2019

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RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR

N°6 - TROISIÈME QUADRIMESTRE 2019

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CHU UCL NAMUR

RECUEIL DES PUBLICATIONS SCIENTIFIQUES DU CHU UCL NAMUR

N°6 - TROISIÈME QUADRIMESTRE 2019

Cher(e)s collègues,
Madame, Monsieur,

Cet ouvrage reprend les publications du troisième quadrimestre de l'année 2019.

Nous vous invitons à poursuivre la transmission de vos publications au Département Recherche et Enseignement afin, non seulement, que nous en prenions connaissance mais également de permettre de les partager avec la communauté du CHU UCL Namur, qui apprendra à connaitre vos travaux dont la publication est le fruit.

Mettre en lumière le dynamisme de nos chercheurs à nos patients, nos collaborateurs et nos partenaires mais également aux collègues de la même institution qui méconnaissent souvent les recherches réalisées dans le service voisin, nous l'espérons, permettra d'établir des collaborations nouvelles entre différents spécialités et métiers.

Sans l'investissement constant des chercheurs dans leurs projets de recherche, ces publications et cette participation au développement des connaissances n'existeraient pas.

En vous souhaitant bonne lecture, nous remercions les chercheurs et leurs équipes pour leur volonté à maintenir et promouvoir le développement de nos missions académiques par leur engagement journalier. Sans eux, ce recueil n'existerait pas !

Professeur Maximilien Gourdin
Directeur aux Affaires Académiques
CHU UCL Namur

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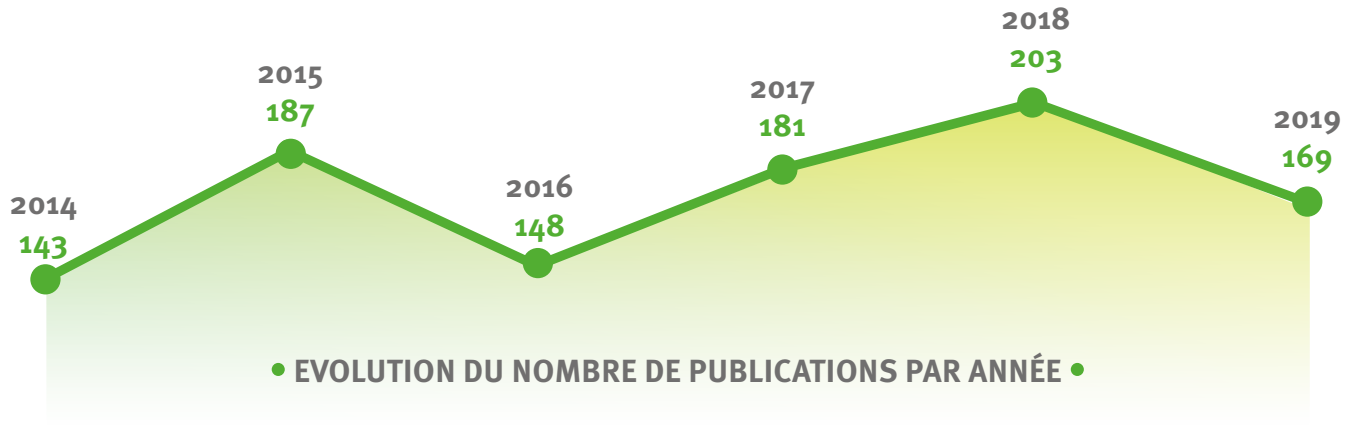

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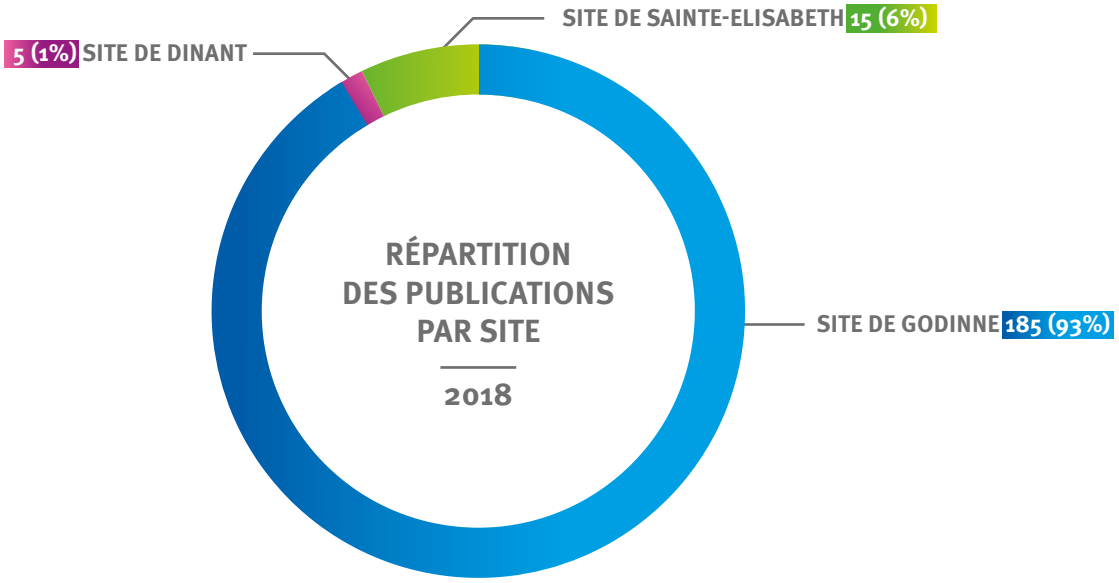

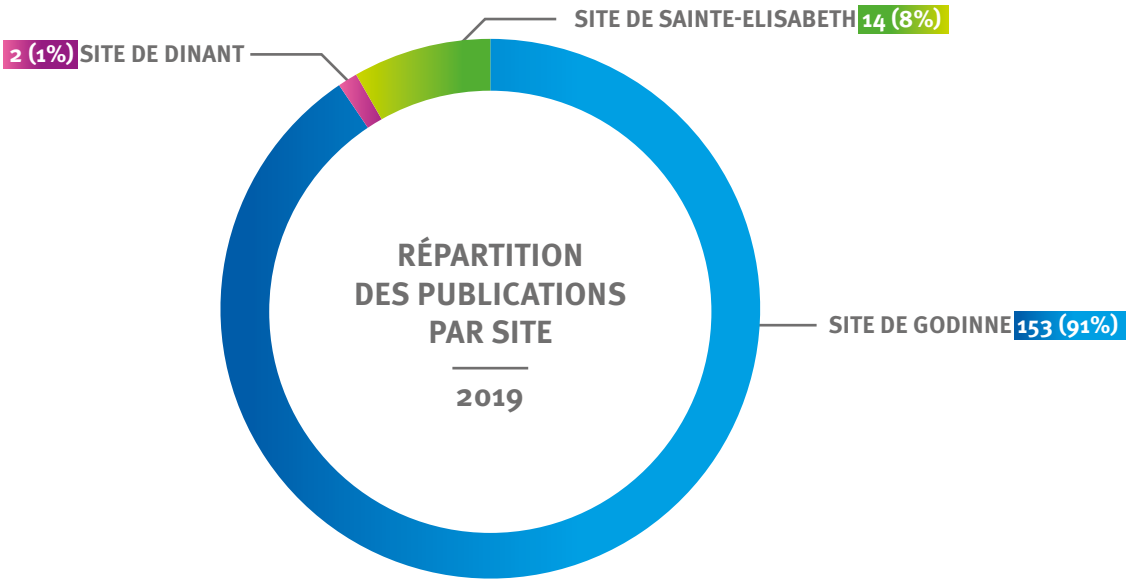

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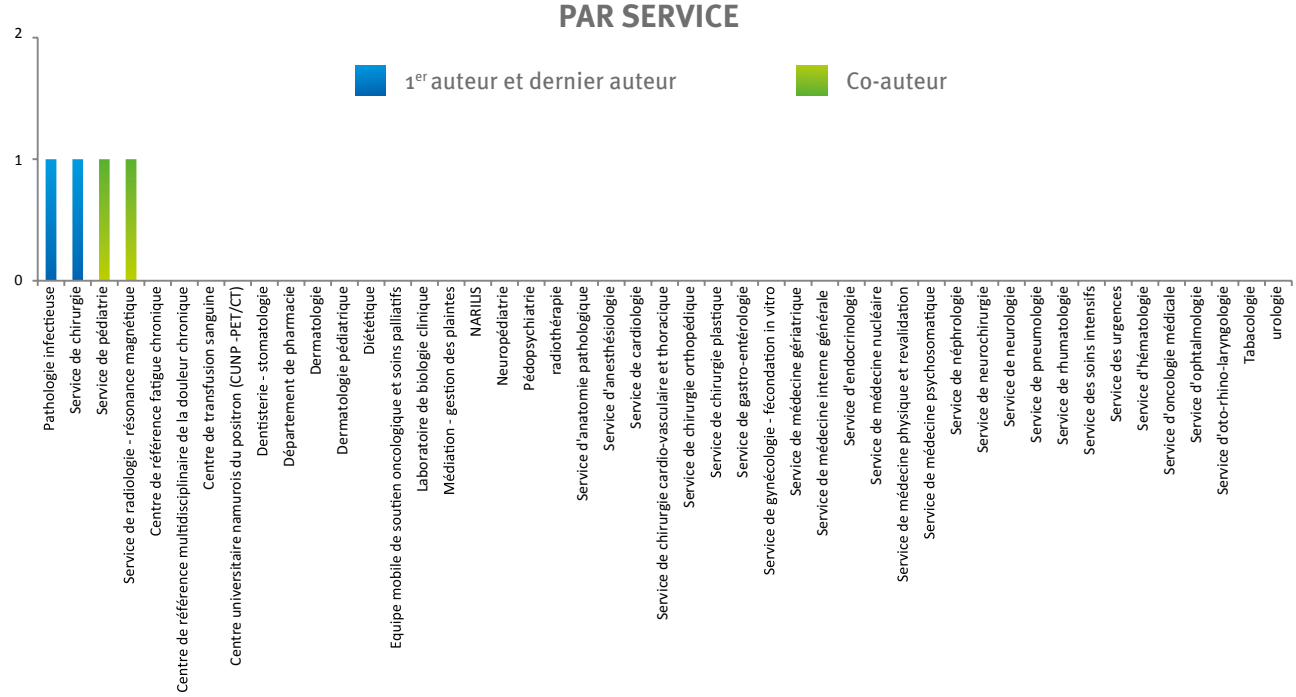

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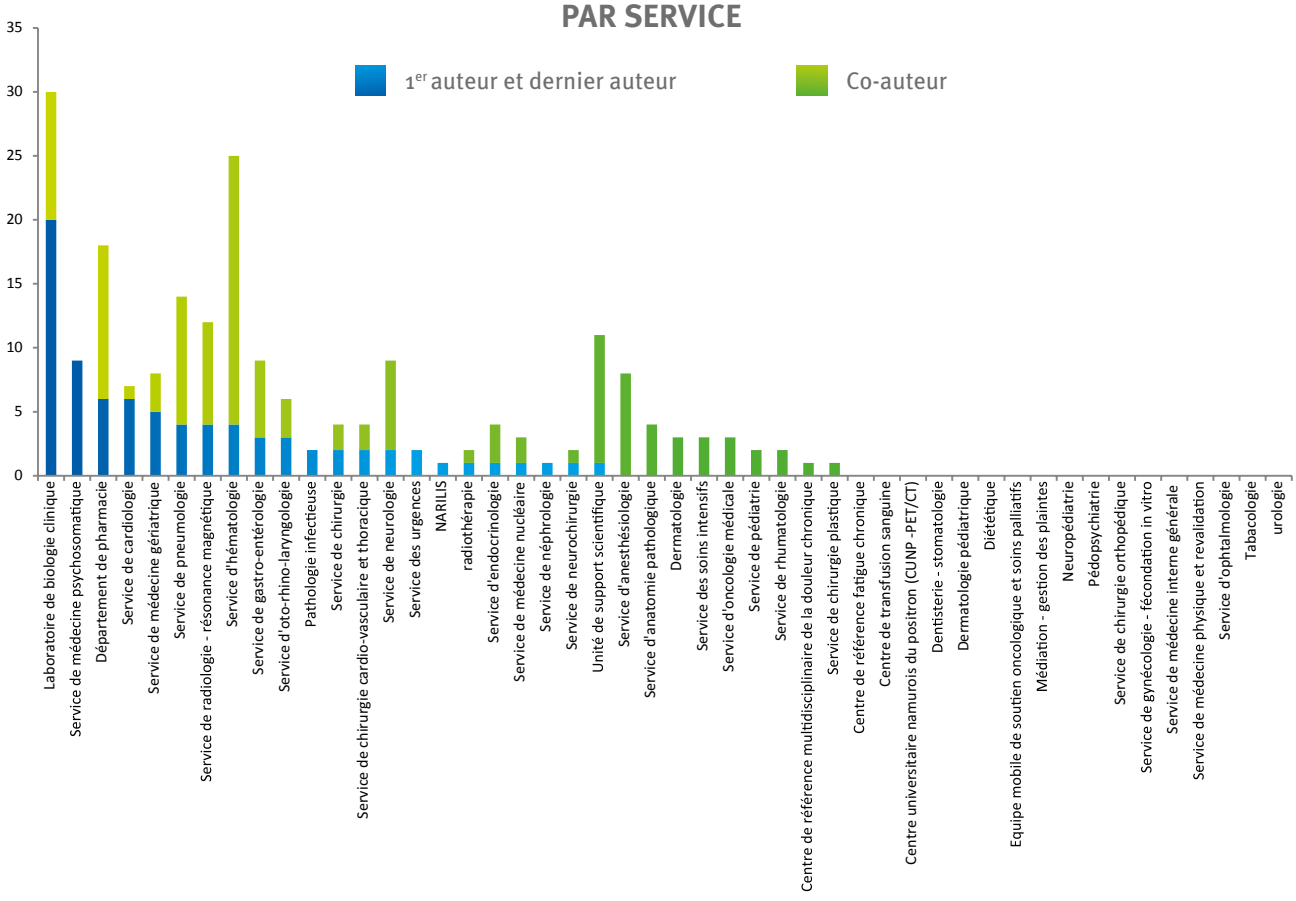


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LA SIGNATURE SCIENTIFIQUE

La signature scientifique des articles et publications que vous rédigez et auxquels vous contribuez est d'une importance capitale pour le financement des missions de Recherche et d'Enseignement au sein du CHU UCL Namur et pour notre visibilité universitaire au niveau national et international.

