6ème Journée et Prix de la Recherche Clinique

Jeudi 16 mai 2013
13h30 – 17h30

HUG – Site Cluse-Roseraie
Nouvel auditoire de pédiatrie, 45 rue de la Roseraie - niveau 2

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

CRC Centre de Recherche Clinique

HUG Hôpitaux Universitaires de Genève

PROGRAMME

13h30 Introduction
Pr. Jérôme Pugin, Vice-doyen à la recherche de la Faculté de médecine de l'Université de Genève, Président du Centre de Recherche Clinique

13h45 Présentations orales – Partie I (9 minutes de présentation, suivie de 3 minutes de discussion)
Modérateur: Pr. Jérôme Pugin

13h45	Dre E. Alirol:	**Nifurtimox-Eflornithine Combination Therapy (NECT) for second-stage gambiense human African trypanosomiasis: MSF experience in the Democratic Republic of the Congo**
13h57	Dr J. Ambrosioni:	**Impact of highly active antiretroviral therapy on the molecular epidemiology of newly diagnosed HIV infections**
14h09	Dre V. Dutoit:	**Exploiting the glioblastoma peptidome to discover novel tumour-associated antigens for immunotherapy**
14h21	Dr I. Guessous:	**1999-2009 Trends in prevalence, unawareness, treatment and control of hypertension in Geneva, Switzerland**
14h33	Dre C. Heidegger:	**Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial**
14h45	Dr J. Klein:	**Assessment of sexual function and conjugal satisfaction prior to and after transplantation**

15h00 Visite des posters et vote du public du meilleur poster
Café et douceurs à disposition

15h30 Présentations orales – Partie II
Modérateur: Pr. Thomas Perneger, Responsable de l'unité d'appui méthodologique du Centre de Recherche Clinique

15h30	Dr R. Meier:	**Increasing Occurrence of Atypical Femoral Fractures Associated With Bisphosphonate Use**
15h42	Dr Y. Mueller:	**Transplanted human pancreatic islets after long-term insulin independence**
15h54	Dr L. Orci:	**Systematic review and meta-analysis of the effect of perioperative steroids on ischaemia–reperfusion injury and surgical stress response in patients undergoing liver resection**
16h06		Présentation annulée
16h18	Dr L. Spahr:	**Transplantation autologue de cellules souches issues de la moelle osseuse lors de cirrhose alcoolique décompensée: une étude clinique controlee**
16h30	Dr A. Trombetti:	**Effect of a multifactorial fall-and-fracture risk assessment and management program on gait and balance performances and disability in hospitalized older adults: a controlled study**

16h45 Conférence par la Dre Françoise Lascombes**,** Adjointe scientifique du Centre de recherche clinique:
La Qualité dans les Essais Cliniques, pourquoi ? Comment ?

17h10 Remise des Prix de la Recherche 2013 et du prix du meilleur poster
Clôture de la journée par le Pr Pierre Dayer, Directeur médical

17h20 Apéritif

MOT DE BIENVENUE

Cher(e) Collègue,

La Journée de la recherche clinique est dorénavant bien établie dans le programme des manifestations de nos institutions : c'est le rendez-vous du mois de mai qui reflète l'activité de recherche par l'intermédiaire des publications soumises.
Un jury dirigé par le Pr Th. Berney a choisi les résumés qui seront présentés oralement et parmi ces résumés, celui qui recevra le Prix de la recherche clinique 2013.
Quant aux posters, c'est vous qui choisirez le meilleur poster car ils seront soumis à l'évaluation du public. Pour que votre choix soit éclairé, les auteurs des posters seront présents pendant la visite entre 15h00 et 15h30 et répondront à vos questions.

Les présentations orales seront suivies par la Conférence de la Docteure Françoise Lascombes, adjointe scientifique du Centre de Recherche Clinique :

La Qualité dans les Essais Cliniques, pourquoi ? Comment ?

Comme d'habitude, la distribution des prix par le Directeur médical, le Pr Pierre Dayer, clôturera la journée.

Nous nous réjouissons de vous voir nombreux le 16 mai 2013 !

Professeur Jérôme Pugin

Docteure Françoise Lascombes

INFORMATION GENERALE

Qui participe?

Tous les chercheurs des HUG et de la Faculté de médecine ayant terminé récemment un projet de recherche clinique dont les résultats sont directement applicables aux soins ou aux patients.
53 recherches provenant de services très variés ont été soumises pour cette sixième édition.

Le jury :

Pr Thierry Berney, chirurgie (Président)
Pr François Pralong, pour le CHUV
Pre Samia Hurst, pour l'Université de Genève, Institut d'éthique biomédicale
Dr Patrick Saudan, néphrologie
Pr Jean-Paul Vallée, radiologie
Pr Michel Boulvain, gynécologie-obstétrique
Dr Patrice Lalive d'Epinay, neurosciences

Le jury a sélectionné les recherches présentées par oral et a désigné l'équipe de recherche lauréate du Prix.

Le Prix de la recherche clinique :

Un diplôme ainsi qu'une somme de CHF 1'000.- sont décernés aux auteurs.

Le Prix du meilleur poster :

Un prix sera attribué au meilleur poster assorti d'une somme de 1'000.- francs, décerné par vote du public.

Pour toute information sur la Journée de la recherche clinique:
http://crc.hug-ge.ch/
corinne.chaudet@hcuge.ch, tél. 022 372 91 34

RECUEIL DES RESUMES

PRESENTATIONS ORALES

ORDRE SELON LE PROGRAMME

NIFURTIMOX-EFLORNITHINE COMBINATION THERAPY (NECT) FOR SECOND-STAGE GAMBIENSE HUMAN AFRICAN TRYPANOSOMIASIS: MSF EXPERIENCE IN THE DEMOCRATIC REPUBLIC OF THE CONGO

***Emilie Alirol**, David Shrumpf, Josué Amici Heradi, Andrea Riedel, Catherine de Patoul, Michel Quere, François Chappuis*

Médecine Internationale et Humanitaire, HUG

Introduction: Existing diagnostic and treatment tools for Human African Trypanosomiasis (HAT) are limited. The recent development of Nifurtimox Eflornithine Combination Therapy (NECT) has brought new hopes for patients in the second stage. While NECT has been rolled out in most endemic countries, safety data are scarce and only derive from clinical trials. The WHO coordinates a pharmacovigilance program to collect additional data on NECT safety and efficacy. We report here the results of 18 months experience of NECT use in treatment centres run by Médecins Sans Frontières (MSF) in Democratic Republic of the Congo (DRC).
Méthode: This cohort study included 684 second-stage HAT patients (including 120 children) treated with NECT in Doruma and Dingila hospitals, northeastern DRC, between January 2010 and June 2011. All treatment emergent Adverse Events (AE) were recorded and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Safety and efficacy data were retrieved from the WHO pharmacovigilance forms and from Epitryps, a program monitoring database.
Résultat: < td>86% of the patients experienced at least one AE during treatment. On average, children experienced less AE than adults. Most AEs were mild (37.9%) or moderate (54.7%). Severe AEs included vomiting (n=32), dizziness (n=16), headache (n=11) and convulsions (n=11). The in-hospital case fatality rate was low (0.15%) and relapses were rare (n=14).
Conclusion: In comparison with previous treatments, NECT was effective, safe and well tolerated in non-trial settings in DRC, further supporting the roll out of NECT as first-line treatment in second-stage T.b. gambiense HAT. Tolerance was particularly good in children.

IMPACT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ON THE MOLECULAR EPIDEMIOLOGY OF NEWLY DIAGNOSED HIV INFECTIONS.

***Juan Ambrosioni,** Thomas Junier, Cécile Delhumeau, Alexandra Calmy, Bernard Hirschel, Evgeny Zdobnov, Laurent Kaiser, Sabine Yerly, Swiss HIV Cohort Study*

Infectious Diseases, HUG

Introduction: Highly active antiretroviral therapy (HAART)reduces viral load and HIV transmission. Our aim was to evaluate HIV-1 transmission trends and the impact of HAART expansion on newly diagnosed HIV infections in Geneva, Switzerland.
Méthode: Retrospective molecular epidemiology analysis of all newly HIV-diagnosed individuals between 2008 and 2010. Phylogenetic analyses were performed using pol sequences of 780 newly HIV-1 diagnosed individuals between 2000 and 2010, and 1058 individuals diagnosed before 2000. All clusters including individuals diagnosed in 2008–2010 were analyzed. Recent HIV infections (<1 year) were determined by documented seroconversion and/or fraction of ambiguous nucleotides. Median viral load and HAART coverage during the study period were obtained from patients included in the Swiss HIV Cohort Study (SHCS).
Résultat: Among 142 newly diagnosed individuals during 2008–2010, 49% had a recent infection and 42% were included in transmission clusters. Among the latter, two thirds were included in new clusters and one-third expanded previously known clusters. Men-having-sex-with-men (MSM) carrying resistant strains were more frequently included in clusters. Only 1.8% of individuals diagnosed before 2000 and 10.8% diagnosed during 2000–2008 were included in clusters involving individuals diagnosed between 2008 and 2010. During 2008–2010, the median population viral load of SHCS-enrolled individuals was significantly lower for individuals diagnosed before 2000 than for those diagnosed during 2000–2008 and 2008–2010 and HAART coverage significantly higher.
Conclusion: MSM with recent HIV infection are a significant source of onward transmission in Geneva. Individuals diagnosed before 2000 were only exceptionally related to newly diagnosed infections between 2008 and 2010 what may be the consequence of their larger HAART coverage. Prevention campaigns need to be focused on improving diagnosis and treatment for recently infected individuals.

EXPLOITING THE GLIOBLASTOMA PEPTIDOME TO DISCOVER NOVEL TUMOUR-ASSOCIATED ANTIGENS FOR IMMUNOTHERAPY

Valérie Dutoit *Christel Herold-Mende Norbert Hilf Oliver Schoor Philipp Beckhove Judith Bucher Katharina Dorsch Sylvia Flohr Jens Fritsche Peter Lewandrowski Jennifer Lohr Hans-Georg Rammensee Stefan Stevanovic Claudia Trautwein Verona Vass Steffen Walter Paul R. Walker Toni Weinschenk Harpreet Singh-Jasuja Pierre-Yves Dietrich*

Laboratoire d'immunologie des tumeurs, Service d'oncologie, HUG

Introduction: Peptides presented at the cell surface reflect the protein content of the cell; those on HLA class I molecules comprise the critical peptidome elements interacting with CD8 T lymphocytes. We hypothesize that peptidomes from ex vivo tumour samples encompass immunogenic tumour antigens.
Méthode: Starting with ex vivo tumor samples, we isolated and sequenced HLA-binding peptides using HPLC and mass spectrometry.
Résultat: We uncover more than 6000 HLA-bound peptides from HLA-A*02+ glioblastoma, of which over 3000 were restricted by HLA-A*02. We prioritized in-depth investigation of 10 glioblastoma-associated antigens based on high expression in tumours, very low or absent expression in healthy tissues, implication in gliomagenesis and immunogenicity. Patients with glioblastoma showed no T cell tolerance to these peptides. Moreover, we demonstrated specific lysis of tumour cells by patients' CD8+ T cells in vitro. In vivo, glioblastoma-specific CD8+ T cells were present at the tumour site.
Conclusion: Overall, our data show the physiological relevance of the peptidome approach and provide a critical advance for designing a rational glioblastoma immunotherapy. The peptides identified in our study are currently being tested as a multipeptide vaccine(IMA950) in patients with glioblastoma.

