-21.

Variability of patient safety culture in Belgian acute hospitals.

Vlayen A, Schrooten W, Wami W, Aerts M, Barrado LG, Claes N, Hellings J.

Abstract

OBJECTIVES: The aim of this study was to measure differences in safety culture perceptions within Belgian acute hospitals and to examine variability based on language, work area, staff position, and work experience.

METHODS: The Hospital Survey on Patient Safety Culture was distributed to hospitals participating in the national quality and safety program (2007-2009). Hospitals were invited to participate in a comparative study. Data of 47,136 respondents from 89 acute hospitals were used for quantitative analysis. Percentages of positive response were calculated on 12 dimensions. Generalized estimating equations models were fitted to explore differences in safety culture.

RESULTS: Handoffs and transitions, staffing, and management support for patient safety were considered as major problem areas. Dutch-speaking hospitals had higher odds of positive perceptions for most dimensions in comparison with French-speaking hospitals. Safety culture scores were more positive for respondents working in pediatrics, psychiatry, and rehabilitation compared with the emergency department, operating theater, and multiple hospital units. We found an important gap in safety culture perceptions between leaders and assistants within disciplines. Administration and middle management had lower perceptions toward patient safety. Respondents working less than 1 year in the current hospital had more positive safety culture perceptions in comparison with all other respondents.

CONCLUSIONS: Large comparative databases provide the opportunity to identify distinct high and low scoring groups. In our study, language, work area, and profession were identified as important safety culture predictors. Years of experience in the hospital had only a small effect on safety culture perceptions.

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