Le nombre d'articles publiés par une Institution de Recherche et d'Enseignement ainsi que les facteurs d'impact des journaux qui les publient sont des critères importants utilisés pour le classement des Universités au niveau mondial.

Actuellement, l'Université catholique de Louvain est deuxième ou troisième université belge en fonction des classements («The World University Ranking», «QS Global World Ranking») et première en Communauté Wallonie-Bruxelles.
Les «ranking» classent l'UCL comme une université avec un «Very High Research Output».

Nous contribuons à ce classement par la publication de nos articles.
Il est donc important d'identifier clairement les travaux scientifiques en accord avec les règles de l'Université et celles de notre institution.
En ce qui concerne la dénomination exacte de notre institution, on utilisera désormais obligatoirement «CHU UCL Namur», sachant qu'il faut toujours privilégier l'appellation «Université catholique de Louvain» avec un petit «c» avant de faire référence au CHU UCL Namur (sans tirets intermédiaires).

Affiliation correcte:

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ERRATUM
2019

Clinical and Electrophysiological Investigation of Spastic Muscle Overactivity in Patients With Disorders of Consciousness Following Severe Brain Injury

Martens G, **Deltombe T,** Foidart-Dessalle M, Laureys S, Thibaut A.

Références	*Doi*	*IF*
Clin Neurophysiol 2019;130(2):207-213	*10.1016/j.clinph.2018.10.021*	*3.675*

Abstract

OBJECTIVE: The clinical and electrophysiological profile of spastic muscle overactivity (SMO) is poorly documented in patients with disorders of consciousness (DOC) following severe cortical and subcortical injury. We aim at investigating the link between the clinical observations of SMO and the electrophysiological spastic over-reactivity in patients with prolonged DOC.

METHODS: We prospectively enrolled adult patients with DOC at least 3 months post traumatic or non-traumatic brain injury. The spastic profile was investigated using the Modified Ashworth Scale and the Hmax/Mmax ratio. T1 MRI data and impact of medication were analyzed as well.

RESULTS: 21 patients were included (mean age: 41 ± 11 years; time since injury: 4 ± 5 years; 9 women; 10 traumatic etiologies). Eighteen patients presented signs of SMO and 11 had an increased ratio. Eight patients presented signs of SMO but no increased ratio. We did not find any significant correlation between the ratio and the MAS score for each limb (all ps › 0.05). The presence of medication was not significantly associated with a reduction in MAS scores or Hmax/Mmax ratios.

CONCLUSIONS: In this preliminary study, the Hmax/Mmax ratio does not seem to reflect the clinical MAS scores in patients with DOC. This supports the fact they do not only present spasticity but other forms of SMO and contracture.
Significance: Patients with DOC are still in need of optimized tools to evaluate their spastic profile and therapeutic approaches should be adapted accordingly.

Mots-clefs

Coma; H/M ratio; Minimally conscious state; Modified Ashworth Scale; Spasticity; Unresponsive wakefulness syndrome.

Successful Pulmonary and Aortic Embolectomies Under Tepid Circulatory Arrest: A Case Report

Kalscheuer G, Schraverus P, Belhaj A, Rondelet B.

Références	*Doi*	*IF*
Am J Gastroenterol. 2018;113(7):1099.	*10.1038/s41395-018-0118-4*	*10,231*

Abstract

Author Pierre Deltenre, MD should appear in the author list in position 25, between Felix Braun and Thomas Berg. He should also have a PhD degree added to his name.

Erratum for

Genetic variants in PNPLA3 and TM6SF2 predispose to the development of hepatocellular carcinoma in individuals with alcohol-related cirrhosis. [Am J Gastroenterol. 2018]

Mots-clefs

RECUEIL DES PUBLICATIONS SCIENTIFIQUES DU CHU UCL NAMUR

N°6 - TROISÈME QUADRIMESTRE 2019

SEPTEMBRE

The Therapeutic Alliance - Its Impact on Antidepressant Therapies in Major Depressive Conditions and on the Overall Health

Sourdeau A, **Zdanowicz N.**

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):411-419		*0.683*

Abstract

BACKGROUND: Based on our 2012 study and a review of the literature on the therapeutic alliance we asked ourselves different questions: does the alliance exert a real influence on the evolution of depressive affects, the rate of remission and the physical and global health?
SUBJECTS AND METHODS: In a two-year study, forty people with major depressive disorder are randomly assigned to groups that receive a SSRI (escitalopram) or a SNRI (duloxetine), each group receive concomitant ASA (100 mg) or a placebo. Sociodemographic data are recorded and patients under went regular assessments with the Hamilton depression scale (HDS) and Clinical Global Impression (CGI) scale, the Helping Alliance Questionnaire (HAQ) and the Short Form Health Survey (SF-12).
RESULTS: There is no significant difference in efficacy between the two antidepressants or between antidepressant treatment with and without ASA. However, subgroup comparisons reveal that the duloxetine + ASA (DASA) subgroup showed a more rapid improvement in HDS score as early as 2 months (t=-3.114, p=0.01), in CGI score at 5 months (t=-2.119, p 0.05) than the escitalopram + placebo (EP) subgroup. Regardless of the treatment arm, the remission rate at 2 years is 50%. Among patients in remission a majority, 65%, have a high level of alliance in opposition to nonresponders who have found mostly a low level of alliance ($\chi 2=6.296$, p 0.012). HAQ scores are not correlated with HAD scores, but a correlation is found with remission rates (r=0.316*). At all times, HAQ scores are correlated with physical health.
CONCLUSION: Our findings suggest that a noradrenergic agent combined with ASA is more effective in treating depression than a serotonergic agent alone. A good alliance improves effectiveness of anti-depressant treatment of 1.85 and leads to an improvement of the physical health rather than directly on the depressive feelings.

Mots-clefs

IQ Over 130 and Phobia: Correlation, Consequences and Other Psychopathologies

Lacour AG, **Zdanowicz N.**

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):386-389		*0.683*

Abstract

BACKGROUND: Nowadays, anxiety disorders are becoming more and more important in our population. And if there is one category of people more vulnerable to this problem, it is the teenagers. In addition, more and more children and teenagers are diagnosed with an IQ greater than 130, causing all the stress and questions that it generates. In this project, we are comparing two groups of adolescents, one with an IQ over 130, the other with an IQ less than 130. We are wondering if there is any difference between these groups, in terms of phobia and other psychopathologies.

SUBJECTS AND METHODS: A sample of 35 teenagers, from 12 to 16 years old, separated in two groups (IQ over 130 and IQ below 130), fulfilled the following questionnaires: the School Rehabilitation Assessment Scale-Revised (SARS-R), the «Family Adaptability and Cohesiveness Evaluation Scale III» (FACES III), and the «Kiddie- SADS-lifetime» (K-SADS-PL), and a social data collection questionnaire.

RESULTS: At the end of this study, we can retain the following relevant elements: adolescents with IQs greater than 130 are statistically more likely to be the eldest siblings (Cochran Test F=9.159, p=0.010). They do not develop more phobias, but are more shy (t=4.375, p=0.036) than the control population. These high-potential and shy teenagers have a whole list of commonalities, such as being easily irritable, being easily distracted, ect... They have fewer friends in real life (t=2.255, p=0.033), fewer virtual friends (t=4.346, p=0.000) and fewer virtual relationships (t=2.431, p=0.021). Their families are very cohesive (Test t=0.004). There is no significant role of the socio-professional class of parents playing in the value of the IQ of their children (t=4.667, p=0.323).

CONCLUSION: To conclude, being a teenager and having an IQ greater than 130 is not always a pleasure. Our results showed us that the majority of these young people consider themselves as shy, unsure of themselves and claim to have many fears. This is evidence of an increased anxiety component compared to the control sample. It seems important to insist on the need to be able and to know how to identify these young people as soon as possible, in order to propose appropriate therapeutic management.

Mots-clefs

Role of Gut Microbiota in the Interaction Between Immunity and Psychiatry: A Literature Review

Dubois T, Reynaert C, Jacques D, Lepiece B, Zdanowicz N.

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):381-385		*0.683*

Abstract

BACKGROUND: Psychiatric disorders may be correlated with a low-grade systemic inflammation but the origin of this inflammatory response remains unclear and both genetics and environmental factors seems to be concerned. Recent researches observed that gut microbiota seems to have an impact on the brain and immune processes.
METHOD: We review recent literature to a better understanding of how microbiota interacts with brain, immunity and psychiatric disorders. We search on Pubmed, PsycINFO, PsycARTICLES and Sciencedirect articles with the keywords «gastrointestinal microbiota» and «mental disorders» or «psychological stress».
RESULTS: We showed links between gut microbiota and brain-gut axis regulation, immune and endocrine system activity, neurophysiological changes, behavior variations and neuropsychiatric disorders. Communications between brain and gut are bidirectional via neural, endocrine and immune pathway. Microbiota dysbiosis and increase gut permeability with subsequent immune challenges seems to be the source of the chronic mild inflammation associated with neuropsychiatric disorders. Repeated immune or stress events early in life may lead to neurodevelopmental disorders or sickness behavior later in life.
CONCLUSIONS: Psychological stress impact gut microbiota with subsequent immune activation leading to neurodevelopmental disorders or sickness behavior and altering neurophysiology and reactivity to stress or lifestyle.

Mots-clefs

Mobius Syndrome and Obsessive Compulsive Disorder: A Case Report

Jacques D, Ossemann M, Timmermans JM, Zdanowicz N, Dubois T.

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):376-380		*0.683*

Abstract

BACKGROUND: Mobius syndrome is characterized by a bilateral congenital paralysis of the facial and abducens nerves which leaves the subject with an expressionless «mask-like» face.
SUBJECTS AND METHODS: Based on a literature review and a case discussion of an adult patient with Mobius syndrome and obsessive-compulsive disorder, initially undiagnosed and confused with a psychotic disorder, we will discuss the influence of Mobius syndrome in psychiatric evaluations.
RESULTS: The lack of facial expressiveness and non-verbal emotional interactions may influence psychiatric evaluations and result in misdiagnosis and the inappropriate prescribing of antipsychotics. In the case analysis, we also observed other associated malformations such as renal atrophy, a bicuspid aortic valve and mitral valve prolapse.
CONCLUSION: We feel that educating the patient about the communicative consequences of impaired facial expressions and facial interactions is a necessary prerequisite for any psychiatric or psychological evaluation in subjects with Mobius syndrome. We also recommend using caution when prescribing antipsychotics in patients with Mobius syndrome given the motor side effects secondary to a potentially pre-existing hypotonia.

Mots-clefs

Family Relationships and Health Locus of Control as Covariables in the Evolution of Major Depressive Disorder

Zdanowicz N, Reynaert C, Jacques D, Lepièce B, Dubois T.