1999-2009 TRENDS IN PREVALENCE, UNAWARENESS, TREATMENT AND CONTROL OF HYPERTENSION IN GENEVA, SWITZERLAND

Guessous I*, Bochud M, Theler JM, Gaspoz JM, Pechère-Bertschi A.*

Idris Guessous, Jean-Marc Theler, Jean-Michel Gaspoz Unit of Population Epidemiology, Division of Primary Care Medicine, Department of Community Medicine, Primary Care and Emergency Medicine, Geneva University Hospitals, Geneva, Switzerland Idris Guessous, Murielle Bochud Community Prevention Unit, University Institute of Social and Preventive Medicine, Lausanne University Hospital, Lausanne, Switzerland Idris Guessous, Antoinette Pechère-Bertschi Unit of Hypertension, Departments of Specialties of Medicine and Community Medicine and Primary Care and Emergency Medicine, Geneva University Hospitals, Geneva, Switzerland

Introduction: There are no time trends in prevalence, unawareness, treatment, and control of hypertension in Switzerland. The objective of this study was to analyze these trends and to determine the associated factors.
Méthode: Population-based study conducted in the Canton of Geneva, Switzerland, between 1999 and 2009. Blood pressure was measured thrice using a standard protocol. Hypertension was defined as mean systolic or diastolic blood pressure ≥ 140/90 mmHg or self-reported hypertension or anti-hypertensive medication. Unawareness, untreated and uncontrolled hypertension was determined by questionnaires/blood pressure measurements. Yearly age-standardized prevalences and adjusted associations for the 1999-2003 and 2004-2009 survey periods were reported.
Résultat: The 10-year survey included 9,215 participants aged 35 to 74 years. Hypertension remained stable (34.4%). Hypertension unawareness decreased from 35.9% to 17.7% (P<0.001). The decrease in hypertension unawareness was not paralleled by a concomitant absolute increase in hypertension treatment, which remained low (38.2%). A larger proportion of all hypertensive participants were aware but not treated in 2004-2009 (43.7%) compared to 1999-2003 (33.1%). Uncontrolled hypertension improved from 62.2% to 40.6% between 1999 and 2009 (P = 0.02). In 1999-2003 period, factors associated with hypertension unawareness were current smoking (OR = 1.27, 95%CI, 1.02-1.59), male gender (OR = 1.56, 1.27-1.92), hypercholesterolemia (OR = 1.31, 1.20-1.44), and older age (OR 65-74 yrs vs 35-49 yrs = 1.56, 1.21-2.02). In 1999-2003 and 2004-2009, obesity and diabetes were negatively associated with hypertension unawareness, high education was associated with untreated hypertension (OR = 1.45, 1.12-1.88 and 1.42, 1.02-1.99, respectively), and male gender with uncontrolled hypertension (OR = 1.49, 1.03-2.17 and 1.65, 1.08-2.50, respectively). Sedentarity was associated with higher risk of hypertension and uncontrolled hypertension in 1999-2003.
Conclusion: Hypertension prevalence remained stable since 1999 in the canton of Geneva. Although hypertension unawareness substantially decreased, more than half of hypertensive subjects still remained untreated or uncontrolled in 2004-2009. This study identified determinants that should guide interventions aimed at improving hypertension treatment and control.

OPTIMISATION OF ENERGY PROVISION WITH SUPPLEMENTAL PARENTERAL NUTRITION IN CRITICALLY ILL PATIENTS: A RANDOMISED CONTROLLED CLINICAL TRIAL

***Claudia Paula Heidegger**, Mette M. Berger, Séverine Graf, Walter Zingg, Patrice Darmon, Michael C. Costanza, Ronan Thibault, Claude Pichard*

Service of Intensive Care (C P Heidegger MD, S Graf BSc), Nutrition Unit (S Graf, P Darmon MD, R Thibault MD, Prof C Pichard MD), and Infection Control Programme (W Zingg MD), Geneva University Hospital, Geneva, Switzerland; Service of Adult Intensive Care, Lausanne University Hospital, Lausanne, Switzerland (Prof M M Berger MD); and Department of Mathematics and Statistics, University of Vermont, Burlington, VT, USA (Prof M C Costanza PhD)

Introduction: Background Enteral nutrition (EN) is recommended for patients in the intensive-care unit (ICU), but it does not consistently achieve nutritional goals. We assessed whether delivery of 100% of the energy target from days 4 to 8 in the ICU with EN plus supplemental parenteral nutrition (SPN) could optimise clinical outcome.
Méthode: This randomised controlled trial was undertaken in two centres in Switzerland. We enrolled patients on day 3 of admission to the ICU who had received less than 60% of their energy target from EN, were expected to stay for longer than 5 days, and to survive for longer than 7 days. We calculated energy targets with indirect calorimetry on day 3, or if not possible, set targets as 25 and 30 kcal per kg of ideal bodyweight a day for women and men,respectively. Patients were randomly assigned (1:1) by a computer-generated randomisation sequence to receive EN or SPN. The primary outcome was occurrence of nosocomial infection after cessation of intervention (day 8), measured until end of follow-up (day 28), analysed by intention to treat. This trial is registered with ClinicalTrials.gov:NCT00802503.
Résultat: We randomly assigned 153 patients to SPN and 152 to EN. 30 patients discontinued before the study end. Mean energy delivery between day 4 and 8 was 28 kcal/kg per day (SD 5) for the SPN group (103% [SD 18%] of energy target), compared with 20 kcal/kg per day (7) for the EN group (77[27%]). Between days 9 and 28, 41 (27%) of 153 patients in the SPN group had a nosocomial infection compared with 58 (38%) of 152 patients in the EN group (hazard ratio 0·65, 95% CI 0·43–0·97; p=0·0338), and the SPN group had a lower mean number of nosocomial infections per patient (−0·42 [−0·79 to −0·05]; p=0·0248).
Conclusion: Individually optimised energy supplementation with SPN starting 4 days after ICU admission could reduce nosocomial infections and should be considered as a strategy to improve clinical outcome in patients in the ICU for whom EN is insufficient.

ASSESSMENT OF SEXUAL FUNCTION AND CONJUGAL SATISFACTION PRIOR TO AND AFTER TRANSPLANTATION

***Jacques Klein**, Sao-Nam Tran, Ariane Mentha-Dugerdil, Emiliano Giostra, Pietro Majno, Isabelle Morard, Thierry Berney, Pascale Dendauw, Philippe Morel, Gilles Mentha, Christophe E. Iselin, Christian Toso*

Service d'Urologie Service de la Chirurgie viscérale et de Transplantation, HUG

Introduction: The aims of this study were to assess sexual function and conjugal satisfaction in patients prior to and after liver transplantation, and in comparison to healthy individuals.
Méthode: A cross-sectional cohort questionnaire assessment was performed in adult liver recipients, including the International Index of Erectile Function (IIEF) for men or the Female Sexual Function Index (FSFI) for women. Conjugal satisfaction was assessed with the Locke-Wallace Marital Adjustment Test. Waitlist candidates and age-matched healthy individuals were used as controls.
Résultat: Questionnaires of 136 patients were assessed (45 women/91 men, mean age: 57 +/-11 years). Overall, sexual function improved after transplantation (male: p=0.065 and female: p=0.072), but remained lower than in aged-matched healthy individuals. The post-transplant level of conjugal satisfaction was stable and similar to healthy controls in men, but improved significantly in women (p=0.008), with higher levels than in healthy subjects (p=0.05).
Conclusion: The present study shows that sexual function improves after transplantation, yet not to the level of healthy controls. It also demonstrates, for the first time, that post-transplant conjugal satisfaction is at least similar to the one of healthy controls.

INCREASING OCCURRENCE OF ATYPICAL FEMORAL FRACTURES ASSOCIATED WITH BISPHOSPHONATE USE

***Raphael P. H. Meier**; Thomas V. Perneger; Richard Stern; Rene Rizzoli; Robin E. Peter*

Department of Surgery (Dr Meier), Division of Clinical Epidemiology and Clinical Research Center (Dr Perneger), Division of Orthopedic Surgery, Department of Surgery (Drs Stern and Peter), and Division of Bone Disease, Department of Medical Specialties (Dr Rizzoli), University Hospitals of Geneva and Faculty of Medicine, Geneva, Switzerland.

Introduction: Current evidence suggests that there is an association between bisphosphonate therapy and atypical femoral fractures, but the extent of this risk remains unclear.
Méthode: Between 1999 and 2010, a total of 477 patients 50 years and older were hospitalized with a subtrochanteric or femoral shaft fracture at a single university medical center. Admission radiographs and medical and treatment records were examined, and patients were classified as having atypical or classic femoral fractures. A random sample of 200 healthy individuals without femoral fracture were also identified. Multivariate logistic regression was used to assess the association of bisphosphonate use and atypical femoral fracture, and the incidence rates of each type of fracture over time were calculated.
Résultat: Thirty-nine patients with atypical fractures and 438 patients with classic fractures were identified. Of the patients with atypical fractures, 32 (82.1%) had been treated with bisphosphonates compared with 28 (6.4%) in the classic fractures group (odds ratios [OR], 66.9; 95% CI, 27.1-165.1) and 11.5% in the group without fracture (OR, 35.2; 95% CI, 13.9-88.8). Bisphosphonate use was associated with a 47% reduction in risk of classic fracture (OR, 0.5; 95% CI, 0.3-0.9). Considering the duration of use, the ORs (95% CIs) for atypical fractures were 35.1 (10.0-123.6) for less than 2 years, 46.9 (14.2-154.4) for 2 to 5 years, 117.1 (34.2-401.7) for 5 to 9 years, and 175.7 (30.0-1027.6) for more than 9 years compared with no use. A contralateral fracture occurred in 28.2% of atypical cases and in 0.9% of classic cases (OR, 42.6; 95% CI, 12.8-142.4). The incidence rate of atypical fractures was low (32 cases per million person-years) and increased by 10.7% per year on average.
Conclusion: Atypical femoral fractures were associated with bisphosphonate use; longer duration of treatment resulted in augmented risk. The incidence of atypical fractures increased over a 12-year period, but the absolute number of such fractures is very small.

TRANSPLANTED HUMAN PANCREATIC ISLETS AFTER LONG-TERM INSULIN INDEPENDENCE

***Yannick D. Muller (1,4)**, Shashank Gupta (2), Philippe Morel (1), Sophie Borot (1), Florence Bettens (3), Marie-Elise Truchetet (4), Jean Villard (4), Jörg D. Seebach (4), Dan Holmberg (2), Christian Toso (1), Johannes A. Lobrinus (5), Domenico Bosco (1), Thierry Berney (1)*

(1) Cell Isolation and Transplantation Center, Department of Surgery, Geneva University Hospitals and University of Geneva, Geneva, Switzerland (2) Centre for Infection and Inflammation Research, Faculty of Health, University of Copenhagen, Denmark (3) National Reference Laboratory for Histocompatibility, Department of Internal Medicine, Geneva University Hospitals and University of Geneva, Geneva, Switzerland (4) Division of Clinical Immunology and Allergology, Department of Internal Medicine, Geneva University Hospitals and University of Geneva, Geneva, Switzerland (5) Department of Pathology, Geneva University Hospitals and University of Geneva, Geneva, Switzerland

Introduction: Long-term insulin independence after islets of Langerhans transplantation is rarely achieved. The aims of this study were to identify the histological and immunological features of islets transplanted in a type 1 diabetic patient who died of a cerebral hemorrhage after >13 years insulin-independence. Islets were pooled from two donors with respectively one and five HLA mismatches.
Méthode: Herein, we assessed the distribution, size and vascularization of insulin positive islets by two-, three-dimensional analysis and optical projection tomography. Moreover, we characterized the different leukocyte subsets including CD68, CD4, CD8, IL-17, Foxp3 and CD20 positive cells in the portal spaces with or without islets. Finally, the donor origins of the islets were identified within the liver by islet microdissection and two-stage nested PCR amplification based on HLA-DRB1 incompatibilities
Résultat: Insulin-positive islets were found throughout the right and left liver, and absent in the pancreas. Two- and three-dimensional analysis showed that islets lost their initial rounded and compact morphology, had a mean diameter of 136µm and were constituted of an unfolded epithelial band of 39.1µm. Leukocyte phenotyping showed no evidence of a tolerogenic environment in the islet-containing portal spaces. Finally, HLA typing of microdissected islets showed HLA from the best matched donor in all 23 microdissection samples, as compared to 1/23 for the least matched donor.
Conclusion: This case report demonstrates that allogeneic islets can survive over 13 years while main taining insulin-independence. Allogeneic islets had unique morphologic features and implanted in the liver regardless of their size. Finally, our results suggest that, in this case, rejection had been prevalent over autoimmunity, although this hypothesis warrants further investigation

SYSTEMATIC REVIEW AND META-ANALYSIS OF THE EFFECT OF PERIOPERATIVE STEROIDS ON ISCHAEMIA–REPERFUSION INJURY AND SURGICAL STRESS RESPONSE IN PATIENTS UNDERGOING LIVER RESECTION

Lorenzo A. Orci*, Christian Toso, G. Mentha, Philippe Morel, Pietro Edoardo Majno*

Service de chirurgie viscérale et de transplantation, département de chirurgie, HUG

Introduction: Several therapeutic strategies, such as ischaemic preconditioning, intermittent or selective pedicle clamping and pharmacological interventions, have been explored to reduce morbidity caused by hepatic ischaemia–reperfusion injury and the surgical stress response. The role of steroids in this setting remains controversial.

Méthode: A comprehensive literature search in MEDLINE, Embase and the Cochrane Register of Clinical Trials (CENTRAL) was conducted (1966 onwards), identifying studies comparing perioperative administration of intravenous steroids with standard care or placebo, in the setting of liver surgery. Randomized Controlled trials (RCTs) and non-RCTs were included. Critical appraisal andmeta-analysis were carried out according to the Preferred Reporting Items for Systematic reviews and Meta-analyses(PRISMA) statement.

Résultat: Six articles were included; five were RCTs. Pooling the results revealed that patients receiving intravenous glucocorticoids were 24 per cent less likely to suffer postoperative morbidity compared with controls (risk ratio 0·76, 95 per cent confidence interval 0·57 to 0·99; P = 0·047). The treated group experienced a significantly greater rise in early postoperative interleukin (IL) 10 levels compared with controls. In addition, steroids significantly reduced postoperative blood levels of bilirubin, and of inflammatory markers such as IL-6 and C-reactive protein. There was no evidence supporting a risk difference in infectious complications and wound healing between study groups.

Conclusion: Perioperative steroids have a favourable impact on postoperative outcomes after liver resection.

PRESENTATION ANNULEE

TRANSPLANTATION AUTOLOGUE DE CELLULES SOUCHES ISSUES DE LA MOELLE OSSEUSE LORS DE CIRRHOSE ALCOOLIQUE DECOMPENSEE: UNE ETUDE CLINIQUE CONTROLEE

***Laurent Spahr**, Yves Chalandon, Sylvain Terraz, Vincent Kindler, Laura Rubbia-Brandt, Jean-Louis Frossard, Romain Breguet, Nicolas Ianthier, Annarita Farina, Jakob Passweg, Christoph D. Becker, Antoine Hadengue*

Gastroentérologie et Hépatologie, Hématologie, Radiologie, Pathologie Clinique, Bioinformatique et Biologie Structurelle

Introduction: Le mauvais pronostic de la cirrhose alcoolique décompensée est en partie associée à un défaut de régénération hépatique. Il a été suggéré que les cellules souches pluripotentes de la moelle osseuse pouvaient participer à la régénération/repopulation du foie malade. A court terme, l'administration de G-CSF stimule la prolifération des cellules hépatiques progénitrices (Spahr et al. Hepatology 2008)
Méthode: 58 patients hospitalisés pour cirrhose alcoolique décompensée (âge moyen 54 ans, score de MELD 19) ont été traités soit de façon standard seule (n=30) ou associé à une mobilisation de cellules souches (GCSFx5jours)suivie d\'aspiration de moelle osseuse/sélection de cellules souches, puis autotransplantation dans l'artère hépatique par artériographie (n=28). Le critère de jugement était l'amélioration d'au moins 3 points du score de MELD à 3 mois. La biopsie de foie était répétée à 4 semaines pour apprécier la régénération hépatique.
Résultat: Les 2 groupes étaient comparables. On déplorait 4 décès dans le bras standard et 2 dans le bras cellules souches. La tolérance à la procédure de transplantation était excellente. A 3 mois, l'évolution du score de MELD était parallèle dans les 2 groupes, ainsi que le nombre de patients ayant atteint le critère de jugement. Le nombre de cellules hépatocytaires en phase de prolifération à 4 semaines était le même dans les 2 groupes.
Conclusion: La transplantation autologue de cellules souches issues de la moelle osseuse est bien supportée lors de cirrhose alcoolique décompensée. Cette stratégie n'apporte toutefois pas de bénéfice en termes d'amélioration de la fonction hépatique à 3 mois de l'épisode initial de décompensation. Ces résultats suggèrent soit un stimulus régénératif insuffisant, soit un blocage prolifératif du foie malade

EFFECT OF A MULTIFACTORIAL FALL-AND-FRACTURE RISK ASSESSMENT AND MANAGEMENT PROGRAM ON GAIT AND BALANCE PERFORMANCES AND DISABILITY IN HOSPITALIZED OLDER ADULTS: A CONTROLLED STUDY

***Andrea Trombetti**, Mélany Hars, François Herrmann, René Rizzoli, Serge Ferrari*

Division of Bone Diseases, Department of Internal Medicine Specialties, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

Introduction: Hospitalization affords a major opportunity for interdisciplinary cooperation to manage fall-and-fracture risk factors in older adults. This study aimed at assessing the effects on physical performances and the level of independence in activities of daily living (ADL) of a multifactorial fall-and-fracture risk assessment and management program applied in a geriatric hospital setting.
Méthode: A controlled intervention study was conducted among 122 geriatric inpatients (mean ± SD age, 84 ± 7 years) admitted with a fall-related diagnosis. Among them, 92 were admitted to a dedicated unit and enrolled into a multifactorial intervention program, including intensive targeted exercise. Thirty patients who received standard usual care in a general geriatric unit formed the control group. Primary outcomes included gait and balance performances and the level of independence in ADL measured 12 ± 6 days apart. Secondary outcomes included length of stay, incidence of in-hospital falls, hospital readmission, and mortality rates.< /td>
Résultat: Compared to the usual care group, the intervention group had significant improvements in Timed Up and Go (adjusted mean difference [AMD] = -3.7s; 95 % CI = -6.8 to -0.7; P = 0.017), Tinetti (AMD = -1.4; 95 % CI = -2.1 to -0.8; P < 0.001), and Functional Independence Measure (AMD = 6.5; 95 %CI = 0.7-12.3; P = 0.027) test performances, as well as in several gait parameters (P < 0.05). Furthermore, this program favorably impacted adverse outcomes including hospital readmission (hazard ratio = 0.3; 95 % CI = 0.1-0.9; P = 0.02).
Conclusion: A multifactorial fall-and-fracture risk-based intervention program, applied in a dedicated geriatric hospital unit, was effective and more beneficial than usual care in improving physical parameters related to the risk of fall and disability among high-risk oldest old patients.

PRESENTATIONS POSTERS

EN ORDRE ALPHABETIQUE SELON LE NOM DE L'AUTEUR QUI A SOUMIS

P1

GROUPES DE GESTION DE LA COLERE AUPRES DES PATIENTS TRAUMATISES-CRANIENS: FAISABILITE ET EFFICACITE INITIALE

Tatiana Aboulafia Brakha, *Carole Greber Buschbeck, Lucien Rochat, Jean-Marie Annoni*

Services de Neurologie et de Neurorééducation-Département de Neurosciences cliniques

Introduction: Parmi les patients traumatisés crâniens (TCC), nous retrouvons une haute prévalence de problèmes de gestion de la colère, avec d'importants retentissements au niveau de la réinsertion socio-professionnelle. Malgré l'importance de la problématique, peu d'études ont décrit les effets d'interventions psychologiques pour une meilleure gestion de colère auprès des patients TCC.
Méthode: 10 patients ayant eu un TCC modéré ou sévère, au moins un an après l'accident, ont participé à un programme de gestion de la colère en petits groupes, pendant huit semaines, à raison d'une séance hebdomadaire. Les participants ont rempli des questionnaires d'auto-évaluation du comportement avant l'intervention (T1), une semaine après l'intervention (T2) et quatre mois après (T3). La faisabilité du protocole a également été évaluée par des critères spécifiques, notamment la demande, la praticité, la mise en place et l'acceptabilité de la part des participants.
Résultat: Les scores dans le questionnaire d'auto-évaluation d'agressivité (AQ-12, mesure principale d'intérêt) ont diminué de manière significative en T3 par rapport à T1, avec une taille d'effet large et une puissance modérée. L'acceptabilité et la praticité ont été entièrement confirmées. Quelques aspects du recrutement et de la mise en place doivent être reconsidérés.
Conclusion: Une prise en groupe de gestion de la colère avec les patients TCC est faisable et utile. Par ailleurs, les résultats positifs de cette étude préliminaire incitent la mise en place d'une étude contrôlée afin de mieux évaluer les effets du programme psychothérapeutique.

P2

PHARMACOKINETIC INTERACTION BETWEEN PRASUGREL AND RITONAVIR IN HEALTHY VOLUNTEERS

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Introduction: The new antiaggregating agent prasugrel is bioactivated by cytochromes P450 (CYP) 3A and 2B6. Ritonavir is a potent CYP3A inhibitor and was shown in vitro as a CYP2B6 inhibitor. The aim of this open-label crossover study was to assess the effect of ritonavir on prasugrel active metabolite (prasugrel-AM) pharmacokinetics in healthy volunteers.
Méthode: Ten healthy male volunteers received 10mg prasugrel. After at least a week washout, they received 100mg ritonavir, followed by 10mg prasugrel 2 hours later. We used dried blood spot sampling method to monitor prasugrel-AM pharmocokinetics (Cmax, t1/2, tmax, AUC0-6h) at 0, 0.25, 0.5, 1, 1.5, 2, 4 and 6 hours after prasugrel administration. A "cocktail" approach was used to measure CYP2B6, 2C9, 2C19 and 3A activities.
Résultat: In the presence of ritonavir, prasugrel-AM Cmax and AUC were decreased by 45% (Mean ratio: 0.55, CI95%: 0.37-0.73, p = 0.008) and 38% (Mean ratio: 0.62, CI95%: 0.52-0.71, p = 0.001), respectively, while t1/2 and tmax were not affected. Midazolam metabolic ratio (MR) dramatically decreased in presence of ritonavir (6.7 ± 2.6 vs. 0.13 ± 0.07) reflecting an almost complete inhibition of CYP3A4, whereas omeprazole, flurbiprofen and bupropion MR were not affected.
Conclusion: These data demonstrate that ritonavir is able to block prasugrel CYP3A4 bioactivation. This CYP-mediated drug-drug interaction might lead to a significant reduction of prasugrel efficacy in HIV-infected patients with acute coronary syndrome.

P3

INHIBITION OF PUTATIVE HYALUROSOME PLATFORM IN KERATINOCYTES AS A MECHANISM FOR CORTICOSTEROID-INDUCED EPIDERMAL ATROPHY

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Introduction: The main limitation of the use of topical corticosteroids in dermatology is their atrophic effects on the skin. We have previously proposed a molecular platform composed of CD44, EGFR and hyaluronate synthase (HAS) which is functionally defective in dermatoporosis, a chronic cutaneous insufficiency/fragility syndrome. In this study we explored the molecular mechanisms of the skin atrophy induced by corticosteroids.
Méthode: An in vivo murine model of a corticosteroid-induced skin atrophy was developed, toghether with an in vitro model with human keratinocytes in order to insights about the atrophy mechanism.
Résultat: We observed an important skin atrophy and a significant decrease of HA, its main cell surface receptor CD44 and F-actin in mouse skin treated with topical clobetasol propionate (CP). Human keratinocytes exposed to CP showed an impaired HA secretion and diminished expression of CD44 and HA synthase 3 (HAS3). CP also abolished filopodia of keratinocytes exposed to CP together with a redistribution of CD44 and F-actin depolymerization. We also showed that HA fragments of intermediary size (HAFi) induced keratinocyte filopodia and protected them against CP. Topical HAFi induced hyperplasia in mouse epidermis and prevented CP-induced atrophy.
Conclusion: Our results suggest that a CD44/EGFR/HAS platform associated with F-actin and filopodia of keratinocytes is the target of corticosteroids for their atrophogenic effects. These observations may le! ad to th e development of novel treatment and prevention strategies for corticosteroid-induced skin atrophy.