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):237-241		*0.683*

Abstract

BACKGROUND: In a two-year study, we compared the efficacy of noradrenergic and serotonergic antidepressants with and without the addition of 100 mg acetylsalicylic acid (ASA) in subjects suffering from major depressive disorder (MDD). In this article we examine the influence of the health locus of control, family relationships and personality traits on the progress of MDD.

SUBJECTS AND METHODS: 40 people with MDD (MDD group) were randomly assigned to the different treatment groups. They were followed in parallel with a group of 20 'healthy' subjects (HG). At the beginning of the study, sociodemographic data were collected, and patients were asked to complete the Multidimensional Health Locus of Control (MHLC) scale, the NEO Five-Factor Inventory (NEO-FFI), and the Family Adaptation and Cohesion Scale (FACES III). During the study subjects were regularly assessed using the Hamilton Depression Scale (HDS), the Short Form Health Survey (SF-12) and the Clinical Global Impression scale (CGI).

RESULTS: Regardless of the type of treatment, physical health is the best predictor of variation at two years in the MDD group; 45% of variance is explained by a linear regression model that includes three variables from the MHLC, FACES III and NEO-FFI scales. Similarly, 40% of CGI and 24% of HDS variance is predicted. These explanatory variables are statistically less powerful in the MDD group than the HG group.

CONCLUSION: While drug treatment is a determinant in changes on the HDS, CGI and SF12 scales, factors such as family relationships, MHLC or personality are important covariates of these changes. The question remains whether we can influence these covariates to improve the response to antidepressants.

Mots-clefs

Adolescents in Transition to Young Adulthood: Evolution of Mental Health Status and Risk Factors Associated With Depressive and Anxiety Disorder

Lepiège B, Zdanowicz N, de Becker E, de Timary P, Lorant V.

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):371-375		*0.683*

Abstract

BACKGROUND: In this paper we focus on adolescents in transition towards young adulthood (ATYA). We know from international studies that the transition process makes adolescents vulnerable to mental illness. However, little is known about Belgian ATYA mental-health status. Nor are risk factors associated with their mental illness understood, in particular with regard to depressive and anxiety disorder. The aim of this study is (1) to discuss evolution in time of prevalence of depressive disorder (DD) and anxiety disorder (AD) among Belgian ATYA and (2), to identify risk factors associated with these disorders among ATYA.

SUBJECTS AND METHODS: Data was extracted from the Belgian Health Interview Survey (BHIS), which is a cross-sectional population survey, carried out in 2001, 2004, 2008, and 2013. Information about the population's background characteristics, health services utilization, health behaviours and mental health status were extracted and statistically analyzed.

RESULTS: ATYA prevalence of DD and AD was higher in 2013 in comparison with previous years. These changes were significant only for DD (F=4.466, p=0.004). In contrast with younger adolescents, among ATYA odds of DD were 28.2% higher (OR 1.282, 95% CI 0.967-1.698, p=0.084) and, odds of AD were 55.2% higher (OR 1.552, 95% CI 1.137-2.119, p=0.006). For ATYA, a poor quality of social support was the most predictive factor of DD (OR 11.187, 95% CI 5.530-22.629, p<0.0001) and AD (OR 6.238, 95% CI 2.845-13.676, p<0.0001); whereas, having a paid job was the most protective factor with regard to DD (OR 0.282, 95% CI 0.169-0.470, p<0.0001) and AD (OR 0.552, 95% CI 0.330-0.924, p<0.024).

CONCLUSION: Prevalence of mental illness among Belgian ATYA appears to worsen in time. In comparison with younger adolescents, ATYA are more vulnerable to anxiety disorders. Adverse and protective risk factors were identified and discussed in a way to improve access, continuity and mental healthcare pathways for Belgian ATYA.

Mots-clefs

Cannabinoid Hyperemesis Syndrome: A Review of the Literature

Deceuninck E, Jacques D.

Références	*Doi*	*IF*
Psychiatr Danub 2019;31(suppl 3):390-394		*0.683*

Abstract

BACKGROUND: Cannabinoid Hyperemesis Syndrome (CHS) is characterized by cyclic vomiting and compulsive need to take hot showers in the context of chronic cannabis use. Physicians' lack of knowledge of CHS often results in a diagnostic delay of several years. The purpose of this article is to describe CHS in order to enable physicians, and more particularly psychiatrists, to diagnose it as quickly as possible and thus avoid unnecessary additional invasive examinations.

SUBJECTS AND METHODS: Bibliographic search for scientific articles published between 2004 and 2019 in the Cochrane, Medline, PubMed, and Psycinfo databases. Key words used were «hyperemesis», «cannabis», «cannabinoid».

RESULTS: CHS is associated with chronic cannabis use and typically manifests as incoercible cyclical vomiting, diffuse abdominal pain, and relief of symptoms by taking hot showers. Patients suffering from CHS generally visit emergency departments very regularly and undergo numerous additional examinations, both invasive and unnecessary. Since no organic cause can explain these symptoms, these patients are referred to the psychiatry department. The only curative treatment is the complete cessation of cannabis use.

CONCLUSION: CHS is an under-diagnosed pathology because it is little known to physicians. This syndrome has unique clinical characteristics. Early recognition of CHS avoids repeated visits to the emergency room and unnecessary follow-up examinations.

Mots-clefs

Prevalence and Risk Factors of Postprandial Hypotension Among Elderly People Admitted in a Geriatric Evaluation and Management Unit : An Observational Study

Schoevaerdts D, Iacovelli M, Toussaint E, Sibille FX, de Saint-Hubert M, Cremer G.

Références	*Doi*	*IF*
Nutr Health Aging 2019;23(10):1026-1033	*10.1007/s12603-019-1271-1*	*2.868*

Abstract

OBJECTIVES: To explore the prevalence and potential risk factors of postprandial hypotension (PPH) among elderly patients in an acute geriatric ward.
DESIGN: A prospective observational study.
SETTING: Geriatric Unit in a Belgian tertiary-care University Hospital.
Participants: Seventy-six hospitalized elderly patients after stabilization of their acute conditions.
MEASUREMENTS: PPH and orthostatic hypotension (OH) measured by a non-invasive automated blood pressure device, demographic data, Katz's Basic Activities of Daily Living (ADL) and Lawton's instrumental ADL, Short Physical Performance Battery, Charlson Comorbidity Index, Mini Nutritional Assessment-Short Form, Timed Up and Go test, Get-up Early test, grip strength and 7 classes of drugs.
RESULTS: Overall, the prevalence of PPH was 46% (n=35/76), and it was symptomatic in 31% of the patients (n=11/35). PPH is associated with OH in one-third of the cases (n=12/35). Two-thirds of the patients with HPP had a significant drop in systolic blood pressure within the first 75 minutes after a meal. In univariate analyses, risk factors of PPH were nursing home residence, alpha-blocker consumption, help needed for eating and a good level of global functional status. However, patients with a good functional status were at increased risk of alpha-blocker exposure. In multivariate analyses, only alpha-blocker consumption and help needed for eating remained statistically significant.
CONCLUSION: PPH is frequent among hospitalized elderly people in a Geriatric Evaluation and Management Unit, affecting nearly one out of two people. The use of alpha-blockers is an important risk factor and may alert clinicians to the risk of PPH.

Mots-clefs

Postprandial hypotension; elderly; epidemiology; orthostatic hypotension; risk factors

Next-generation ARIA Care Pathways for Rhinitis and Asthma: A Model for Multimorbid Chronic Diseases

Bousquet JJ, **Vandenplas O**, at al.

Références	*Doi*	*IF*
Clin Transl Allergy 2019;9(44):eCollection	*10.1186/s13601-019-0279-2*	*3.539*

Abstract

BACKGROUND: In all societies, the burden and cost of allergic and chronic respiratory diseases are increasing rapidly. Most economies are struggling to deliver modern health care effectively. There is a need to support the transformation of the health care system into integrated care with organizational health literacy.

MAIN BODY: As an example for chronic disease care, MASK (Mobile Airways Sentinel NetworK), a new project of the ARIA (Allergic Rhinitis and its Impact on Asthma) initiative, and POLLAR (Impact of Air POLLution on Asthma and Rhinitis, EIT Health), in collaboration with professional and patient organizations in the field of allergy and airway diseases, are proposing real-life ICPs centred around the patient with rhinitis, and using mHealth to monitor environmental exposure. Three aspects of care pathways are being developed: (i) Patient participation, health literacy and self-care through technology-assisted «patient activation», (ii) Implementation of care pathways by pharmacists and (iii) Next-generation guidelines assessing the recommendations of GRADE guidelines in rhinitis and asthma using real-world evidence (RWE) obtained through mobile technology. The EU and global political agendas are of great importance in supporting the digital transformation of health and care, and MASK has been recognized by DG Santé as a Good Practice in the field of digitally-enabled, integrated, person-centred care.

CONCLUSION: In 20 years, ARIA has considerably evolved from the first multimorbidity guideline in respiratory diseases to the digital transformation of health and care with a strong political involvement.

Mots-clefs

ARIA; Care pathways; Health care transformation; MASK; POLLAR; Rhinitis.

Long-term Physiochemical Stability of Concentrated Solutions of Salbutamol (Albuterol) in Polypropylene Syringes for Use in the Intensive Care Unit and in Obstetrics

Lardinois B, Baltzis A, Delcave C, Soumoy L, Jamart J, Bihin B, Hecq JD, Galanti L.

Références	*Doi*	*IF*
Int J Pharm Compd 2019;23(5):434-437		*0.07*

Abstract

In order to avoid fluid overload, the use of more concentrated drug solutions in intensive care units and obstetrics is common. The objective of this study was to quantify the physicochemical stability of a concentrated solution of salbutamol (albuterol) in polypropylene syringes during 30 days of storage at 5°C ± 3°C with protection from light. Four 50-mL syringes containing 0.060mg/mL of salbutamol (albuterol) in 0.9% NaCl were prepared and stored at 5°C ± 3°C with protection from light during 30 days of storage. Immediately after preparation and periodically during the storage, salbutamol (albuterol) concentrations were measured by an ultra-performance liquid chromatography. Spectrophotometric absorbance at different wavelengths, pH measurement, and microscopic observations were also performed. All solutions were physicochemically stable during the entire period of storage at 5°C ± 3°C: no color change, turbidity, precipitation or opacity, significant pH variations, or optic densities were observed in the solutions. No crystals were seen by microscopic analysis. Concentrations of salbutamol remained stable during the storage period. Solutions of salbutamol (albuterol) 0.060 mg/mL in syringes of 0.9% NaCl are physically and chemically stable for at least 30 days when stored in syringes at 5°C ± 3°C with protection from light and may be prepared in advance by a centralized intravenous additive service.

Mots-clefs

Development of a Process-Oriented Quality Improvement Strategy for the Medicines Pathway in Nursing Homes Using the SEIPS Model

Strauven G, Vanhaecht K, Anrys P, De Lapeleire J, **Spinewine A**, Foulon V.

Références	*Doi*	*IF*
Res Social Adm Pharm 2019; [Online ahead of print]	*10.1016/j.sapharm.2019.06.003*	*2.719*

Abstract

BACKGROUND AND OBJECTIVE: Medication errors in nursing homes are highly prevalent and occur in different stages of the medicines pathway. The application of the SEIPS (System Engineering Initiative for Patient Safety) model facilitates the identification of work system factors that contribute to errors. Therefore, the aim of our research was to investigate in-depth the medicines pathway in nursing homes by using the SEIPS model and to develop a set of key activities and aggregated key interventions to be used as a basis for quality-improvement strategies.
METHODS: A variety of qualitative methods, including observations, semi-structured interviews, the development of a flowchart, an expert meeting and a working symposium, were used to identify processes and work system components. Key interventions and activities were developed in three rounds (one development and two validation rounds) across the different research methods to fine-tune the defined key interventions and activities.
RESULTS: Our analysis revealed a large variety of tasks as well as persons elements, aspects related to technology and tools, organisational factors and environmental elements that all interact and influence the medicines pathway. The large number of tasks could be linked to eight overarching processes: prescribing, purchase and ordering, delivery, storage, preparation, administration, monitoring and (re-)admission. After three rounds (one development and two validation rounds), a final set of 137 key activities and 27 aggregated key interventions, concretising the eight processes, was obtained.
CONCLUSION: The in-depth analysis of processes within the medicines pathway in nursing homes resulted in a set of key activities and aggregated key interventions which may serve as a basis for the nursing home sector and policy makers to enhance a safe and efficient medicines pathway.

Mots-clefs
Key interventions; Medicines pathway; Nursing homes; Quality; SEIPS model; Safety.

Extra-axonal Restricted Diffusion as an In-Vivo Marker of Reactive Microglia

Taquet M, **Jankovski A,** Rensonnet G, Jacobs D, des Rieux A, Macq B, Warfield S, Scherrer B.

Références	*Doi*	*IF*
Sci Rep 2019;9(1):13874	*10.1038/s41598-019-50432-5*	*4.011*

Abstract

Reactive microgliosis is an important pathological component of neuroinflammation and has been implicated in a wide range of brain diseases including brain tumors, multiple sclerosis, Parkinson's disease, Alzheimer's disease, and schizophrenia. Mapping reactive microglia in-vivo is often performed with PET scanning whose resolution, cost, and availability prevent its widespread use. The advent of diffusion compartment imaging (DCI) to probe tissue microstructure in vivo holds promise to map reactive microglia using MRI scanners. But this potential has never been demonstrated. In this paper, we performed longitudinal DCI in rats that underwent dorsal root axotomy triggering Wallerian degeneration of axons-a pathological process which reliably activates microglia. After the last DCI at 51 days, rats were sacrificed and histology with Iba-1 immunostaining for microglia was performed. The fraction of extra-axonal restricted diffusion from DCI was found to follow the expected temporal dynamics of reactive microgliosis. Furthermore, a strong and significant correlation between this parameter and histological measurement of microglial density was observed. These findings strongly suggest that extra-axonal restricted diffusion is an in-vivo marker of reactive microglia. They pave the way for MRI-based microglial mapping which may be important to characterize the pathogenesis of neurological and psychiatric diseases.

Mots-clefs

A Recurrent and Transesophageal Echocardiography-Associated Outbreak of Extended-Spectrum β-Lactamase-Producing Enterobacter cloacae Complex in Cardiac Surgery Patients

Van Maerken T, De Brabandere E, **Noel A**, Coorevits L, De Waegemaeker P, Ablorh R, Bouchez S, Herck I, Peperstraete H, Bogaerts P, Verhasselt B, Glupczynski Y, Boelens J, Leroux-Roels I.

Références	*Doi*	*IF*
Antimicrob Resist Infect Control 2019;8(152):eCollection	*10.1186/s13756-019-0605-4*	*1.96*

Abstract

BACKGROUND: We report a recurrent outbreak of postoperative infections with extended-spectrum β-lactamase (ESBL)-producing E. cloacae complex in cardiac surgery patients, describe the outbreak investigation and highlight the infection control measures.
METHODS: Cases were defined as cardiac surgery patients in Ghent University Hospital who were not known preoperatively to carry ESBL-producing E. cloacae complex and who postoperatively had a positive culture for this multiresistant organism between May 2017 and January 2018. An epidemiological investigation, including a case-control study, and environmental investigation were conducted to identify the source of the outbreak. Clonal relatedness of ESBL-producing E. cloacae complex isolates collected from case patients was assessed using whole-genome sequencing-based studies.
RESULTS: Three separate outbreak episodes occurred over the course of 9 months. A total of 8, 4 and 6 patients met the case definition, respectively. All but one patients developed a clinical infection with ESBL-producing E. cloacae complex, most typically postoperative pneumonia. Overall mortality was 22% (4/18). Environmental cultures were negative, but epidemiological investigation pointed to transesophageal echocardiography (TEE) as the outbreak source. Of note, four TEE probes showed a similar pattern of damage, which very likely impeded adequate disinfection. The first and second outbreak episode were caused by the same clone, whereas a different strain was responsible for the third episode.
CONCLUSIONS: Health professionals caring for cardiac surgery patients and infection control specialists should be aware of TEE as possible infection source. Caution must be exercised to prevent and detect damage of TEE probes.

Mots-clefs

Cardiac surgery; Enterobacter cloacae complex; Extended-spectrum β-lactamase; Outbreak; Transesophageal echocardiography

Are Biosimilars the Future of Oncology and Haematology?

Zinzani PL, Dreyling M, Gradishar W, **André M**, Esteva FJ, Boulos S, Gonzalez Barca E, µCu-rigliano G.

Références	*Doi*	*IF*
Drugs 2019;79(15):1609-1624	*10.1007/s40265-019-01193-y*	*4.993*

Abstract

Biological drugs are vital but often high-cost components of cancer treatment. Several biosimilar versions of these drugs have been approved in Europe and/or the USA, with many more in development. However, there is some disconnect between the biosimilars that are approved for use and those accessible in clinical practice, with availability impacted by factors including patent litigation and complex healthcare insurance policies, particularly in the USA. Provided the barriers to widespread uptake can be overcome, biosimilars offer potential benefits including cost savings and improved patient access versus the reference product (RP). This article provides an up-to-date and focused perspective on the development and use of biosimilars in the haemato-oncology setting. European and US regulatory pathways governing biosimilar licensing demand that there are no clinically meaningful differences between a biosimilar and its RP. Pathways are rigorously enforced and involve comprehensive non-clinical evaluations and clinical trials in selected indications to establish the equivalence or non-inferiority of efficacy, and the comparability of safety, of the biosimilar versus its RP. 'Indication extrapolation' is only permitted if scientifically justifiable considering mechanism(s) of action, pharmacokinetics, immunogenicity and safety in relevant patient populations. Switching treatment from RP to biosimilar is supported by most available data, predominantly from indications other than cancer, and post-marketing pharmacovigilance programmes are warranted. Notably, the potential benefits of biosimilar cancer treatment may extend beyond direct cost savings: for example, the availability of biosimilars of common regimen components may help incentivise the evaluation and/or clinical use of new treatment approaches and novel drugs.

Mots-clefs

Gene signature-MELD Score and Alcohol Relapse Determine Long-Term Prognosis of Patients With Severe Alcoholic Hepatitis

Deltenre P, Trepo E, Fujiwara N, Goossens N, **Marot A,** Dubois M, Spahr L, Henrion J, Moreno C, Hosgida Y

Références	*Doi*	*IF*
Liver Int 2019; [Online ahead of print]	*10.1111/liv.14265*	*5.542*

Abstract

Biological drugs are vital but often high-cost components of cancer treatment. Several biosimilar versions of these drugs have been approved in Europe and/or the USA, with many more in development. However, there is some disconnect between the biosimilars that are approved for use and those accessible in clinical practice, with availability impacted by factors including patent litigation and complex healthcare insurance policies, particularly in the USA. Provided the barriers to widespread uptake can be overcome, biosimilars offer potential benefits including cost savings and improved patient access versus the reference product (RP). This article provides an up-to-date and focused perspective on the development and use of biosimilars in the haemato-oncology setting. European and US regulatory pathways governing biosimilar licensing demand that there are no clinically meaningful differences between a biosimilar and its RP. Pathways are rigorously enforced and involve comprehensive non-clinical evaluations and clinical trials in selected indications to establish the equivalence or non-inferiority of efficacy, and the comparability of safety, of the biosimilar versus its RP. 'Indication extrapolation' is only permitted if scientifically justifiable considering mechanism(s) of action, pharmacokinetics, immunogenicity and safety in relevant patient populations. Switching treatment from RP to biosimilar is supported by most available data, predominantly from indications other than cancer, and post-marketing pharmacovigilance programmes are warranted. Notably, the potential benefits of biosimilar cancer treatment may extend beyond direct cost savings: for example, the availability of biosimilars of common regimen components may help incentivise the evaluation and/or clinical use of new treatment approaches and novel drugs.

Mots-clefs

L'Hôpital de jour gériatrique : une interface ambulatoire au service des personnes âgées

Schoevaerdts D, Dumont C, Hanotier P, Fournier A, Piette D, Almpanis C, Detraux F, Sentrie M, **Sibille FX,** Cornette P.

Références	*Doi*	*IF*
Louvain Médical 2019;138(7):417-422		*0.010*

Abstract

L'hôpital de jour gériatrique est une structure ambulatoire qui propose une prise en charge diagnostique et thérapeutique aux personnes âgées en tant qu'alternative aux hospitalisations classiques. Cet article a pour but de mieux faire connaître la structure aux cliniciens de terrain. Il en décrit l'historique dans le monde et en Belgique, y commente les résultats d'une méta-analyse et d'enquêtes nationales réalisées depuis 2007, date de parution du Programme de Soins pour le Patient Gériatrique. Comparés aux données publiées,les hôpitaux de jours gériatriques belges proposent une approche plutôt à orientation diagnostique alors que certains développent la revalidation. Ils offrent, à l'aide d'une équipe multidisciplinaire, une évaluation gériatrique globale des syndromes gériatriques (déclin fonctionnel,fragilité,chutes, troubles de la mémoire, malnutrition,...) en étroite collaboration avec la première ligne et le réseau de soins. L'évaluation gériatrique standardisée a prouvé des bénéfices significatifs lors d'une hospitalisation conventionnelle qui malheureusement comporte toutefois des risques (déclin fonctionnel, chutes, confusion aiguë, iatrogénie et infections nosocomiales). L'hôpital de jour gériatrique propose donc un accès à un plateau spécifique (examens techniques et avis spécialisés) associé à une évaluation gériatrique standardisée en vue d'élaborer un plan de soin en soutien au travail de première ligne tout en évitant une hospitalisation classique.

Mots-clefs

Is Antiretroviral Two-Drug Regimen the New Standard for HIV Treatment in Naive Patients?

Dupont E, Yombi JC.

Références	*Doi*	*IF*
AIDS Rev. 2019;21(3):143-156	*10.24875/AIDSRev.19000061.*	*1.13*

Abstract

The use of a combination antiretroviral therapy (cART) has changed dramatically the prognosis and the life expectancy of people living with HIV. The current treatment guidelines continue the convention of preferred cART based on combining a dual nucleoside reverse-transcriptase inhibitor (NRTI) backbone with a third «anchor» agent, such as a ritonavir (r)- or cobicistat (c)-boosted protease inhibitor (PI), a non-NRTI (NNRTI), or an integrase inhibitor (INI) boosted or unboosted. However, due to toxicities of NRTIs, sparing NRTI regimen has been studied for a long time with moderate success due to low efficacy (especially in patients with high viral load and low CD4) compare to standard triple therapy. New strategy with lamivudine (3TC) plus a boosted PI or INI showed promise results and indicated that modern two-drug regimens might now, in fact, become a reliable treatment for HIV-infected naïve patients. This article discusses recent data from dual therapy studies in naïve HIV-infected patients and the challenges behind this strategy.

Mots-clefs

3TC; Antiretroviral therapy; Dual therapy; Integrase inhibitor; Naïve human immunodeficiency virus-infected patients; Protease inhibitor

Interobserver variability in upfront dichotomous histopathological assessment of ductal carcinoma in situ of the breast: the DCISion study.

Dano H, Altinay S, Arnould L, Bletard N, Colpaert C, Dedeurwaerdere F, Dessauvagie B, Duwel V, Floris G, Fox S, Gerosa C, Jaffer S, Kurpershoek E, Lacroix-Triki M, Laka A, Lambein K, MacGrogan GM, Marchió C, Martinez DM, Nofech-Mozes S, Peeters D, Ravarino A, Reisenbichler E, Resetkova E, Sanati S, Schelfhout AM, Schelfhout V, Shaaban AM, Sinke R, **Stanciu-Pop CM**, Stobbe C, van Deurzen CHM, Van de Vijver K, Van Rompuy AS, Verschuere S, Vincent-Salomon A, Wen H, Bouzin C, Galant C, Van Bockstal MR.

Références	*Doi*	*IF*
Mod Pathol. 2019 Sep 18 [Epub ahead of print]	*10.1038/s41379-019-0367-9*	*6.365*

Abstract

Histopathological assessment of ductal carcinoma in situ, a nonobligate precursor of invasive breast cancer, is characterized by considerable interobserver variability. Previously, post hoc dichotomization of multicategorical variables was used to determine the «ideal» cutoffs for dichotomous assessment. The present international multicenter study evaluated interobserver variability among 39 pathologists who performed upfront dichotomous evaluation of 149 consecutive ductal carcinomas in situ. All pathologists independently assessed nuclear atypia, necrosis, solid ductal carcinoma in situ architecture, calcifications, stromal architecture, and lobular cancerization in one digital slide per lesion. Stromal inflammation was assessed semiquantitatively. Tumor-infiltrating lymphocytes were quantified as percentages and dichotomously assessed with a cutoff at 50%. Krippendorff's alpha (KA), Cohen's kappa and intraclass correlation coefficient were calculated for the appropriate variables. Lobular cancerization (KA = 0.396), nuclear atypia (KA = 0.422), and stromal architecture (KA = 0.450) showed the highest interobserver variability. Stromal inflammation (KA = 0.564), dichotomously assessed tumor-infiltrating lymphocytes (KA = 0.520), and comedonecrosis (KA = 0.539) showed slightly lower interobserver disagreement. Solid ductal carcinoma in situ architecture (KA = 0.602) and calcifications (KA = 0.676) presented with the lowest interobserver variability. Semiquantitative assessment of stromal inflammation resulted in a slightly higher interobserver concordance than upfront dichotomous tumor-infiltrating lymphocytes assessment (KA = 0.564 versus KA = 0.520). High stromal inflammation corresponded best with dichotomously assessed tumor-infiltrating lymphocytes when the cutoff was set at 10% (kappa = 0.881). Nevertheless, a post hoc tumor-infiltrating lymphocytes cutoff set at 20% resulted in the highest interobserver agreement (KA = 0.669). Despite upfront dichotomous evaluation, the interobserver variability remains considerable and is at most acceptable, although it varies among the different histopathological features. Future studies should investigate its impact on ductal carcinoma in situ prognostication. Forthcoming machine learning algorithms may be useful to tackle this substantial diagnostic challenge.