P4

FULL BODY GAIT ANALYSIS MAY IMPROVE DIAGNOSTIC DISCRIMINATION BETWEEN HEREDITARY SPASTIC PARAPLEGIA AND SPASTIC DIPLEGIA: A PRELIMINARY STUDY

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Introduction: Hereditary spastic paraplegia (HSP) and spastic diplegia (SD) patients share a strong clinical resemblance. Thus, HSP patients are frequently misdiagnosed with a mild form of SD. Clinical gait analysis (CGA) has been highlighted as a possible tool to support the differential diagnosis of HSP and SD. Previous analysis has focused on the lower-body but not the upper-body, where numerous compensations during walking occur. The aim of this study was to compare the full-body movements of HSP and SD groups and, in particular, the movement of the upper limbs.
Méthode: Ten HSP and 12 SD patients were evaluated through a CGA between 2008 and 2012. The kinematic parameters were computed using the ViconPeak software. The mean amplitude of normalised (by the patient's height) arm swing was also calculated. All patients were asked to walk at a self-selected speed. The mean kinematic parameters for the two populations were analysed with Mann-Whitney comparison tests.
Résultat: The results demonstrated that HSP patients used more spine movement to compensate for lower limb movement alterations, whereas SD patients used their arms for compensation. SD patients had increased shoulder movements in the sagittal plane and frontal plane compared to HSP patients. These arm postures are similar to the description of the guard position that toddlers exhibit during the first weeks of walking. To increase speed, SD patients have larger arm swings in the sagittal, frontal and transversal planes.
Conclusion: Upper-body kinematics, and more specifically arm movements and spine movements, may support the differential diagnosis of HSP and SD.

P5

REDUCTION OF PEAK OXYGEN CONSUMPTION IN PATIENTS WITH NON-SMALL CELL LUNG CANCER TREATED WITH NEO-ADJUVANT CHEMOTHERAPY

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Introduction: Fitness is best assessed with cardio-pulmonary exercise testing (CPET) in patients with non-small cell lung cancer (NSCLC) eligible for lung resection surgery. Peak oxygen consumption (VO2 peak) is predictive of short-term complications after elective thoracic surgery and long-term survival in patients who cannot undergo surgery because of advanced cancer. Anti-neoplastic drugs have toxic effects on cellular metabolism and therefore on VO2 peak. Effect of neo-adjuvant chemotherapy on cardiopulmonary fitness has received little attention.
Méthode: We compared CPET results in patients with (n=9) or without (n=91) neo-adjuvant chemotherapy before elective surgery for NSCLC. We performed linear regression to compare CPET results in patients with or without neo-adjuvant chemotherapy with adjustment for anthropomorphic variables and comorbidities.
Résultat: NSCLC patients with neo-adjuvant chemotherapy were younger, reported comorbid conditions less often and had lower hematocrit value. Overall, VO2 was low in both groups (VO2 peak 1424 ml/min, SD 444 ml/min; 20.3 ml/min/kg, SD 5.7). After adjustment for age, sex, height, weight, hematocrit, FEV1% and comorbid conditions, peak VO2 was lower in patients with neoadjuvant chemotherapy (-290 ml/min/kg [CI95%-509; -70] p=0.010). Adjusted peak VO2/kg was reduced by 23% (-4.7 ml/min/kg [CI95% -8.0; -1.3]) as well as anaerobic threshold (- 12.3% [I95%-20.9%, -3.7%])ompared to patients without chemotherapy. Peak heart rate and ventilatory equivalents at anaerobic threshold tended to be higher in patients with chemotherapy.
Conclusion: Pre-operative Oxygen consumption was markedly reduced in NSCLC patients with neo-adjuvant chemotherapy after adjustment for confounders. CPET pattern might be explained by a complex toxic effect of anti-neoplastic drugs on lung interstitium, muscle metabolism and heart function. Because of low VO2 peak, patients with neo-adjuvant chemotherapy may thus be at risk of being denied surgery. Cardiopulmonary fitness might be preferably measured before neo-adjuvant chemotherapy in patients with NSCLC.

P6

SIX OF 12 RELAPSED/REFRACTORY INDOLENT LYMPHOMA PATIENTS TREATED 12 YEARS AGO WITH 131I-TOSITUMOMAB REMAIN IN COMPLETE REMISSION

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Introduction: Advanced stage indolent non-Hodgkin's lymphoma (NHL) cannot be cured by conventional therapy while localized stage I/II disease may be cured by radiotherapy as suggested by very low recurrence rates observed after 10 years progression free survival (J Clin Oncol 1996;14:1282).
Méthode: Over 11 years ago, we treated in Switzerland 12 indolent and 4 transformed, relapsed/refractory lymphoma patients with a single, non-myeloablative therapy of 131I-tositumomab in the frame of the Bexxar/GlaxoSmithKline open-label phase II study. The 16 patients had had a mean of 3.1 (range 1 to 6) chemotherapy/antibody treatments.
Résultat: Three of four transformed lymphomas were progressive after RIT and only 1 patient had a partial response lasting 10 months. 12/12 patients with indolent lymphoma responded, 4 (33%) with partial and 8 (67 %) with com! plete re mission (CR/CRu). Side effects were mostly mild and transient except for 1 patient who developed a myelodysplastic syndrome 34 months after RIT and 74 months after initial diagnosis and treatment with CHOP. Today, 6 of the 8 CR/CRu patients remain disease free 11.8 years (range 11.0 to 12.8 years) after RIT.
Conclusion: Our results show that even in relapse after 1–6 chemo- and/or immunotherapies, particularly long lasting complete remissions were observed in half of the patients with recurrent indolent lymphoma after a single course of RIT. Since indolent lymphoma cannot be cured by conventional chemotherapy, it would seem that patients in continued CR 12 years after RIT given in relapse/resistance should imperatively be followed further aiming to demonstrate potential cures at 15 to 20 years after treatment. Research Support : Swiss Cancer League (KFS 991-02-2000)

P7

FRACTURES IN HEALTHY FEMALES FOLLOWED FROM CHILDHOOD TO EARLY ADULTHOOD ARE ASSOCIATED WITH LATER MENARCHEAL AGE AND WITH IMPAIRED BONE MICROSTRUCTURE AT PEAK BONE MASS

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Introduction: Whether fractures observed in healthy children are associated with microstructural alterations and strength deficit that persists by the end of the growth period is not established. Considering the importance of pubertal timing in bone development, we also quantified the fracture risk related to later menarchal age.
Méthode: We followed 124 healthy girls from mean age 7.9±0.5 to 20.4±0.6 (±SD) y. Fractures, menarcheal age and radius areal (a) bone mineral density (BMD) were recorded at regular intervals. At a mean age of 20.4 y, microstructural and strength variables of the distal radius were determined by high-resolution peripheral computerized tomography and micro-finite element analysis.
Résultat: Sixty-one fractures occurred in 42 subjects. At 20.4 y, subjects with fractures had lower aBMD at radial diaphysis (P=0.005) and metaphysis (P=0.008), lower distal radius trabecular (Tb) volumetric density (vBMD) (P=0.010) and ! thicknes s (P=0.014), and reduction in stiffness (P=0.013), failure load (P=0.013) and apparent modulus (P=0.046). Odd ratios revealed an increased risk of fracture for 1 SD reduction in radial aBMD diaphysis: 1.97 (P=0.006) and metaphysis: 1.97 (P=0.008); distal radius Tb vBMD: 1.89 (P=0.011), thickness: 1.97 (P=0.017), stiffness: 2.02 (P=0.014), failure load: 2.00 (P=0.014) and apparent modulus: 1.79 (P=0.043). Menarcheal age occurred at a later age in subjects with fractures (P=0.003). For 1 SD (1.2 y) later menarcheal age, the increase of fracture risk was: 2.1 (P=0.002).
Conclusion: In healthy young women, low trabecular volumetric density and thickness in the distal radius are associated with reduced bone strength and increased fracture risk during growth. This study also documents that later pubertal timing is associated with increased incidence of fracture during childhood and adolescence.

P8

MODELISATION DE L'EFFET DANS LES META-ANALYSES D'ETUDES DE SURVIE

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Introduction: Les méta-analyses requièrent des méthodes statistiques adaptées aux données extraites des publications, telles que les survies estimées à différents temps du suivi des patients. Nous proposons une méthode statistique pour modéliser l'effet d\'une intervention médicale à partir des courbes des survies des études de la méta-analyse.
Méthode: L'effet de l'intervention, mesuré par le hazard ratio (HR), est modélisé en fonction du temps de suivi. Les paramètres sont estimés par maximum de vraisemblance et la variabilité inter-étude est prise en compte. L'hypothèse que l'effet de l'intervention est constant au cours du temps est peut être testée. La méthode présentée est appliquée aux données de deux méta-analyses publiées: 1) détection précoce versus tardive d'une rechute locale chez des patientes atteintes d'un cancer du sein, 2) transplantation de moelle osseuse versus chimiothérapie chez des patients avec une leucémie non lymphocytaire.
Résultat: La méthode proposée permet d'analyser l'évolution de l'effet d'une intervention médicale au cours du temps. Dans la première méta-analyse, la survie des patientes était meilleure dans le groupe avec une détection précoce (HR=0.58, (95CI% 0.48;0.70)) et l'effet restait stable sur les 4 années de suivi (p=0.93). Dans la deuxième méta-analyse, l'effet de la transplantation osseuse sur la survie variait au cours du temps (p=0.02) : HR=0.64 (95%CI: 0.52;0.79), HR=0.51 (95%CI: 0.42;0.63) et HR=0.51 (95%CI: 0.42;0.63) les 1ère, 2ème et 3ème années.
Conclusion: Ce travail méthodologique a permis de développer une méthode de méta-analyse pour étudier les variations de l'effet au cours du temps de suivi, ce qui n'est possible avec les méthodes classiques.

P9

VALIDATION OF A 10-ITEM CARE-RELATED REGRET INTENSITY SCALE (RIS-10) FOR HEALTH CARE PROFESSIONALS

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Introduction: Regret after one of the many decisions and interventions that health care professionals make every day can have an impact on their own health and quality of life, and on their patient care practices.The aim of this study is to validate a new care-related regret intensity scale. (RIS) for health care professionals.
Méthode: Retrospective cross-sectional cohort study with a 1- month follow-up (test-retest) in a French-speaking University Hospital. A total of 469 nurses and physicians responded to the survey, and 175 answered the retest. Instruments: RIS, self-report questions on the context of the regret-inducing event, its consequences for the patient, involvement of the health care professionals, and changes in patient care practices after the event. We measured the impact of regret intensity on health care professionals with the satisfaction with life scale, the SF-36 first question (self-reported health), and a question on self-esteem.
Résultat: On the basis of factor analysis and item response analysis, the initial 19-item scale was shortened to 10 items. The resulting scale (RIS-10) was unidimensional and had high internal consistency (a = 0.87) and acceptable test-retest reliability (0.70). Higher regret intensity was associated with (a) more consequences for the patient; (b) lower life satisfaction and poorer self-reported health in health care professionals; and (c) changes in patient care practices. Nurses reported analyzing the event and apologizing, whereas physicians reported talking preferentially to colleagues, rather than to their supervisor, about changing practices.
Conclusion: The RIS is a valid and reliable measure of carerelated regret intensity for hospital-based physicians and nurses.

P10

EFFICACY OF SUGAMMADEX FOR THE REVERSAL OF MODERATE AND DEEP ROCURONIUM-INDUCED NEUROMUSCULAR BLOCK IN PATIENTS PRETREATED WITH MAGNESIUM SULFATE

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Introduction: Sugammadex, a modified gamma cyclodextrin, is a selective binding agent specifically designed to encapsulate the neuromuscular blocking agent rocuronium. Pre-treatment with intravenous magnesium sulfate (MgSO4) prolongs spontaneous recovery time after a single intubation dose of rocuronium by about 25%. Our hypothesis was that after pre-treatment with intravenous MgSO4, the time to reverse a moderate and a deep neuromuscular block induced by an intubation dose of rocuronium with standard doses of sugammadex was significantly prolonged.
Méthode: Thirty-two men (18-65 years) were randomly allocated to receive MgSO4 60 mg kg-1 or matching placebo (saline) in a double-blinded manner. Study drugs were given intravenously for 15 min before induction of anesthesia with propofol, sufentanil and rocuronium 0.6 mg kg-1. Anesthesia was maintained with a target-controlled propofol infusion. Neuromuscular transmission was quantified using train-of-four (TOF)-Watch SX acceleromyography. In part I of the study, sugammadex 2 mg kg-1 was administered in 16 patients (8 MgSO4 and 8 placebo) at reappearance of the second twitch (“moderate” block). In part II, sugammadex 4 mg kg-1 was administered in 16! patient s (8 MgSO4 and 8 placebo) at post-tetanic count 1-2 (“deep” block). The primary endpoint was the time in seconds from injection of sugammadex to a T4/T1 ratio ≥0.9.
Résultat: Data from all 32 randomized patients could be analyzed. In part I (moderate block), time from injection of sugammadex to a T4/T1 ratio ≥0.9 was on average 72 [SD=19] seconds with MgSO4 and was 74 [30] seconds with saline (P=0.874). In part II (deep block), time was 74 [27] seconds with MgSO4 and was 75 [17] seconds with saline (P=0.922).
Conclusion: Pre-treatment with intravenous MgSO4 has no impact on the efficacy of recommended doses of sugammadex for the reversal of moderate and deep rocuronium-induced neuromuscular block. Trial Registration. clinicaltrials.gov identifier: NCT0144093.

P11

HOMING OF HUMAN B CELLS TO LYMPHOID ORGANS AND B-CELL LYMPHOMA ENGRAFTMENT ARE CONTROLLED BY CELL ADHESION MOLECULE JAM-C

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Introduction: Homing of malignant B cells to bone marrow and secondary lymphoid organs is of critical importance in disease progression of lymphoproliferative syndromes. The junctional adhesion molecules (JAMs) localize at endothelial tight junctions and have been involved in leukocyte transmigration. JAM-C is also expressed in human B cells, allowing the classification of JAM-Cpos and JAM-Cneg B-cell lymphomas. In the current study, we investigated the role of JAM-C in the homing and engraftment of normal and malignant B cells.
Méthode: Human B cells were isolated from peripheral blood of healthy donors and lymphoma patients. To study the role of JAM-C in B cell migration, B cells were injected into NOD/SCID mice and homing of cells to lymphoid organs (bone marrow, spleen, lymph nodes) was analyzed one hour later by flow cytometry and immunohistochemistry. To identify the interactions of JAM-C on B cells, binding, adhesion, immunofluorescence and surface plasmon resonance assays were performed. To investigate the role of JAM-C in lymphoma dissemination, the JAM-C positive B-cell line Jeko-1 was injected into NOD/SCID mice and animals were treated for three weeks with anti-JAM-C antibodies. Tumor burden was evaluated in lymphoid organs on day 26.
Résultat: Treatment with anti-JAM-C antibodies reduced the homing of normal and JAM-Cpos lymphoma B cells to lymph nodes, bone marrow and spleen by 50-60%. Adhesion, immunofluorescence analysis and plasmon resonance studies identified JAM-B as the major ligand for JAM-C. Accordingly, anti-JAM-C antibodies red! uced the adhesion and binding of JAM-C expressing B cells to the ligand JAM-B by 50%. Long-term administration of anti-JAM-C antibodies reduced the engraftment of JAM-Cpos Jeko-1 cells in the bone marrow (21%), spleen (94%) and lymph nodes (93%) of NOD/SCID mice.
Conclusion: Our results demonstrate a functional role of JAM-C in B cell homing and engraftment into lymphoid organs. Anti-JAM-C antibodies could thus represent a potential therapeutic approach preventing lymphoma B cells from reaching supportive lymphoid microenvironments in bone marrow, lymph nodes and spleen.

P12

POS3D MRSA

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Introduction: Les infections nosocomiales représentent un problème majeur dans les établissements hospitaliers. Les HUG ont mis en place une stratégie consistant à la fois à prévenir et à surveiller l'infection. En collaboration avec le SPCI (Service de prévention et contrôle de l'infection), le projet Pos3D MRSA propose un outil de surveillance et d'analyse.
Méthode:Cet outil va projeter l'ensemble des données caractérisant le statut de l'infection dans le modèle 3D de l'hôpital. On pourra notamment suivre les trajectoires des patients positifs et visualiser les intersections avec les patients négatifs, mettant en évidence des foyers d'infections potentiels.
Résultat: Le résultat de ce projet est une application web en html5 en utilisant la technologie 3D WebGL.
Conclusion: Le mécanisme de modélisation 3D de l'hôpital et de la projection de données mis en oeuvre pour ce projet ouvre des perspectives intéressantes pour un grand nombre d'applications tant au niveau médical (trajectoires des patients, suivi d'infections, etc..), qu'au niveau logistique (suivi de stocks) et également sur le plan de la communication (accueil des patients et/ou des visiteurs).

P13

PHYSICAL ACTIVITY, COGNITIVE MOTOR INTERFERENCE AND SLEEP IN PATIENTS WITH STROKE: PRELIMINARY RESULTS

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Introduction: Stroke is a major cause of physical and cognitive disability, and the influence of sleep on recovery is well known. However, the influence of these three parameters (motor skills, cognitive performance and sleep) on physical activity has not been evaluated.
Méthode: Physical activity was measured by actigraphy, sleep was measured by pulse oximetry and various questionnaires. Gait parameters were measured by a GAITRite mat whilst individuals walked under single and dual task conditions. We will be focusing on the sleep questionnaire data and the dual task data.
Résultat: Thus far 13 patients have been included (Mean ± sd: age 62 ± 11years) have been included in this study. Significant differences were seen between the dual-task and single task conditions as far the number of enumerated figures were concerned ($p < 0.01$ for forward counting and $p < 0.05$ for backward counting), Results for questionnaires relating to sleep were as follows, mean ± SD: Epworth Sleepiness Scale (ESS) 7 ± 4, Pittsburg Sleep Quality Index (PSQI) 8 ± 4, STOP-Bang (SB) 3 ± 1 and the Fatigue Severity Scale (FSS) 4.3 ± 1.8.
Conclusion: These results demonstrate that the dual task conditions had an effect on the two counting tasks (forward and backward counting) performed. Indicating that focus of attention was compromised whilst performing these tasks. These preliminary results demonstrate that as yet there is no indication of sleep disturbances in individuals with stroke. However the sample size is small and so this is unlikely to be a true reflection of sleep issues in individuals with stroke.

P14

SMARTPHONES : EVIDENCE-BASED USER-INTERFACE DESIGN

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Introduction: Nowadays, many caregivers rely on handheld devices to consult medical references and don't understand why they should stop using their smartphones at the hospital's door. Stakeholders remain cautious towards these new tools because the quality of the medical data recorded by this mean still raises many concerns. Based on the hypothesis that the quality of recorded data is influenced by the input interface, we have set up a usability study to find out the most appropriate one.
Méthode: Since smartphones are well adapted to record vital signs at patients' bedside, this task is used to compare the use of six data entry interfaces. We recruited a user panel and recorded their performance while they performed the task. These measures were then used to find out what interface is the most accurate, the most efficient and the friendliest for users.
Résultat: Results show that users take significantly less time to enter measures with the numeric keyboard. Regarding the accuracy, the numeric keyboard doesn't dominate but stand in the first ranks. The evaluation made by users reflects perfectly these results. Indeed, users have unanimously elected the numeric keyboard as their favorite interface.
Conclusion: All the indicators show clearly that the numeric keyboard is the most adapted interface to enter numeric measures. This is not only the fastest and most accurate interface but also the one that have received users' approbation. These results are very important for the future development of handheld a! pplicati ons to insure the quality of the recorded data as well as users' acceptance.

P15

IMPACT OF ADVANCE DIRECTIVES AND OF HEALTH CARE PROXY ON DOCTORS' DECISIONS: A RANDOMIZED TRIAL

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Introduction: Advance directives or proxy designations are widely recommended, but how they affect doctors' decision-making is not well known. The aim of this study was to quantify their influence on doctors' decisions.
Méthode: We mailed to all the generalists and internists in French-speaking Switzerland (N=1962) three vignettes describing difficult decisions involving incapacitated patients. In each case the advance directive requested that further care be withheld. One vignette tested the impact of a written advance directive vs a proxy. Another compared the impact of a hand-written directive vs a formalized document. The third vignette compared the impact of family vs a doctor as a proxy. Each vignette was prepared in 3 or 4 versions, including a control version where no directive or proxy was present. Vignettes were randomly allocated to respondents. We used logistic regression to predict the decision to forgo a medical intervention.
Résultat: Compared to the control condition, the odds of forgoing a medical intervention was increased by the written advance directive (OR 7.3; p<0.001), the proxy (OR 7.9; p<0.001), and the combination of the two (OR 35.7; p<0.001). The hand-written directive had the same impact (OR 13.3) as the formalized directive (OR 13.8). The effect of proxy opinion was slightly stronger when provided by a doctor (OR 11.3) rather than by family (OR 7.8).
Conclusion: Advance directives and proxy opinions are equally effective in influencing doctors' decisions, but having both has the strongest effect. The for! mat of t he advance directive and the identity of the proxy have little influence on decisions.

P16

SENSITIVITY, SPECIFICITY, AND LIKELIHOOD RATIOS OF POLYMERASE CHAIN REACTION IN THE DIAGNOSIS OF SYPHILIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Syphilis is a sexually-transmitted infection of concern worldwide. While its treatment is simple, low cost, and effective, its diagnosis remains challenging. Treponema pallidum polymerase chain reaction (Tp-PCR) has been viewed as an interesting tool and we aimed to estimate pooled sensitivity and specificity of Tp-PCR compared to recommended reference tests in the diagnosis of suspected syphilis at various stages and in various biological materials.
Méthode: Systematic review and meta-analysis. Search of 3 electronic bibliographic databases from January 1990 to January 2012 and the abstract books of five specialized congresses (1999-2011). Search key terms included syphilis, Treponema pallidum or neurosyphilis and molecular amplification, polymerase chain reaction or PCR. We included studies that used both reference tests to diagnose syphilis plus PCR in various biological materials.
Résultat: Of 1160 identified abstracts, 69 were selected and 46 studies used adequate reference tests. Sensitivity was highest in the swabs from primary genital or anal chancres (78.4%; 95% CI: 68.2-86.0) and in blood from neonates with congenital syphilis (83.0%; 55.0-95.2). Pooled specificities were ~95%, except those in blood. A positive Tp-PCR is highly informative with a positive LR around 20. in ulcers or skin lesions In the blood, the positive LR was <10.
Conclusion: The pooled values of LR showed that T. pallidum Tp-PCR was more efficient to confirm than to exclude syphilis i! n lesion s. Tp-PCR is a useful diagnostic tool in ulcers, especially when serology is still negative and in settings with a high prevalence of syphilis.

P17

SUBCLINICAL THYROID DYSFUNCTION AND THE RISK OF HEART FAILURE EVENTS: AN INDIVIDUAL PARTICIPANT DATA ANALYSIS FROM 6 PROSPECTIVE COHORTS

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Introduction: American College of Cardiology/American Heart Association guidelines for the diagnosis and management of heart failure recommend investigating exacerbating conditions such as thyroid dysfunction, but without specifying the impact of different thyroid-stimulation hormone (TSH) levels. Limited prospective data exist on the association between subclinical thyroid dysfunction and heart failure events.
Méthode: We performed a pooled analysis of individual participant data using all available prospective cohorts with thyroid function tests and subsequent follow-up of heart failure events. Individual data on 25 390 participants with 216 248 person-years of follow-up were supplied from 6 prospective cohorts in the United States and Europe. Euthyroidism was defined as TSH of 0.45 to 4.49 mIU/L, subclinical hypothyroidism as TSH of 4.5 to 19.9 mIU/L, and subclinical hyperthyroidism as TSH <0.45 mIU/L, the last two with normal free thyroxine levels.
Résultat: Among 25 390 participants, 2068 (8.1%) had subclinical hypothyroidism and 648 (2.6%) had subclinical hyperthyroidism. In age- and sex-adjusted analyses, risks of heart failure events were increased with both higher and lower TSH levels (P for quadratic pattern <0.01); the hazard ratio was 1.01 (95% confidence interval, 0.81-1.26) for TSH of 4.5 to 6.9 mIU/L, 1.65 (95% confidence interval, 0.84-3.23) for TSH of 7.0 to 9.9 mIU/L, 1.86 (95% confidence interval, 1.27-2.72) for TSH of 10.0 to 19.9 mIU/L (P for trend <0.01) and 1.31 (95% confidence interval, 0.88-1.95) for TSH of 0.10 to 0.44 mIU/L and 1.94 (95% confidence interval, 1.01-3.72) for TSH <0.10 mIU/L (P for trend=0.047). Risks remained similar after adjustment for cardiovascular risk factors.
Conclusion: Risks of heart failure events were increased with both higher and lower TSH levels, particularly for TSH ≥10 and <0.10 mIU/L.