Mots-clefs

A Step Toward a Patient-Tailored Therapy in TAVR.

Ibrahim R, **Simon F**.

Références	*Doi*	*IF*
JACC Cardiovasc Interv. 2019 Sep 23;12(18):1794-1795.	*10.1016/j.jcin.2019.06.033.*	*9.544*

Abstract

Mots-clefs
TAVR; pacemaker; right bundle branch block (RBBB)

Low level CpG island promoter methylation predicts a poor outcome in adult T-cell acute lymphoblastic leukemia.

Touzart A, Boissel N, Belhocine M, Smith C, **Graux C**, Latiri M, Lhermitte L, Mathieu E, Huguet F, Lamant L, Ferrier P, Ifrah N, Macintyre E, Dombret H, Asnafi V, Spicuglia S.

Références	*Doi*	*IF*
Haematologica. 2019 Sep [Epub ahead of print]	*10.3324/haematol.2019.223677*	*7.570*

Abstract

Cancer cells undergo massive alterations in their DNA methylation patterns which result in aberrant gene expression and malignant phenotypes. Abnormal DNA methylation is a prognostic marker in several malignancies, but its potential prognostic significance in adult T-cell acute lymphoblastic leukemia is poorly defined. Here, we performed methylated DNA immunoprecipitation to obtain a comprehensive genome-wide analysis of promoter methylation in adult T-cell Acute Lymphoblastic Leukemia (n=24) compared to normal thymi (n=3). We identified a CpG hypermethylator phenotype that distinguishes two T-cell acute lymphoblastic leukemia subgroups and further validate it in an independent series of 17 T-Lymphoblastic Lymphoma. Next, we identified a methylation classifier based on 9 promoters which accurately predict the methylation phenotype. This classifier was applied to an independent series of 168 primary adult T-cell Acute Lymphoblastic Leukemias treated accordingly to the GRAALL03/05 trial using methylation-specific multiplex ligation-dependent probe amplification. Importantly hypomethylation correlated with specific oncogenic subtypes of T-cell Acute Lymphoblastic Leukemias and identified patients associated with a poor clinical outcome. This methylation-specific multiplex ligation-dependent probe amplification based methylation profiling could be useful for therapeutic stratification of adult T-cell Acute Lymphoblastic Leukemias in routine practice. The GRAALL-2003 and -2005 studies were registered at http://www.clinicaltrials.gov as #NCT00222027 and #NCT00327678, respectively.

Mots-clefs

Adult Acute Lymphoblastic Leukemia; Cytogenetics and Molecular Genetics; methylation

Biomarkers of extracellular matrix turnover in patients with idiopathic pulmonary fibrosis given nintedanib (INMARK study): a randomised, placebo-controlled study

Maher TM, Stowasser S, Nishioka Y, White ES, Cottin V, Noth I, Selman M, Rohr KB, Michael A, Ittrich C, Diefenbach C, Jenkins RG; INMARK trial investigators
(**Dahlqvist C**, Investigator)

Références	*Doi*	*IF*
Lancet Respir Med. 2019 Sep;7(9):771-779	*10.1016/S2213-2600(19)30255-3*	*22.992*

Abstract

BACKGROUND:cA hallmark of idiopathic pulmonary fibrosis is the excess accumulation of extracellular matrix in the lungs. Degradation of extracellular matrix generates free-circulating protein fragments called neoepitopes. The aim of the INMARK trial was to investigate changes in neoepitopes as predictors of disease progression in patients with idiopathic pulmonary fibrosis and the effect of nintedanib on these biomarkers.
METHODS: In this randomised, double-blind, placebo-controlled trial, patients with a diagnosis of idiopathic pulmonary fibrosis within the past 3 years and forced vital capacity (FVC) of 80% predicted or higher were eligible to participate. Patients were recruited from hospitals, private practices, clinical research units, and academic medical centres. Patients were randomly assigned (1:2) with the use of a pseudo-random number generator to receive oral nintedanib 150 mg twice a day or placebo for 12 weeks in a double-blind fashion, followed by open-label nintedanib for 40 weeks. The primary endpoint was the rate of change in C-reactive protein (CRP) degraded by matrix metalloproteinases 1 and 8 (CRPM) from baseline to week 12 in the intention-to-treat population. The trial has been completed and is registered with ClinicalTrials.gov, number NCT02788474, and with the European Clinical Trials Database, number 2015-003148-38.
FINDINGS: Between June 27, 2016, and May 15, 2017, 347 patients were randomly assigned to the nintedanib group (n=116) or to the placebo group (n=231). One patient from the placebo group was not treated owing to a randomisation error. At baseline, mean FVC was 97•5% (SD 13•5) predicted. In the double-blind period, 116 patients received nintedanib and 230 patients received placebo. The rate of change in CRPM from baseline to week 12 was -2•57 × 10-3 ng/mL/month in the nintedanib group and -1•90 × 10-3 ng/mL/month in the placebo group (between-group difference -0•66 × 10-3 ng/mL/month [95% CI -6•21 × 10-3 to 4•88 × 10-3]; p=0•8146). The adjusted rate of change in FVC over 12 weeks was 5•9 mL in the nintedanib group and -70•2 mL in the placebo group (difference 76•1 mL/12 weeks [31•7 to 120•4]). In patients who received placebo for 12 weeks followed by open-label nintedanib, rising concentrations of CRPM over 12 weeks were associated with disease progression (absolute decline in FVC ≥10% predicted or death) over 52 weeks. In the double-blind period, serious adverse events were reported in eight (7%) patients given nintedanib and 18 (8%) patients given placebo. Grade 3 diarrhoea was reported in two (2%) patients in the nintedanib group and two (1%) patients in the placebo group. No patients had grade 4 diarrhoea.
INTERPRETATION: In patients with idiopathic pulmonary fibrosis and preserved lung function, treatment with nintedanib versus placebo for 12 weeks did not affect the rate of change in CRPM but was associated with a reduced rate of decline in FVC. These results suggest that change in CRPM is not a marker of response to nintedanib in patients with idiopathic pulmonary fibrosis.
FUNDING: Boehringer Ingelheim.

Mots-clefs

OCTOBRE

Fibromyalgia syndrome-A Laser-Evoked Potentials Study Unsupportive of Small Nerve Fibre Involvement

Van Assche D, Plaghki L, **Masquelier E**, Hatem S.

Références	*Doi*	*IF*
Eur J Pain 2019; [Online ahead of print]	*10.1002/ejp.1501*	*3.188*

Abstract

BACKGROUND: Fibromyalgia syndrome (FMS) is a chronic pain syndrome characterized by widespread pain and a variety of non-pain symptoms. Central sensitivity phenomena are found consistently in FMS. Additionally, several researchers proclaimed that a subgroup of FMS patients may present with unrecognized peripheral small fibre neuropathy (SFN). Laser-evoked brain potentials (LEP) are considered as a reliable method for the functional assessment of the thermo-nociceptive system, including the evaluation of SFN.
OBJECTIVES: The aim of this retrospective study was to estimate the prevalence of thermo-nociceptive system dysfunction based on LEPs in FMS.
METHODS: LEP recordings of 92 FMS patients and 39 age and gender-matched healthy controls were selected from a database collected between 2003 and 2012 with standardized settings for laser stimulation and EEG recording. The N1, N2 and P2 LEP components were identified and characterized by peak latency and amplitude.
RESULTS: None of the FMS patients showed signs of loss of function of the nociceptive responses evoked by A δ-nociceptor activation, compared to healthy controls. 6.5% of the FMS patients had N2-P2 peak-to-peak amplitudes above the upper limit of the 99%-confidence interval. N2-P2 peak-to-peak amplitudes were negatively correlated with age, without age-related differences between groups.
CONCLUSIONS: The characteristic signs of a damaged thermo-nociceptive system as revealed by LEPs were absent in this large cohort of FMS patients.
SIGNIFICANCE: The present research does not support the hypothesis that small fibre neuropathy is a significant contributor to the pathophysiology of FMS.

Mots-clefs

Systematic Review With Meta-Analysis: Automated Low-Flow Ascites Pump Therapy for Refractory Ascites

Lepida A, **Marot A**, Trépo E, Degré D, Moreno C, Deltenre P.

Références	*Doi*	*IF*
Aliment Pharmacol Ther 2019;50(9):978-987	*10.1111/apt.15502*	*3.40*

Abstract

BACKGROUND: Few effective treatments are available for patients with cirrhosis and refractory ascites. New treatment modalities are needed for these patients.
AIM: To synthesise the available evidence on the efficacy and safety of automated low-flow ascites pump therapy in patients with cirrhosis and refractory ascites.
Methods: Electronic databases were searched for trials evaluating automated low-flow ascites pump therapy in patients with refractory ascites.
RESULTS: Nine studies were included. Eight were case series, one was a randomised controlled trial. Pooled estimate rates were 0.62 (95% CI = 0.49-0.74) for the absence of requirement of large volume paracentesis (LVP) after pump insertion, 0.30 (95% CI = 0.17-0.47) for acute kidney injury, 0.27 (95% CI = 0.13-0.49) for bacterial peritonitis and 0.20 (95% CI = 0.09-0.37) for urinary tract infection. There was high heterogeneity between studies which was often reduced or eliminated in sensitivity analyses by excluding studies of patients with a mean or median model for end-stage liver disease (MELD) score › 15. Results of sensitivity analyses were similar to those of overall analyses. Mean increase in serum creatinine level after pump insertion was 23 µmol/L (95% CI = 10-35) with no heterogeneity between studies. The pooled estimate rate for pump-related side effects was 0.77 (95% CI = 0.64-0.87) with low heterogeneity between studies.
CONCLUSION: This meta-analysis demonstrates that most patients treated with automated low-flow ascites pump therapy do not require LVP after pump insertion. Acute kidney injury occurs in 30% of patients and creatinine levels increase by a mean of 23 µmol/L after pump insertion. Bacterial peritonitis and urinary tract infection occur in 27% and 20% of patients respectively.

Mots-clefs

Optimization of the MALDIxin Test for the Rapid Identification of Colistin Resistance in Klebsiella Pneumoniae Using MALDI-TOF MS

Dortet L, Broda A, Bernabeu S, **Glupczynski Y**, **Bogaerts P**, Bonnin R, Naas T, Filloux A, Larrouy-Maumus G.

Références	*Doi*	*IF*
J Antimicrob Chemother 2019;75(1):110-116	*10.1093/jac/dkz405*	*5.113*

Abstract

BACKGROUND: With the dissemination of carbapenemase producers, a revival of colistin was observed for the treatment of infections caused by MDR Gram-negatives. Unfortunately, the increasing usage of colistin led to the emergence of resistance. In Klebsiella pneumoniae, colistin resistance arises through addition of 4-amino-l-arabinose (l-Ara4N) or phosphoethanolamine (pEtN) to the native lipid A. The underlying mechanisms involve numerous chromosome-encoded genes or the plasmid-encoded pEtN transferase MCR. Currently, detection of colistin resistance is time-consuming since it still relies on MIC determination by broth microdilution. Recently, a rapid diagnostic test based on MALDI-TOF MS detection of modified lipid A was developed (the MALDIxin test) and tested on Escherichia coli and Acinetobacter baumannii.

OBJECTIVES: Optimize the MALDIxin test for the rapid detection of colistin resistance in K. pneumoniae.

METHODS: This optimization consists of an additional mild-acid hydrolysis of 15 min in 1% acetic acid. The optimized method was tested on a collection of 81 clinical K. pneumoniae isolates, including 49 colistin-resistant isolates (45 with chromosome-encoded resistance, 3 with MCR-related resistance and 1 with both mechanisms).

RESULTS: The optimized method allowed the rapid (<30 min) identification of l-Ara4N- and pEtN-modified lipid A of K. pneumoniae, which are known to be the real triggers of polymyxin resistance. At the same time, it discriminates between chromosome-encoded and MCR-related polymyxin resistance.