P18

DRUG-INDUCED LONG QT IN ADULT PSYCHIATRIC INPATIENTS: THE 5-YEAR CROSS-SECTIONAL ESOP STUDY

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Introduction: To determine the prevalence of drug-induced long QT at admission to a public psychiatric hospital and document associated factors in a cross-sectional approach.
Méthode: All ECG recordings over a 5-year period were reviewed for drug-induced long QT (QTc ≥ 500 ms; certain or probable drug imputability) and associated conditions. Patients with drug-induced long QT (n=62) were compared to a sample of patients with normal ECG (n=143).
Résultat: Among 6\'790 inpatients, 27.3% had abnormal ECG, 1.6% had long QT and 0.9% were detected as drug-induced long QT cases. Sudden cardiac death was recorded in five patients and Torsades de Pointes in seven other patients. Drug-induced long QT patients had significantly higher frequencies of hypokalemia (19.4% vs. 5.6%, p=0.004), hepatitis C virus infection (41.9% vs. 9.8%, p<0.001), HIV infection (24.2% vs. 6.3%, p=0.001), and abnormal T-wave morphology (35.5% vs. 15.4%, p=0.003). Haloperidol, sertindole, clotiapine, phenothiazines, fluoxetine, (es-) citalopram, and methadone were significantly more frequent in drug-induced long QT patients. After adjustment for hypokalemia, hepatitis C virus infection, HIV infection and abnormal T-wave morphology, effects of haloperidol, clotiapine, phenothiazines and (es-)citalopram remained statistically significant. Receiver operating characteristic curve analysis based on the number of endorsed factors per patient indicated that 85.5% of drug-induced long QT patients had 2 or more factors, whereas 81.1% of normal ECG patients had less than 2 factors.
Conclusion: Drug-induced long QT and arrhythmia propensity substantially increase when specific psychotropic drugs are administered to patients with hypokalemia, abnormal T-wave morphology, hepatitis C virus infection, and HIV infection.

P19

RESPIRATORY CHANGE IN ECG-WAVE AMPLITUDE IS A RELIABLE PARAMETER TO ESTIMATE INTRAVASCULAR VOLUME STATUS.

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Introduction: Electrocardiogram (ECG) is a standard type of monitoring in intensive care medicine. Several studies suggest that changes in ECG morphology may reflect changes in volume status. The ‘‘Brody effect’’, a theoretical analysis of left ventricular (LV) chamber size influence on QRS-wave amplitude, is the key element of this phenomenon. It is characterised by an increase in QRS-wave amplitude that is induced by an increase in ventricular preload. This study investigated the influence of changes in intravascular volume status on respiratory variations of QRS-wave amplitudes (ΔECG) compared with respiratory pulse pressure variations (ΔPP), considered as a reference standard.
Méthode: In 17 pigs, ECG and arterial pressure were recorded. QRS-wave amplitude was measured from the Biopac recording to ensure that in all animals ECG electrodes were always at the same location. Maximal QRS amplitude (ECGmax) and minimal QRS amplitude (ECGmin) were determined over one respiratory cycle. ΔECG was calculated as 100 × [(ECGmax-ECGmin)/(ECGmax+ECGmin)/2]. ΔECG and ΔPP were simultaneously recorded. Measurements were performed at different time points: during normovolemic conditions, after haemorrhage (25 mL/kg), and following re-transfusion (25 mL/kg) with constant tidal volume (10 mL/kg) and respiration rate (15 breath/min).
Résultat: At baseline, ΔPP and ΔECG were both < 12%. ΔPP were significantly correlated with ΔECG (r2=0.89, p<0.001). Volume loss induced by haemorrhage increased significantly &# 916;PP and ΔECG. Moreover, during this state, ΔPP were significantly correlated with ΔECG (r2=0.86, p<0.001). Re-transfusion significantly decreased ΔPP and ΔECG, and ΔPP were significantly correlated with ΔECG (r2=0.90, p<0.001).
Conclusion: The observed correlations between ΔPP and ΔECG at each time point of the study suggest that ΔECG is a reliable parameter to estimate the changes in intravascular volume status and provide experimental confirmation of the “Brody effect.”

P20

ULTRASOUND-GUIDED CONTINUOUS INTERSCALENE BLOCK: THE INFLUENCE OF LOCAL ANESTHETIC DELIVERY METHOD (AUTOMATED BOLUS VERSUS CONTINUOUS INFUSION) ON POSTOPERATIVE ANALGESIA AFTER SHOULDER SURGERY.

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Introduction: Background: Compared with a continuous infusion, an intermittent bolus regimen has been recently shown to reduce local anesthetic (LA) consumption and improve analgesia involving continuous sciatic and epidural block. During a continuous interscalene block (CISB), the influence of LA delivery method on pain relief and side-effects has been the subject of little investigation. This prospective, randomized study tested the hypothesis that, in CISB, automated boluses of LA combined with PRN (pro re nata) boluses would provide better analgesia after shoulder surgery compared with continuous infusion in conjunction with PRN boluses.
Méthode: Methods: One hundred and one patients, scheduled for elective shoulder surgery under general anesthesia with continuous interscalene analgesia were recruited. All the nerve blocks were ultrasound-guided using an out-of-plane approach and nerve stimulator in sentinel mode (> 0.5 mA). Following ultrasound confirmation of the catheter tip immediately lateral to C5/C6 roots, ropivacaine 0.5%+lidocaine 1% (50:50) 20 ml were administered preoperatively via the catheter before surgery. They were randomly assigned to receive via interscalene e! nd-hole catheter either a continuous infusion of 0.2% ropivacaine at an infusion rate of 4ml/h (group CI, n=50) or an automated hourly 4 ml bolus of the same LA (group AB, n=50). Both method deliveries are combined with 5 ml patient controlled boluses of 0.2 % ropivacaine with a lockout time of 30 min. Postoperative pain scores, incremental doses delivered by PCA, LA consumption, rescue morphine analgesia and side-effects were recorded.
Résultat: Postoperative pain was similar between the groups [Group CI day 2 median (IQR) average VAS pain=4 (2-6) vs 3 (2–5) in the groupe AB, p=0.54] as were the number of PRN ropivacaine bolus requirement at 24 and 48 h. The need for rescue morphine was similar in the two groups on both days 1 and 2.
Conclusion: Conclusions: In CISB under ultrasound guidance, automated regular bolus of LA combined with PRN boluses provide similar quality of analgesia after shoulder surgery without reduction of LA and morphine consumption as compared with continuous infusion technique combined with PRN boluses.

P21

ACOUSTIC RADIATION FORCE IMPULSE (ARFI) ELASTOGRAPHY FOR THE NONINVASIVE DIAGNOSIS OF LIVER FIBROSIS IN CHILDREN

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Introduction: Acoustic radiation force impulse (ARFI) imag- ing) is correlated with histopathological findings using METAVIR and semiquantitative scoring system (SSS) criteria for liver fibrosis.To compare acoustic radiation force impulse imaging with biopsy results in the evaluation of liver fibrosis in children.
Méthode: Children with chronic liver disease and healthy children underwent acoustic radiation force impulse imaging liver measurements. ARFI gives a shear-wave velocity corresponding to tissue elasticity. In 39 children with liver disease, the values obtained were correlated with biopsy results. Receiver-operating characteristic (ROC) curves were used to determine the reliability of ARFI in estimating liver fibrosis in children.
Résultat: ARFI mean value was 1.12 in the healthy group and 1.99 in children with chronic liver disease. ROC curves show that an ARFI cutoff of 1.34 m/s is predictive of both METAVIR and SSS scores with a sensitivity of SSS > 2:0.85; METAVIR > F0:0.82. A cutoff of 2 m/s yielded a sensitivity of 100% to detect SSS > 4 or METAVIR > F2.
Conclusion: Acoustic radiation force impulse imaging is a reliable, noninvasive and rapid method to estimate moderate to severe liver fibrosis in children. It might prove useful to clinicians for fibrosis monitoring in children with liver dis- ease and postpone the time of liver biopsy.

P22

ANTIBODY-MEDIATED STATUS EPILEPTICUS: A RETROSPECTIVE MULTICENTER SURVEY

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Introduction: In recent years, an increasing number of autoantibodies (AB) have been detected in the CSF and serum of patients with new onset epilepsy. Some of these patients develop convulsive or nonconvulsive status epilepticus (ABSE), necessitating intensive medical care and administration of multiple antiepileptic and immunomodulatory treatments of uncertain effectiveness. In this retrospective multicenter survey we aimed to determine the spectrum of gravity, the duration and the prognosis of the disorder. In addition, we sought to identify the antibodies associated with this condition, as well as determine whether there is a most effective treatment regime.
Méthode: 12 European Neurology University Clinics, with extensive experience in the treatment of SE patients, were sent a detailed questionnaire regarding symptoms and treatment of AB-SE patients. Seven centers responded positively, providing a total of 13 patients above the age of 16.
Résultat: AB-SE affects mainly women (12/13, 92%) with a variable age at onset (17–69 years, median: 25 years). The duration of the disease is also variable (10 days to 12 years, median: 2 months). Only the 3 oldest patients died (55–69 years). Most patients were diagnosed with anti NMDAR encephalitis (8/13) and had oligoclonal bands in the CSF (9/13). No specific treatment regimen (antiepileptic, immunomodulatory) was found to be clearly superior. Most of the surviving 10 patients (77%) recovered completely or nearly so within 2 years of index poststatus.
Conclusion: AB-SE is a severe but potentially reversible condition. Long duration does not seem to imply fatal outcome; however, age older than 50 years at time of onset appears to be a risk factor for death. There was no evidence for an optimal antiepileptic or immunomodulatory treatment. A prospective multicenter study is warranted in order to stratify the optimal treatment algorithm, determine clear risk factors of unfavorable outcome and long-term prognosis.

P23

DECOLONIZATION OF INTESTINAL CARRIAGE OF EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIACEAE WITH ORAL COLISTIN AND NEOMYCIN: A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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Introduction: Beta-lactamase producing Enterobacteriaceae (ESBL-E) are an increasingly frequent cause of infections in the community and the healthcare setting. In this study we aimed to investigate whether intestinal carriage of ESBL-E can be eradicated.
Méthode: We conducted a double-blind, randomized, placebo-controlled single-center trial to assess the efficacy of an oral decolonization regimen on intestinal ESBL-E carriage in adult patients with an ESBL-E positive rectal swab. 58 patients were allocated 1:1 to either placebo or colistin sulfate (50mg 4x/day) and neomycin sulfate (250mg 4x/day) for 10 days plus nitrofurantoin (100mg 3x/day) for 5 days in the presence of ESBL-E bacteriuria. The primary outcome was detection of ESBL-E by rectal swab 28+/-7 days after the end of treatment. Missing primary outcome data were imputed based on the last available observation. Additional cultures (rectal, inguinal, urine) were taken on day 6 of treatment (d6t) and on days 1 (d1p) and 7 (d7p) post-treatment.
Résultat: Among 54 patients (27 in each group) included in the primary analysis, there was no statistically significant difference between the groups with regard to the primary outcome (14/27 [52%] versus 10/27 [37%], p=0.27). During treatment and shortly afterwards there was significantly lower rectal ESBL-E carriage in the treatment group: 9/26 versus 19/22 on d6t (p<0.001) and 8/25 versu! s 20/26 on d1p (p=0.001). This effect had disappeared by d7p (18/27 versus 17/25, p=0.92). Liquid stools were more common in the treatment group (7/27 versus 2/29, p=0.05).
Conclusion: The regimen used in this study temporarily suppressed ESBL-E carriage, but had no long-term effect.

P24

INTERET DE L'ETUDE DU CONTROLE MOTEUR DANS LA SCLEROSE LATERALE AMYOTROPHIQUE

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Introduction: Le Timed Up and Go (TUG) mesure le temps nécessaire pour se lever d'une chaise, faire le tour d'un objet situé à 3 mètres puis revenir s'asseoir. Le vieillissement et le déclin cognitif entraînent des modifications du contrôle cortical de la marche et de l'équilibre. Il a été démontré de l'intérêt d'une version imaginée du TUG (iTUG) pour évaluer l'impact du vieillissement pathologique sur le contrôle de la marche. Le but de notre travail est d'étudier la performance du TUG et du iTUG chez des patients souffrant d'une Sclérose Latérale Amyotrophique (SLA).
Méthode: Nous avons inclus consécutivement 25 patients (âge moyen: 64 ± 12.2 ans) ayant bénéficié d'un TUG/iTUG lors de leur première évaluation à la consultation SLA des HUG entre mars 2011 et septembre 2012. Le score fonctionnel ALSFRS-R a été évalué en même temps.
Résultat: Il existe une corrélation positive entre l'âge des participants, le TUG (R2=0.18, p=0.04) et le iTUG (R2=0.12, p=0.05). Le score ALSFRS-R est inversement proportionnel au TUG (R2=0.40, p=0.001) et au iTUG (R2=0.30, p=0.007). En tenant compte du type de SLA (bulbaire ou non bulbaire), un iTUG inférieur à 8.4s est corrélé à une augmentation du risque de décès (modèle de Cox, p=0.01).
Conclusion: Cette étude montre que le TUG et le iTUG sont réalisables chez les patients souffrant d'une SLA et que ces 2 paramètres sont corrélés au score fonctionnel ALSFRS-R. De plus, le iTUG, tenant compte de la composante cognitive du contrôle moteur pourrait constituer un marqueur intéressant de l'évolution de la maladie.

P25

CITATION BIAS FAVORING STATISTICALLY SIGNIFICANT STUDIES IS PRESENT IN MEDICAL RESEARCH

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Introduction: Statistically significant studies may be cited more than negative studies on the same topic. We aimed to assess here whether such citation bias is present across the medical literature.
Méthode: We conducted a cohort study of the association between statistical significance and citations. We selected all therapeutic intervention studies included in meta-analyses published between January and March 2010 in the Cochrane database, and retrieved citation counts of all individual studies using ISI Web of Knowledge. The association between the statistical significance of each study and the number of citations it received between 2008 and 2010 was assessed in mixed Poisson models.
Résultat: We identified 89 research questions addressed in 458 eligible papers. Significant studies were cited twice as often as non-significant studies (multiplicative effect of significance 2.14, 95% confidence interval 1.38 to 3.33). This association was in part due to the higher impact factor of journals where significant studies are published (adjusted multiplicative effect of significance 1.14, 95% confidence interval 0.87 to 1.51).
Conclusion: A citation bias favouring significant results occurs in medical research. As a consequence, treatments may seem more effective to the readers of medical literature than they really are.

P26

IMPACT OF A BOARD GAME APPROACH ON CURRENT SMOKERS

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Introduction: The main objective of our study was to assess the impact of a board game on smoking status and smoking-related variables in current smokers.
Méthode: Randomized controlled trial comparing the game group with a psychoeducation group and a waiting-list control group. The following measures were performed at participant inclusion, as well as after a 2-week and a 3-month follow-up period: “Attitudes Towards Smoking Scale” (ATS-18), “Smoking Self-Efficacy Questionnaire” (SEQ-12),“Attitudes Towards Nicotine Replacement Therapy” scale (ANRT-12), number of cigarettes smoked per day, stages of change, quit attempts, and smoking status. Furthermore, participants were assessed for concurrent psychiatric disorders and for the severity of nicotine dependence with the Fagerström Test for Nicotine Dependence (FTND).
Résultat: A time × group effect was observed for subscales of the ANRT-12 and SEQ-12, as well as for the number of cigarettes smoked per day. The percentage of nonsmokers at 3 month follow-up was significantly higher in the game group and the psychoeducation group, whereas no change was observed in the waiting-list group. Outcomes at 3 months were not predicted by gender, age, FTND, stage of change, or psychiatric disorders at inclusion.
Conclusion: The board game seems to be a goodoption for smokers. The game led to improvements in variables known to predict quitting in smokers. Furthermore, it increased smoking-cessation rates at 3-month follow-up. The game is also an interesting alternative for smokers in the precontemplation stage.

P27

SCN1A MUTATIONS IN A POPULATION OF CHILDREN WITH STATUS EPILEPTICUS

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Introduction: Status epilepticus (SE) may present as an isolated episode in normal infants during a febrile illness, or repeatedly in severe epileptic syndromes of infancy, with which the differential diagnosis is difficult initially. Abnormalities on the gene that encodes SCN1A, are frequently found in various epilepsy syndromes that share a propensity for SE. The objective of this study was to know if SCN1A mutations predispose certain children to develop SE.
Méthode: Swiss multicenter case-control study. Children, who presented with at least one episode of SE between 1 month and 16 years, were tested for SCN1A mutations. Their results were compared to those of children with short seizures only, after a minimal follow-up of 2.5 years. To detect any partial or complete deletion/duplication on SCN1A, multiplex ligation-dependent probe amplification was performed. Prescreening for potential DNA point mutations was carried out by high-resolution melting curve analysis (HRMCA). SCN1A was divided into 40 fragments. DNA from patients was tested in parallel and normalized temperature-shifted difference plots were compared between samples. Fragments showing abnormal HRMCA profiles were amplified by PCR. Direct sequencing of the purified products was performed and further analyzed on capillary electrophoresis using primers designed to cover all exons and their flanking sequences. Blood samples from the parents of children with abnormal genetic results were also analyzed to check for potential heritability. Epilepsy syndrome diagnoses were made according to established clinical criteria.
Résultat: 109 children were included, 71 with SE (Group A) and 38 without SE (Group B). SCN1A mutations were found in 12 (16.9%) patients of group A and in 3 (7.9%) patients of group B (p=0.25). In group A, the median age at first SE was 8 months for children with Dravet syndrome (DS), and 41 months for those with another diagnostic (p<0.001). All children with DS (10/10, 100%) had at least one SE recurrence, in a mean interval of 2 months after the initial episode, whereas only 25/61 (41%) of those with another diagnosis had presented more than one SE episode at the time of inclusion (p=0.005). Among the 26 patients aged less than 18 months at the time of their initial SE episode, the risk of having DS was higher in those who had 2 episodes than in those with a single SE event (56.3% (95% CI 29.9-80.21) vs 0.0% (95% CI 0.0-30.8), p=0.005).
Conclusion: SCN1A mutations are found in almost 17% patients with SE. Children with DS present their initial SE episode earlier than those with another epilepsy diagnosis, and all recur in a short interval. This suggests that one can wait for a second SE event before testing SCN1A in children suspect of having DS. Finally, the presence of SCN1A mutations is unlikely if the initial SE occurs after 18 months.

P28

APPORT DE L'EVALUATION NEUROPSYCHOLOGIQUE DANS L'IDENTIFICATION DES PATIENTS AVEC HYDROCEPHALIE A PRESSION NORMALE

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Introduction: L'hydrocéphalie à pression normale (HPN) fait partie des rares causes de démences réversibles. Elle est caractérisée par une triade clinique associant des déficits cognitifs, des troubles de la marche et une incontinence urinaire. Cette symptomatologie est peu spécifique puisque retrouvée dans d'autres pathologies neurodégénératives ou cérébrovasculaires. Du fait de l'existence d'un traitement, l'identification des patients avec HPN est cruciale. L'objectif de cette étude était de comparer l'effet de la ponction lombaire (PL) soustractive sur les performances neuropsychologiques de patients avec un diagnostic d'HPN avec celles de patients présentant une symptomatologie mimant ce diagnostic.
Méthode: Parmi les 36 patients inclus dans cette étude, 26 présentaient un diagnostic d'HPN et 10 avaient une pathologie neurologique mimant ce diagnostic. Des tests neuropsychologiques évaluant le fonctionnement exécutif, les capacités attentionnelles, ainsi que le transfert inter-hémisphérique ont été utilisés. Les comparaisons intergroupes ont été effectuées avec le test de Mann-Whitney ou le test de Fisher.
Résultat: Les deux groupes présentaient des caractéristiques cliniques équivalentes (Age moyen : 76 ± 7 ans ; score moyen au MMSE : 24 ± 5 points). Le groupe de patients avec HPN montrait une amélioration après PL significativement plus importante que les patients non HPN au niveau des capacités de mémoire de travail (empan verbal endroit ; P = 0.04) et de flexibilité mentale (color trails test, P = 0.02). Les autres fonctions montraient des performances équivalentes.
Conclusion: Une évaluation neuropsychologique avant et après ponction lombaire soustractive constitue un élément important dans le processus diagnostique afin d'identifier les patients avec une HPN de ceux présentant une pathologie similaire.

P29

STATINS MAY REDUCE FEMORAL OSTEOLYSIS IN PATIENTS WITH TOTAL HIP ARTHROPLASTY

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Introduction: In experimental studies, statin use has been associated with reduction of osteoclastic activity and promotion of bone formation around implants. Moreover, a large clinical study recently reported a substantially reduced risk of revision for aseptic loosening among statin users with THA. Our objective was to evaluate the influence of statin use on the development of femoral osteolysis within 5 years after THA.
Méthode: We conducted a case-cohort study including all THAs presenting with femoral osteolysis at the 5 year visit (cases) and compared them with those without osteolysis (controls). Cases and controls were identified from a cohort of primary THAs operated between 2001 and 2005 with the same uncemented cup and the same 28mm head size. Periprosthetic osteolysis was assessed on standardised radiographs by a surgeon blinded to the patient's exposure status.
Résultat: Seven hundred thirty-five THAs were included, mean age 68 years. Five years after surgery osteolysis had developed around the femoral component of 40 THAs (5.4%). Ever-use of statins was much less frequent among cases (5 of 40, 12.5%) than among controls (199 of 695, 28.6%). The crude risk ratio of femoral osteolysis among statin users was 0.36 (95% CI 0.14;0.92). After adjusting for age, sex, activity level, BMI, diagnosis, bearing surface, and type of stem, the adjusted risk ratio was 0.38 (95% CI 0.15; 0.99).
Conclusion: In conclusion, statin use was associated with a reduced risk of developing femoral osteolysis 5 years after THA. Statins may be useful for reducing the risk of implant failure following THA.

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USEFULNESS OF PET-CT IN THE DIAGNOSIS OF PATIENTS WITH "VULNERABLE" CAROTID PLAQUES: CORRELATION TO CLINICAL SYMPTOMS, PRESENCE OF MICRO-EMBOLIC SIGNALS AND TO PLASMATIC MARKERS OF INFLAMMATION

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Introduction: Vulnerable atherosclerotic plaques responsible for ischemic strokes are characterized by high numbers of inflammatory cells and proteins. The glucose analogue 18F-fluorodeoxyglucose (FDG) can be used to image inflammatory cell activity by positron emission tomography (PET). The aim of our study was to evaluate whether PET-CT showed a higher accumulation of FDG in carotid plaques in symptomatic patients and in plaques generating micro-embolic signals (MES+). Furthermore we investigated whether plasmatic inflammatory biomarkers also correlated with the different clinical and imaging parameters.
Méthode: Patients with 50 to 99% symptomatic or asymptomatic carotid disease were included. FDG-PET-CT was performed within 2-3 days after symptoms onset. MES detection by transcranial Doppler was carried out for 60 minutes. Further workup included brain MRI and blood samples for analysis of inflammatory parameters (MMP-9,-8, rantes). Analysis of PET-CTs included mean and maximum standardized uptake values (SUV) of the carotid plaque and jugular veins. The uptake was calculated by the ratio of maximal SUV of the plaque and average SUV of the jugular veins.
Résultat: 123 carotid plaques were analyzed, 61 symptomatic and 62 asymptomatic. The uptake index was significantly higher in symptomatic ($p=0.0007$) and in MES+ plaques ($p=0.01$). Analysis of biomarkers showed a significant correlation between FDG uptake and the cheomokine rantes ($p=0.006$, $rho=0.25$).
Conclusion: PET - CT had the potential to identify vulnerable plaques and may therefore improve our selection criteria of patients eligible for carotid surgery or stenting.

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LA DANSE THERAPIE AMELIORE L'IMAGE DU CORPS CHEZ LES PERSONNES OBESES

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Introduction: l'obésité et les troubles du comportement alimentaire sont associés à une mauvaise estime de soi et à une image du corps altérée. Le but de cette étude est de déterminer l'influence d'un programme de danse thérapie sur l'évolution des représentations mentales associées à l'image du corps chez les patients obèses. Les changements de l'image du corps chez ces personnes ont été évalués dans les 4 dimensions : physique, psychologique, cognitive et social.
Méthode: Cette étude s'est déroulée pendant 36 semaines. Les patients ont dansé à raison de deux heures par semaine. Les 18 patients obèses ont été évalués à trois reprises : avant, à 18 semaines et à 36 semaines. Des questionnaires ont été utilisés pour évaluer la distorsion de l'image du corps, l'estime de soi, la qualité de vie liée à la santé, la perception sensorielle moteur et les représentations mentales associées au schéma corporel et à l'image du corps.
Résultat: Les résultats indiquent une amélioration significative de la qualité de vie ($p<0.03$), de la conscience corporelle ($p<0.001$) et des représentations mentales associées à l'image du corps ($p<0.001$).
Conclusion: En conclusion, des ateliers de danse thérapie permettent aux patients obèses d'ajuster leur ressenti corporel et psychique à leur image. Application pratique : En général les patients obèses sont réticents aux activités physiques. La danse thérapie améliore non seulement l'image du corps mais améliore également l'aspect psychosocial de leur personnalité Mots clé : obésité, danse thérapie, image du corps

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CHARACTERISTICS OF 41 PATIENTS HOSPITALIZED WITH A TAKO-TSUBO SYNDROME IDENTIFIED BY A SYSTEMATIC COMPUTERIZED SEARCH.