CONCLUSIONS: The MALDIxin test has the potential to become an accurate tool for the rapid determination of colistin resistance in clinically relevant Gram-negative bacteria.

Mots-clefs

Effect of Selepressin vs Placebo on Ventilator- And Vasopressor-Free Days in Patients With Septic Shock: The SEPSIS-ACT Randomized Clinical Trial

Laterre PF, Berry SM, Blemings A, Carlsen JE, François B, Graves T, Jacobsen K, Lewis RJ, Opal SM, Perner A, Pickkers P, Russell JA, Windeløv NA, Yealy DM, Asfar P, Bestle MH, Muller G, Bruel C, Brulé N, Decruyenaere J, **Dive A**, Dugernier T, Krell K, Lefrant JY, Megarbane B, Mercier E, Mira JP, Quenot JP, Steen Rasmussen B, Thorsen-Meyer HC, Vander Laenen M, Lauridsen Vang M, Vignon P, Vinatier I, Wichmann S, Wittebole X, Kjølbye AL, Angus DC, SEPSIS-ACT Investigators

Références	*Doi*	*IF*
JAMA 2019;322(15):1476-1485	*10.1001/jama.2019.14607*	*51.273*

Abstract

Importance: Norepinephrine, the first-line vasopressor for septic shock, is not always effective and has important catecholaminergic adverse effects. Selepressin, a selective vasopressin V1a receptor agonist, is a noncatecholaminergic vasopressor that may mitigate sepsis-induced vasodilatation, vascular leakage, and edema, with fewer adverse effects.

Objective: To test whether selepressin improves outcome in septic shock.

Design, setting, and participants: An adaptive phase 2b/3 randomized clinical trial comprising 2 parts that included adult patients (n = 868) with septic shock requiring more than 5 µg/min of norepinephrine. Part 1 used a Bayesian algorithm to adjust randomization probabilities to alternative selepressin dosing regimens and to trigger transition to part 2, which would compare the best-performing regimen with placebo. The trial was conducted between July 2015 and August 2017 in 63 hospitals in Belgium, Denmark, France, the Netherlands, and the United States, and follow-up was completed by May 2018.

Interventions: Random assignment to 1 of 3 dosing regimens of selepressin (starting infusion rates of 1.7, 2.5, and 3.5 ng/kg/min; n = 585) or to placebo (n = 283), all administered as continuous infusions titrated according to hemodynamic parameters.

Main outcomes and measures: Primary end point was ventilator- and vasopressor-free days within 30 days (deaths assigned zero days) of commencing study drug. Key secondary end points were 90-day mortality, kidney replacement therapy-free days, and ICU-free days.

Results: Among 868 randomized patients, 828 received study drug (mean age, 66.3 years; 341 [41.2%] women) and comprised the primary analysis cohort, of whom 562 received 1 of 3 selepressin regimens, 266 received placebo, and 817 (98.7%) completed the trial. The trial was stopped for futility at the end of part 1. Median study drug duration was 37.8 hours (IQR, 17.8-72.4). There were no significant differences in the primary end point (ventilator- and vasopressor-free days: 15.0 vs 14.5 in the selepressin and placebo groups; difference, 0.6 [95% CI, -1.3 to 2.4]; P = .30) or key secondary end points (90-day mortality, 40.6% vs 39.4%; difference, 1.1% [95% CI, -6.5% to 8.8%]; P = .77; kidney replacement therapy-free days: 18.5 vs 18.2; difference, 0.3 [95% CI, -2.1 to 2.6]; P = .85; ICU-free days: 12.6 vs 12.2; difference, 0.5 [95% CI, -1.2 to 2.2]; P = .41). Adverse event rates included cardiac arrhythmias (27.9% vs 25.2% of patients), cardiac ischemia (6.6% vs 5.6%), mesenteric ischemia (3.2% vs 2.6%), and peripheral ischemia (2.3% vs 2.3%).

Conclusions and relevance: Among patients with septic shock receiving norepinephrine, administration of selepressin, compared with placebo, did not result in improvement in vasopressor- and ventilator-free days within 30 days. Further research would be needed to evaluate the potential role of selepressin for other patient-centered outcomes in septic shock.

Mots-clefs

Interstitial and Granulomatous Lung Disease in Inflammatory Bowel Disease Patients

Eliadou E, Moleiro J, Ribaldone DG, Astegiano M, Rothfuss K, Taxonera C, Ghalim F, Carbonnel F, Verstockt B, Festa S, Maia L, Berrozpe A, Zagorowicz E, Savarino E, Ellul P, Vavricka SR, Calvo M, Koutroubakis I, Hoentjen F, Salazar Luis F, Callela F, Cañete Pizarro F, Soufleris K, Sonnenberg E, Cavicchi M, Wypych J, **Hommel C**, Ghiani A, Fiorino G, ECCO CONFER COMMITTEE

Références	*Doi*	*IF*
J Crohns Colitis 2019; [Online ahead of print]	*10.1093/ecco-jcc/jjz165*	*7.827*

Abstract

BACKGROUND: Interstitial lung (ILD) disease and Granulomatous lung disease (GLD) are rare respiratory disorders that have been associated with inflammatory bowel disease (IBD). Clinical presentation is polymorphic and aetiology is unclear.

METHODS: This was an ECCO-CONFER project. Cases of concomitant ILD or GLD and IBD or drug induced ILD/GLD were collected. The criteria for diagnosing ILD and GLD were based on definitions from the American Thoracic Society and European Respiratory Society and on the discretion of reporting clinician.

RESULTS: We identified 31 patients with ILD, majority had ulcerative colitis (UC) (n=22). Drug related ILD was found in 64% of patients. Twenty five patients (80.6%) required hospitalization and 1 required non-invasive ventilation. Causative drug was stopped in all drug related ILD and 87% of patients received systemic steroids. At follow up 16% of patients had no respiratory symptoms, 16% had partial improvement, 55% had ongoing symptoms, no data in 13%. One patient was referred for lung transplantation and 1 death from lung fibrosis was reported. We also identified 22 GLD patients, most had Crohn's disease (CD) (n=17). Drug related GLD was found in 36% of patients. Ten patients (45.4%) required hospitalization. Causative drug was stopped in all drug related GLD and 81% of patients received systemic steroids. Remission of both conditions was achieved in almost all patients.

CONCLUSIONS: ILD and GLD although rare can cause significant morbidity. In our series over half of cases were drug related and therefore focused pharmacovigilance is needed to identify and manage these cases.

Mots-clefs

Association Between Symptoms, Quality of Life, and Gastric Emptying in Dyspeptic Patients

Wuestenberghs F, Juge M, Melchior C, Desprez C, Leroi AM, Gourcerol G.

Références	*Doi*	*IF*
J Neurogastroenterol Motil 2019;25(4):534-543	*10.5056/jnm19060*	*3.179*

Abstract

BACKGROUND/AIMS: Association between symptoms, quality of life and gastric emptying in dyspepsia is inconsistent in the literature. The aim of our study is to investigate if gastric emptying is associated with specific symptoms and quality of life in dyspeptic patients.

METHODS: We reviewed retrospectively gastric emptying measured by 13C-labelled octanoate breath testing for more than 6 hours in 198 consecutive patients with dyspepsia complaints. Gastrointestinal symptoms were assessed using a 5-points Likert scale and by a symptomatic composite score, whereas quality of life was measured by the GIQLI.

RESULTS: In our cohort, 90 patients (45%) had a delayed gastric emptying (half emptying time above 166 minutes when assessed over 6-8 hours). There was no difference in symptoms or quality of life between patients with or without delayed gastric emptying. However, patients with severely delayed gastric emptying (half emptying time above 200 minutes) had increased postprandial fullness (P = 0.012), abdominal pain (P = 0.026), bloating (P = 0.044), early satiety (P = 0.018), symptomatic composite score (P = 0.005), and a lower quality of life (P = 0.018). This association was no longer observed if the calculation of gastric emptying was limited to the first 4-hour samples.

CONCLUSIONS: There is no association between symptoms, quality of life and gastric emptying in an overall dyspeptic population. However, there is an association between symptoms, quality of life of delayed gastric emptying in the subgroup of patients with severely delayed gastric emptying. An 8-hour measurement of gastric emptying should be recommended.

Mots-clefs

Breath tests; Dyspepsia; Gastric emptying; Gastroparesis; Quality of life.

Illustration of a Fatal Radiation-Induced Lung Aneurysm: Is Central Lung Stereotactic Radiotherapy to Be Banned?

Ledoux B, Dupont M, Duplaquet F, Pirard L, Ocak S, Wanet M, Remouchamps V.

Références	*Doi*	*IF*
Cancer Radiother 2019;23(8):926-929	*10.1016/j.canrad.2019.05.016*	*1.263*

Case report

Stereotactic body radiation therapy is still controversial for inoperable patients with central lung lesion. We report the case of a 59-year-old woman with previous history of head and neck squamous cell carcinoma who was treated by lung stereotactic body irradiation for an inoperable lymph node in station 10R. One year after, a fibroscopy showed a necrosis of the right main bronchus mucosae and the CT showed a radio-induced aneurysm protruding into the right inferior lobular bronchus. The patient eventually died a few hours later with a massive haemoptysis. This case highlights the potential toxicity of central lung stereotactic body radiation therapy and raises the question of its legitimacy.

Mots-clefs

Aneurysm; Anévrisme; Central tumour; Haemoptysis; Hémoptysie; Long-term toxicity; Lung lesion; Lésion pulmonaire; SBRT; Stéréotaxie; Toxicité à long terme; Tumeur centrale.

A Breathing Pacemaker

Robaye B, Melly L, Kalscheuer G, Xhaët O, Blommaert D.

Références	*Doi*	*IF*
Eur Heart J Cardiovasc Imaging 2019. [Online ahead of print]	*10.1093/ehjci/jez273*	*5.260*

Abstract

A 59-year-old man suffered from a pacemaker infection. He was born with a complex cardiac malformation (dextrocardia, transposition of the great arteries, and atrial switch). He was implanted of a bicameral pacemaker for complete atrioventricular block in 1995. The pocket of the pacemaker was inflamed, inflated, and grew in size when the patient coughed or expirated against resistance. Chest computed tomography (CT) scan showed an aerial fistula (Panels A, axial plane and B, sagittal plane arrows) between an abscess of the upper segment of the right lung and the pocket of the pacemaker, along the extravascular path of the leads. Echocardiographies were of poor quality...

Mots-clefs

ALK Immunohistochemistry Positive, FISH Negative NSCLC Is Infrequent, but Associated With Impaired Survival Following Treatment With Crizotinib

Thunnissen E, Lissenberg-Witte BI, van den Heuvel MM, Monkhorst K, Skov BG, Sørensen JB, Mellemgaard A, Dingemans AMC, Speel EJM, de Langen AJ, Hashemi SMS, Bahce I, van der Drift MA, Looijen-Salamon MG, Gosney J, Postmus PE, Samii SMS, **Duplaquet F, Weynand B**, Durando X, Penault-Llorca F, Finn S, Grady AO, Oz B, Akyurek N, Buettner R, Wolf J, Bubendorf L, Duin S, Marondel I, Heukamp LC, Timens W, Schuuring EMD, Pauwels P, Smit EF.

Références	*Doi*	*IF*
Lung Cancer 2019;138:13-18	*10.1016/j.lungcan.2019.09.023*	*4.599*

Abstract

OBJECTIVE: Metastasized non-small cell lung cancer (NSCLC) with an anaplastic lymphoma kinase (ALK) rearrangement is usually sensitive to a range of ALK-tyrosine kinase inhibitors. ALK-positive NSCLC have been identified in pivotal phase III trials with fluorescence in situ hybridization (ALK FISH+). These tumors are also expressing the fusion product (ALK immunohistochemistry (IHC)+). However, discrepant cases occur, including ALK IHC + FISH-. The aim of this study was to collect ALK IHC + cases and compare within this group response to crizotinib treatment of ALK FISH + cases with ALK FISH- cases.

MATERIALS AND METHODS: In this European prospective multicenter research study patients with Stage IV ALK IHC + NSCLC treated with crizotinib were enrolled. Tumor slides were validated centrally for ALK IHC and ALK FISH.

RESULTS: Registration of 3523 ALK IHC tests revealed a prevalence of 2.7% (n = 94) ALK IHC + cases. Local ALK FISH analysis resulted in 48 concordant (ALK IHC+/FISH+) and 16 discordant (ALK IHC+/FISH-) cases. Central validation revealed 37 concordant and 7 discordant cases, 5 of which had follow-up. Validation was hampered by limited amount of tissue in biopsy samples. The PFS at 1 year for ALK concordant and discordant was 58% and 20%, respectively (HR = 2.4; 95% CI: 0.78-7.3; p = 0.11). Overall survival was significantly better for concordant cases than discordant cases after central validation (HR=4.5; 95% CI= 1.2-15.9; p=0.010.

CONCLUSION: ALK IHC + FISH- NSCLC is infrequent and associated with a worse outcome on personalized treatment. A suitable predictive testing strategy may be to screen first with IHC and then confirm with FISH instead of considering ALK IHC equivalent to ALK FISH according to the current guidelines.

Mots-clefs

alk; fluorescence in situ hybridisation; immunohistochemistry; non-small cell lung cancer; prognosis; treatment.

Role of Focal Adhesion Kinase in Small-Cell Lung Cancer and Its Potential as a Therapeutic Target

Aboubakar Nana F, Vanderputten M, **Ocak S.**

Références	*Doi*	*IF*
Cancer (Basel) 2019;11(11)	*10.3390/cancers11111683*	*6.162*

Abstract

Small-cell lung cancer (SCLC) represents 15% of all lung cancers and it is clinically the most aggressive type, being characterized by a tendency for early metastasis, with two-thirds of the patients diagnosed with an extensive stage (ES) disease and a five-year overall survival (OS) as low as 5%. There are still no effective targeted therapies in SCLC despite improved understanding of the molecular steps leading to SCLC development and progression these last years. After four decades, the only modest improvement in OS of patients suffering from ES-SCLC has recently been shown in a trial combining atezolizumab, an anti-PD-L1 immune checkpoint inhibitor, with carboplatin and etoposide, chemotherapy agents. This highlights the need to pursue research efforts in this field. Focal adhesion kinase (FAK) is a non-receptor protein tyrosine kinase that is overexpressed and activated in several cancers, including SCLC, and contributing to cancer progression and metastasis through its important role in cell proliferation, survival, adhesion, spreading, migration, and invasion. FAK also plays a role in tumor immune evasion, epithelial-mesenchymal transition, DNA damage repair, radioresistance, and regulation of cancer stem cells. FAK is of particular interest in SCLC, being known for its aggressiveness. The inhibition of FAK in SCLC cell lines demonstrated significative decrease in cell proliferation, invasion, and migration, and induced cell cycle arrest and apoptosis. In this review, we will focus on the role of FAK in cancer cells and their microenvironment, and its potential as a therapeutic target in SCLC.

Mots-clefs

focal adhesion kinase; small-cell lung cancer; targeted therapy.

Treatment Failure and Hospital Readmissions in Severe COPD Exacerbations Treated With Azithromycin Versus Placebo - A Post-Hoc Analysis of the BACE Randomized Controlled Trial

Vermeersch K, Belmans A, Bogaerts K, Gyselinck I, Cardinaels N, Gabrovska M, Aumann J, Demedts IK, Corhay JL, **Marchand E**, Slabbynck H, Haenebalcke C, Vermeersch S, Verleden GM, Troosters T, Ninane V, Brusselle GG, Janssens W, BACE trial investigators

Références	*Doi*	*IF*
Respir Res 2019;20(1):237	*10.1186/s12931-019-1208-6*	*3.829*

Abstract

BACKGROUND: In the BACE trial, a 3-month (3 m) intervention with azithromycin, initiated at the onset of an infectious COPD exacerbation requiring hospitalization, decreased the rate of a first treatment failure (TF); the composite of treatment intensification (TI), step-up in hospital care (SH) and mortality.

OBJECTIVES: (1) To investigate the intervention's effect on recurrent events, and (2) to identify clinical subgroups most likely to benefit, determined from the incidence rate of TF and hospital readmissions.

METHODS: Enrolment criteria included the diagnosis of COPD, a smoking history of ≥10 pack-years and ≥ 1 exacerbation in the previous year. Rate ratio (RR) calculations, subgroup analyses and modelling of continuous variables using splines were based on a Poisson regression model, adjusted for exposure time.

RESULTS: Azithromycin significantly reduced TF by 24% within 3 m (RR = 0.76, 95%CI:0.59;0.97, p = 0.031) through a 50% reduction in SH (RR = 0.50, 95%CI:0.30;0.81, p = 0.006), which comprised of a 53% reduction in hospital readmissions (RR = 0.47, 95%CI:0.27;0.80; p = 0.007). A significant interaction between the intervention, CRP and blood eosinophil count at hospital admission was found, with azithromycin significantly reducing hospital readmissions in patients with high CRP (› 50 mg/L, RR = 0.18, 95%CI:0.05;0.60, p = 0.005), or low blood eosinophil count (‹300cells/µL, RR = 0.33, 95%CI:0.17;0.64, p = 0.001). No differences were observed in treatment response by age, FEV1, CRP or blood eosinophil count in continuous analyses.

CONCLUSIONS: This post-hoc analysis of the BACE trial shows that azithromycin initiated at the onset of an infectious COPD exacerbation requiring hospitalization reduces the incidence rate of TF within 3 m by preventing hospital readmissions. In patients with high CRP or low blood eosinophil count at admission this treatment effect was more pronounced, suggesting a potential role for these biomarkers in guiding azithromycin therapy.

Mots-clefs

CRP; Eosinophil count; Macrolide; Readmission; Recurrent event.

Increased Expression and Activation of FAK in Small-Cell Lung Cancer Compared to Non-Small-Cell Lung Cancer

Aboubakar Nana F, Hoton D, Ambroise J, Lecocq M, Vanderputten M, **Sibille Y,** Vanaudenaerde B, Pilette C, Bouzin C, Ocak S.

Références	*Doi*	*IF*
Cancer (Basel) 2019;11(10)	*10.3390/cancers11101526*	*6.162*

Abstract

INTRODUCTION: Focal adhesion kinase (FAK) plays a crucial role in cancer development and progression. FAK is overexpressed and/or activated and associated with poor prognosis in various malignancies. However, in lung cancer, activated FAK expression and its prognostic value are unknown.

METHODS: FAK and activated FAK (phospho-FAK Y397) expressions were analyzed by multiplex immunofluorescence staining in formalin-fixed paraffin-embedded tissues from 95 non-small-cell lung cancer (NSCLC) and 105 small-cell lung cancer (SCLC) patients, and 37 healthy donors. The FAK staining score was defined as the percentage (%) of FAK-stained tumor area multiplied by (×) FAK mean intensity and phospho-FAK staining score as the (% of phospho-FAK-stained area of low intensity × 1) + (% of phospho-FAK-stained area of medium intensity × 2) + (% of the phospho-FAK-stained area of high intensity × 3). FAK and phospho-FAK staining scores were compared between normal, NSCLC, and SCLC tissues. They were also tested for correlations with patient characteristics and clinical outcomes.

RESULTS: The median follow-up time after the first treatment was 42.5 months and 6.4 months for NSCLC and SCLC patients, respectively. FAK and phospho-FAK staining scores were significantly higher in lung cancer than in normal lung and significantly higher in SCLC compared to NSCLC tissues ($p < 0.01$). Moreover, the ratio between phospho-FAK and FAK staining scores was significantly higher in SCLC than in NSCLC tissues ($p < 0.01$). However, FAK and activated FAK expression in lung cancer did not correlate with recurrence-free and overall survival in NSCLC and SCLC patients.

CONCLUSIONS: Total FAK and activated FAK expressions are significantly higher in lung cancer than in normal lung, and significantly higher in SCLC compared to NSCLC, but are not prognostic biomarkers in this study.

Mots-clefs

FAK; expression; lung cancer; multiplex immunofluorescence staining; non-small-cell lung cancer; phospho-FAK; prognosis; small-cell lung cancer; targeted therapy.

Infections in the Older Population: What Do We Know?

Schoevaerdts D, Sibille FX, Gavazzi G.

Références	*Doi*	*IF*
Aging Clin Exp Res 2019; [Online ahead of print]	*10.1007/s40520-019-01375-4*	*0.80*

Abstract

The incidence of infections increases with age and results in a higher risk of morbidity and mortality. This rise is not mainly related to chronological age per se but has been linked mostly to individual factors such as immunosenescence; the presence of comorbidities; the occurrence of geriatric syndromes such as poor nutrition, polypharmacy, and cognitive disorders; and the presence of functional impairment concomitant with environmental, healthcare-related and microbiological factors such as the increasing risk of multidrug-resistant microorganisms. The geriatric concept of frailty introduces a new approach for considering the risk of infection; this concept highlights the importance of functional status and is a more comprehensive and multicomponent approach that may help to reverse the vulnerability to stress. The aim of this article is to provide some typical hallmarks of infections among older adults in comparison to younger individuals. The main differences among the older population that are presented are an increased prevalence of infections and potential risk factors, a higher risk of carrying multidrug-resistant microorganisms, an increase in barriers to a prompt diagnosis related to atypical presentations and challenges with diagnostic tools, a higher risk of under- and over-diagnosis, a worse prognosis with a higher risk of acute and chronic complications and a particular need for better communication among all healthcare sectors as they are closely linked together.

Mots-clefs

Aged; Clinical presentation; Frail elderly; Infections; Signs and symptoms

Longitudinal Clinical Outcomes in a Real-World Population of Patients With Idiopathic Pulmonary Fibrosis: The PROOF Registry

Wuyts WA, **Dahlqvist C**, Slabbynck H, Schlesser M, Gusbin N, Compere C, Maddens S, Lee YC, Kirchgaessler KU, Bartley K, Bondue B.

Références	*Doi*	*IF*
Respir Res 2019;20(1):231	*10.1186/s12931-019-1182-z*	*3.829*

Abstract

BACKGROUND: The PROOF registry is an observational study initiated in October 2013 with the aim to monitor disease progression in a real-world population of patients with idiopathic pulmonary fibrosis (IPF). Here, we present longitudinal clinical outcomes from the PROOF registry.

METHODS: Patients with IPF were enrolled across eight centers in Belgium and Luxembourg. For all patients, clinical outcomes data were collected, including mortality, lung transplant, acute exacerbations, and pulmonary hypertension. For patients treated with pirfenidone at any time during follow-up (2013-2017), for any duration of treatment (the pirfenidone-treated population): pirfenidone treatment patterns were collected; changes in pulmonary function (forced vital capacity [FVC] and carbon monoxide diffusing capacity [DLco]) were reviewed up to 24 months post-inclusion; and time-to-event analyses from the time of registry inclusion were performed.

RESULTS: The PROOF registry enrolled a total of 277 patients. During follow-up, 23.1% of patients died, 5.1% received a lung transplant, 5.4% experienced an acute exacerbation, and 6.1% had comorbid pulmonary hypertension. In the pirfenidone-treated population (N = 233, 84.1%), 12.9% of patients had a temporary dose discontinuation and 31.8% had a temporary dose reduction; 4.3% of patients permanently discontinued pirfenidone due to an adverse drug reaction. Mean percent predicted FVC was 81.2% (standard deviation [SD] 19.0) at Month 0 and 78.3% (SD 25.0) at Month 24, and mean percent predicted DLco was 47.0% (SD 13.2) and 45.0% (SD 16.5), respectively. Rates of ≥ 10% absolute decline in percent predicted FVC and ≥ 15% absolute decline in percent predicted DLco over 24 months were 31.0% and 23.2%, respectively. Mean times from registry inclusion to categorical absolute decline in percent predicted FVC and percent predicted DLco were 20.1 (standard error [SE] 0.6) months and 23.4 (SE 0.5) months, respectively; mean time from registry inclusion to death was 31.0 (SE 0.9) months.

CONCLUSIONS: The PROOF registry is a source of European data characterizing longitudinal clinical outcomes of patients with IPF. Over 12 months of follow-up, pulmonary function remained largely stable in patients with IPF who received pirfenidone for any duration of treatment. Pulmonary function remained similar at 24 months of follow-up, although patient numbers were lower.

Mots-clefs

Phenotyping Occupational Asthma Caused by Acrylates in a Multicenter Cohort Study

Suojalehto H, Suuronen K, Cullinan P, Lindström I, Sastre J, Walusiak-Skorupa J, Munoz X, Talini D, Klusackova P, Moore V, Merget R, Svanes C, Mason P, dell'Omo M, Moscato G, Quirce S, Hoyle J, Sherson D, Preisser A, Seed M, **Rifflart C**, Godet J, de Blay F, **Vandenplas O**, European Network for the Phenotyping of Occupational Asthma (E-PHOCAS) investigators

Références	*Doi*	*IF*
J Allergy Clin Immunol Pract 2019 [Online ahead of print]	*10.1016/j.jaip.2019.10.017*	*7.550*

Abstract

BACKGROUND: While acrylates are well-known skin sensitizers, they are not classified as respiratory sensitizers although several cases of acrylate-induced occupational asthma (OA) have been reported.

Objective: To evaluate the characteristics of acrylate-induced OA in a large series of cases and compare those with OA induced by other low-molecular-weight (LMW) agents.