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Introduction: Tako-Tsubo syndrome (TS) also known as transient left ventricular apical ballooning syndrome, stress cardiomyopathy, or broken heart syndrome, mimics acute coronary syndrome. Acute, reversible left ventricular dysfunction is observed in the presence of normal coronary arteries and often there is precipitating emotional or physical stress. TS only constitutes a small proportion of all coronary syndromes. Epidemiological data are available on TS, but as the disease is not uncommonly encountered in large centers it is useful to have recent estimates at disposal. Our objective was to systematically identify cases of TS in our institution and we present preliminary data here that describe the characteristics of patients presenting with TS.
Méthode: We systematically identified all cases of TS hospitalized between 2008 and 2011 in our institution. Patients were identified by a computerized search by keywords in all available electronic hospital records. We subsequently manually reviewed each record and only patients in whom the diagnosis of TS was retained were kept.
Résultat: The 41 cases of TS were predominantly female (88.2%) as extensively described in the literature. The mean age was 73.5 years [49-89 years]. We observed a highly variable number of cases of TS over the observation period (3-17 cases per year) with no clear trend over time.
Conclusion: Our retrospective study reproduces findings by others on the large female predominance of TS. TS patients tend to be older than patients with coronary syndrome. The highly variable number of cases observed per year is either due to diagnostic bias, an unknown confounder, or due to true variations in incidence.

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ANTI-APOLIPOPROTEIN A-1 IGG IN PATIENTS WITH MYOCARDIAL INFARCTION PROMOTES INFLAMMATION THROUGH TLR2/CD14 COMPLEX.

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Introduction: Toll-like receptors (TLRs) mediated vascular inflammation, inducible by- amongst other factors- auto-antibodies, is increasingly recognized as a potential mediator of cardiovascular disease. We investigated whether anti-apolipoprotein A-1 (ApoA-1) IgG were associated with a pro-inflammatory cytokine profile in myocardial infarction (MI) patients, and whether anti-ApoA-1 IgG elicited a pro-inflammatory response by activating TLRs.
Méthode: As surrogate markers of atherosclerotic plaque vulnerability, interleukin (IL)-6, tumor necrosis factor (TNF)-α, matrix-metalloproteinase (MMP)-9 and MMP-3 levels were assessed on 221 consecutive MI patients. Using human monocyte-derived macrophages (HMDMs) we investigated i) the anti-ApoA-1 IgG interaction with TLRs using proximity ligation assay (PLA), and ii) anti-ApoA-1 IgG-dependent IL-6/TNF-α production. TLR involvement was further confirmed using HEK293-Blue TLR-2/-4 cells and by computational docking simulations.
Résultat: In MI patients, anti-ApoA-1 IgG positivity was associated with higher levels of IL-6, TNF-α, MMP-9, but lower MMP-3 levels. In in vitro experiments, anti-ApoA-1 antibodies bound to HDMDs in a TLR2-dependent manner, resulting in nuclear translocation of NFκB and a significant increase in TNF-α and IL-6 production. Subsequent functional studies highlighted the importance of CD14 as co-receptor in the anti-ApoA-1 IgG-TLR2- induced cytokine production. Additional bioinformatic studies identified structural homologies between TLR2 and ApoA-1, which may explain the observed cross-reactivity between antibodies against these two molecules.
Conclusion: Anti-apoA-1 IgG positivity in MI is associated with a high-risk cytokine profile. These auto-antibodies promote inflammation by stimulating the TLR2/CD14 receptor complex, probably because of molecular mimicry, which may contribute to atherosclerosis-related complications in patients.

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FACILITER LA CREATION DE GUIDES DE BONNES PRATIQUES POUR LE TRAITEMENT DES MALADIES INFECTIEUSES

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Introduction: L'utilisation massive et souvent erronée des antibiotiques mène à une augmentation de la résistance aux antibiotiques, mettant ainsi en péril le traitement des maladies infectieuses. Dans ce contexte, il est indispensable d'améliorer l'utilisation des antibiotiques. Une approche possible est l'utilisation de guides de bonnes pratiques.
Méthode: Nous avons développé KART, un outil destiné à faciliter la création des guides de bonnes pratiques. La spécificité de KART repose sur l'intégration d'un moteur de recherche de type \"question-réponse\", spécialisé pour le domaine de l'antibiothérapie. Ce moteur utilise différentes collections de littérature biomédicale, telle que MEDLINE, pour suggérer des antibiotiques à des questions cliniques concernant l'antibiothérapie. Cet outil a finalement été évalué par des experts en maladies infectieuses.
Résultat: L'évaluation de KART a montré que pour 53% des questions posées, le premier traitement proposé par notre outil est consistant avec les recommandations existantes. L'évaluation par les utilisateurs a permis de mettre en évidence des cas spécifiques dans lesquels KART a des difficultés à répondre, tels que les cas pour lesquels les antibiotiques doivent être évités.
Conclusion: Notre approche permet un accès simplifié à la littérature biomédicale en proposant des réponses courtes, ainsi que la possibilité de comprendre les réponses de KART grâce à la littérature pertinente associée à chaque proposition. Nous avons donc développé une approche innovatrice pour faciliter le processus de développement des guides de bonnes pratiques dans un contexte où les connaissances disponibles augmentent à un taux qui ne peut pas être suivi par les humains.

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CHILDHOOD MALTREATMENT AND METHYLATION OF THE GLUCOCORTICOID RECEPTOR GENE (NR3C1) IN BIPOLAR DISORDER

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Introduction: Childhood maltreatments are more frequently observed in bipolar disorder (BD) patients compared to control populations and are associated with higher severity of the disorder. In animals and humans, increased methylation of the glucocorticoid receptor (GR) gene (NR3C1) has been associated with early life adverse events.
Méthode: We collected peripheral blood DNA from 99 BD patients and characterized the levels of childhood maltreatment using the Childhood Trauma Questionnaire (CTQ). Using this sample of BD patients, we sought to determine whether the severity of early life stress correlated with the methylation status of the exon 1F NR3C1 promoter.
Résultat: The higher was the number of childhood maltreatments the higher was the percentage of NR3C1 methylation (b=0.52; p=3.23*10-27; 95%CI from 0.46 to 0.59). Percentage of NR3C1 metyhlation was significantly associated with the severity of each type of maltreatment independently, emotional abuse being the most significantly associated (b=0.64; p=4.21*10-18; 95%CI from 0.52 to 0.76). Percentage of methylation was significantly associated with a history of alcohol use disorder.
Conclusion: Child maltreatment has a sustained effect on the methylation status of the exon 1F NR3C1 promoter, an effect that may be measured in the peripheral blood. Epigenetic processes, through enduring alteration of the HPA axis, may mediate the impact of early life adversities on adulthood psychopathologies.

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THE STAPHYLOCOCCUS AUREUS THIOL/OXIDATIVE STRESS SENSOR SPX CONTROLS TRFA/MECA, A MEMBER OF THE CELL-WALL STRESS REGULON

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Introduction: Cell-wall active antibiotics (glycopeptides and β-lactams) are non-penetrating antibiotics and phospho-signalling systems play an important role in transduction of signalling to promote resistance. While recent data indicate that glycopeptide resistance mechanisms may be linked with oxidative stress response pathways, the molecular pathways linking cell-wall active antibiotics resistance and oxidative stress remain to be explored.
Méthode: We examined the transcriptional regulation of trfA gene, a gene of unknown function whose deletion leads to almost complete loss of resistance to oxacillin and glycopeptide antibiotics in glycopeptide-intermediate S. aureus (GISA) derivatives of methicillin-susceptible or methicillin-resistant (MRSA) clinical or laboratory isolates.
Résultat: Northern blot analysis and 5' RACE mapping revealed that trfA was expressed by three monocistronic transcripts driven by three promoters, named P1, P2 and P3. Exposure to cell-wall active antibiotics led to increased trfA transcription and translation, indicating that TrfA likely belongs to the S. aureus cell-wall stress regulon. Noteworthy, trfA transcription was found to be regulated in dependen tly from the cell-wall stress transcriptional regulator VraR. In contrast, post-transcriptional modification of the oxidative stress regulator Spx played a major role in the induction of trfA transcription by S. aureus exposed to cell-wall targeting antibiotics.
Conclusion: These data provide further evidence for a link between glycopeptide resistance and oxidative stress responses by still incompletely understood molecular pathways. We proposed a model that may account for the role of the oxidative stress regulator Spx in cell-wall antibiotic resistance independent from phospho- signalling systems.

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THE SHORT-TERM PROGNOSIS OF CARDIOGENIC SHOCK CAN BE DETERMINED USING HEMODYNAMIC VARIABLES: A RETROSPECTIVE COHORT STUDY

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Introduction: Few reports address the relationship between hemodynamic parameters and the cardiogenic shock (CS) outcome in critically ill patients. The present study aimed to investigate the association between hemodynamic variables and early cardiogenic shock mortality in critically ill patients

Méthode: This observational study examined a retrospective cohort of patients with CS. we retrospectively analyzed medical information and the hemodynamic variables (recorded during the first 24 hours following admission to the ICU) of patients with cardiogenic shock. For all the patients, the Simplified Acute Physiology Score (SAPS) II score, cardiac index, cardiac power index, continuous hemodynamic values following the first 24 h hours of admission were reviewed. The patients were classified as survivors or non-survivors. All the variables were then compared with survival and non-survival status and those variables with a significant association in the univariate analysis were entered into a multivariate logistic regression model.71 patients were included. Among them, 26 (37%) died within 28 days after ICU admission and were classified as "non-survivors.

Résultat: The minimum value for diastolic arterial blood pressure (DAP) during the first 24 h was independently associated with the 28-day mortality in the univariate and multivariate analyses model. This model performed better than the model using the SAPS II score, even when assessing the effect of inotrope and vasoactive treatments at 24, 48 and 72 hours

Conclusion: According to the data collected from the present study, DAP deserves a role in evaluating patients with CS.The advantages of this parameter are the ease of monitoring,even in a moderately equipped center,and its reliability in determining CS prognosis.However, a more profound analysis of this parameter and further evaluation are required to better understand its prognostic significance in CS.

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DOES KNEE ALIGNMENT INFLUENCE GAIT IN PATIENTS WITH SEVERE KNEE OSTEOARTHRITIS?

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Introduction: Patients with knee osteoarthritis present an altered gait pattern. Amongst many factors, the lower limb alignment (varus, valgus) has been identified as an important risk factor for the progression of knee osteoarthritis. Among the large number of studies on knee osteoarthritis gait, only a few have included patients with a valgus deformity. The aims of this study were to determine how knee alignment influences full-body gait in patients with knee osteoarthritis and if knee malalignment is associated with pain and functional capacity.

Méthode: Sixty patients with severe knee osteoarthritis scheduled for a total knee arthroplasty were included in this study. Twenty-six subjects were recruited as the control group. The spatio-temporal parameters, three-dimensional full-body kinematics, and lower body kinetics were evaluated during a comfortable gait and compared between the groups. Pain and function were assessed with the WOMAC questionnaire.

Résultat: The full-body gait analysis demonstrated substantially different gait patterns and compensation mechanisms between the three groups. Patients with varus knee alignment significantly augmented their trunk movements in sagittal and frontal planes in comparison with patients with a valgus knee. In addition, patients with a valgus knee reported lower pain and lower functional deficits compared to patients with a varus knee.

Conclusion: We found that gait compensations were significantly influenced by lower limb alignment. These new insights related to different knee osteoarthritis gait patterns might help in the understanding of gait compensation behavior prior to total knee arthroplasty and better manage the strategies of rehabilitation following surgery.

NOTES