METHODS: Jobs and exposures, clinical and functional characteristics, and markers of airway inflammation were analyzed in an international, multicenter, retrospective cohort of subjects with OA ascertained by a positive inhalation challenge to acrylates (n = 55) or other LMW agents (n = 418) including isocyanates (n = 125).

RESULTS: Acrylate-containing glues were the most prevalent products, and industrial manufacturing, dental work, and beauty care were typical occupations causing OA. Work-related rhinitis was more common in acrylate-than in isocyanate-induced asthma (P < .001). The increase in postchallenge fractional exhaled nitric oxide was significantly greater in acrylate-induced OA (26.0; 8.2 to 38.0 parts per billion [ppb]) than in OA induced by other LMW agents (3.0; -1.0 to 10.0 ppb; P < .001) or isocyanates (5.0; 2.0 to 16.0 ppb; P = .010). Multivariable models confirmed that OA induced by acrylates was significantly and independently associated with a postchallenge increase in fractional exhaled nitric oxide (≥17.5 ppb).

CONCLUSIONS: Acrylate-induced OA shows specific characteristics, concomitant work-related rhinitis, and exposure-related increases in fractional exhaled nitric oxide, suggesting that acrylates may induce asthma through different immunologic mechanisms compared with mechanisms through which other LMW agents may induce asthma. Our findings reinforce the need for a reevaluation of the hazard classification of acrylates, and further investigation of the pathophysiological mechanisms underlying their respiratory sensitizing potential.

Mots-clefs

Acrylate; Cyanoacrylate; Fractional exhaled nitric oxide; Low-molecular-weight agent; Methacrylate; Occupational asthma.

Concomitant Assessment of Rivaroxaban Concentration and Its Impact on Thrombin Generation

Bloemen S, Zwaveling S, **Mullier F,** Douxfils J.

Références	*Doi*	*IF*
Thromb Res 2019;184:8-15	*10.1016/j.thromres.2019.09.037*	*3.266*

Abstract

BACKGROUND: Reliable assays to measure direct oral anticoagulant (DOAC) levels and their activity in critical situations are needed. Drug levels alone are not representative of the effect of DOACs on an individual's coagulation. We developed a technique that provides direct assessment of the global effect of rivaroxaban on the individual's coagulation in addition to plasma concentrations.

METHODS: DOAC concentrations were determined in fifty patients using rivaroxaban, with the new assay, Xross-CAT. The effect of rivaroxaban on coagulation (activity) was measured with thrombin generation (TG) in platelet poor plasma using 5 pM tissue factor on the same device. The levels were validated with the Biophen DiXal assay. The prothrombin time (PT) and dilute Russell viper venom time (dRVVT) were performed to estimate the effect on coagulation.

RESULTS: The variability of Xross-CAT was below 12%. Xross-CAT correlates well with Biophen DiXaI (rs = 0.885). The bias, determined by Bland-Altman analysis, was 4.9% and the Passing-Bablok equation was y = 1.1x - 2.1. The correlation of plasma levels with TG was moderate (ETP rs = -0.548; Peak rs = -0.559), as for the PT (rs = 0.739) and the dRVVT (rs = 0.692).

CONCLUSIONS: Xross-CAT shows a good correlation with Biophen DiXaI that was previously confirmed to accurately assess rivaroxaban levels. Bleeding and thrombotic complications are not necessarily associated with drug levels and could be influenced by concomitant risk factors. The main benefit of Xross-CAT is that it can be performed simultaneously with thrombin generation, providing an overview of the global anticoagulation status of a patient in relation to circulating DOAC levels.

Mots-clefs

Coagulation assays; Direct factor Xa inhibitor; Plasma concentrations; Rivaroxaban; Thrombin generation.

Albumin Losses During Hemodiafiltration: All Dialyzers Are Not Created Equal - A Case Report

Cuvelier C, Tintillier M, Migali G, Van Ende C, Pochet JM.

Références	*Doi*	*IF*
BMC Nephrol 2019;20(1):392	*10.1186/s12882-019-1567-8*	*2.088*

Abstract

BACKGROUND: Online hemodiafiltration (OL-HDF) is associated with better removal of both small and middle molecules and might improve survival compared to conventional hemodialysis (HD). Nevertheless, hemodiafiltration (HDF) can lead to an increase in albumin loss across the dialyzer, especially with high permeability membrane and high convective volume (CV). We present the case of a patient treated by OL-HDF who developed severe hypoalbuminemia resulting from massive albumin loss into dialysate.
CASE PRESENTATION: A 71-year-old woman with ESRD started renal replacement therapy in December 2016. She was treated by high volume post-dilution OL-HDF, 4 h, 3 times per week. The dialyzer was the Phylther HF20SD (a 2.0m2 heat sterilized high flux (HF) polyphenylene membrane from Bellco). At the initiation of dialysis, the serum albumin was 4.0 g/dl. During the following months, the patient developed severe hypoalbuminemia. The lowest value observed was 2.26 g/dl in July 2017. Diagnostic workup excluded nephrotic syndrome, hepatic failure and malabsorption. The patient was shifted from OL-HDF to standard HF HD, keeping the same dialyzer and dialysis schedule. During the following months, we observed a progressive correction of the hypoalbuminemia (3.82 g/dl at last follow-up). To precise the impact of the epuration technique on the albumin losses in this patient, we measured the amount of albumin in dialysate during one session with the Phylther HF20SD on OL-HDF and one session with the same filter but on standard HD. The CV was 29.0 l for the HDF session. The total albumin losses were 23.6 g on OL-HDF and 4.6 g on HD.
CONCLUSION: OL-HDF can lead to significant albumin loss into the dialysate, especially with high permeability membrane and high CV. When prescribing post-dilutional OL-HDF, the choice of the dialyzer membrane should be made with caution. Users of the steam sterilized polyphenylene membrane, the Phylther SD, should be informed of the risk of large albumin loss with this membrane during post-dilution OL-HDF.

Mots-clefs

Albumin loss; Convective volume; High permeability membrane; Hypoalbuminemia; Online hemodiafiltration; Phylther SD; Polyphenylene membrane.

Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

Flaherty KR, Wells AU, Cottin V, Devaraj A, Walsh SLF, Inoue Y, Richeldi L, Kolb M, Tetzlaff K, Stowasser S, Coeck C, Clerisme-Beaty E, Rosenstock B, Quaresma M, Haeufel T, Goeldner RG, Schlenker-Herceg R, Brown KK; INBUILD Trial Investigators
(**Dahlqvist C**, Investigator)

Références	*Doi*	*IF*
N Engl J Med. 2019;381(18):1718-1727	*10.1056/NEJMoa1908681*	*70.670*

Abstract

BACKGROUND: Preclinical data have suggested that nintedanib, an intracellular inhibitor of tyrosine kinases, inhibits processes involved in the progression of lung fibrosis. Although the efficacy of nintedanib has been shown in idiopathic pulmonary fibrosis, its efficacy across a broad range of fibrosing lung diseases is unknown.

METHODS: In this double-blind, placebo-controlled, phase 3 trial conducted in 15 countries, we randomly assigned patients with fibrosing lung disease affecting more than 10% of lung volume on high-resolution computed tomography (CT) to receive nintedanib at a dose of 150 mg twice daily or placebo. All the patients met criteria for progression of interstitial lung disease in the past 24 months despite treatment and had a forced vital capacity (FVC) of at least 45% of the predicted value and a diffusing capacity of the lung for carbon monoxide ranging from 30 to less than 80% of the predicted value. Randomization was stratified according to the fibrotic pattern (a pattern of usual interstitial pneumonia [UIP] or other fibrotic patterns) on high-resolution CT. The primary end point was the annual rate of decline in the FVC, as assessed over a 52-week period. The two primary populations for analysis were the overall population and patients with a UIP-like fibrotic pattern.

RESULTS: A total of 663 patients were treated. In the overall population, the adjusted rate of decline in the FVC was -80.8 ml per year with nintedanib and -187.8 ml per year with placebo, for a between-group difference of 107.0 ml per year (95% confidence interval [CI], 65.4 to 148.5; P<0.001). In patients with a UIP-like fibrotic pattern, the adjusted rate of decline in the FVC was -82.9 ml per year with nintedanib and -211.1 ml per year with placebo, for a difference of 128.2 ml (95% CI, 70.8 to 185.6; P<0.001). Diarrhea was the most common adverse event, as reported in 66.9% and 23.9% of patients treated with nintedanib and placebo, respectively. Abnormalities on liver-function testing were more common in the nintedanib group than in the placebo group.

CONCLUSIONS: In patients with progressive fibrosing interstitial lung diseases, the annual rate of decline in the FVC was significantly lower among patients who received nintedanib than among those who received placebo. Diarrhea was a common adverse event. (Funded by Boehringer Ingelheim; INBUILD ClinicalTrials.gov number, NCT02999178.)

Mots-clefs

Functional tungsten disulfide nanotubes; Hemocompatibility; Safety; Thrombin generation

NOVEMBRE

Anatomical-based Classification for Transoral Lateral Oropharyngectomy

De Virgilio A, Kim SH, Scott Magnuson J, Holsinger C, Remacle M, **Lawson G**, Wang CC, Mercante G, Malvezzi L, Iocca O, Di Maio P, Ferreli F, Pellini R, Spriano G.

Références	*Doi*	*IF*
Oral Onco 2019;99:104450	*10.1016/j.oraloncology.2019.104450*	*3.730*

Abstract

PURPOSE: The aim of the study is proposing a classification of different transoral lateral oropharyngectomy procedures in order to ensure better definitions of post-operative results.

METHODS: The classification resulted from the consensus of the different authors and was based on anatomical-surgical principles.

RESULTS: The classification comprises three types of lateral oropharyngectomy: type 1 is the resection of the palatine tonsil deep to the pharyngobasilar fascia; type 2 is performed by removing the entire palatine tonsil, the palatoglossus muscle, the palatopharyngeal muscle and the superior constrictor muscle; type 3 is performed by removing the entire palatine tonsil, the palatoglossus muscle, the palatopharyngeal muscle, the superior constrictor muscle, the buccopharyngeal fascia with extension to the pterygoid muscle and parapharyngeal space fat content. Based on the extension of the dissection we can use the suffix A (soft palate), B (posterior pharyngeal wall), C (base of tongue) and D (retromolar trigone).

CONCLUSION: The proposed classification introduces a simple and easy to use categorization of transoral lateral oropharyngectomies into three classes. Resection extensions are easily described using suffixes.

Mots-clefs

Endoscopic surgery; Oropharynx; Robotic surgery; TORS; Tonsil; Transoral oropharyngectomy

Evaluation of a Hereditary Spherocytosis Screening Algorithm by Automated Blood Count Using Reticulocytes and Erythrocytic Parameters on the Sysmex XN-series

Sottiaux JY, Favresse J, Chevalier C**, Chatelain B, Jacqmin H, Mullier F.**

Références	*Doi*	*IF*
Int J Lab Hematol 2019; [Online ahead of print]	*10.1111/ijlh.13125*	*2.073*

Abstract

Mots-clefs

FER and FES Tyrosine Kinase Fusions in Follicular T-cell Lymphoma

Debackere K, van der Krogt JA, Tousseyn T, Finalet Ferreiro JA, Van Roosbroeck K, Marcelis L, **Graux C**, Dierickx D, Ameye G, Vandenberghe P, Mpm Michaux L, Cools J, Wlodarska I.

Références	*Doi*	*IF*
Blood 2019; [Online ahead of print]	*10.1182/blood.2019002401*	*15.132*

Abstract

Mots-clefs

The Genomic Landscape of Nonsmall Cell Lung Carcinoma in Never Smokers

Boeckx B, Shahi RB, Smeets D, De Brakeleer S, Decoster L, Van Brussel T, Galdermans D, Vercauter P, Decoster L, Alexander P, Berchem G, **Ocak S, Vuylsteke P**, Deschepper K, Lambrechts M, Cappoen N, Teugels E, Lambrechts D, De Greve J.

Références	*Doi*	*IF*
Int J Cancer 2019; [Online ahead of print]	*10.1002/ijc.32797*	*4.982*

Abstract

Lung cancer is the number one cause of cancer-related death worldwide with cigarette smoking as its major risk factor. Although the incidence of lung cancer in never smokers is rising, this subgroup of patients is underrepresented in genomic studies of lung cancer. Here, we assembled a prospective cohort of 46 never-smoking, nonsmall cell lung cancer (NSCLC) patients and performed whole-exome and low-coverage whole-genome sequencing on tumors and matched germline DNA. We observed fewer somatic mutations, genomic breakpoints and a smaller fraction of the genome with chromosomal instability in lung tumors from never smokers compared to smokers. The lower number of mutations, enabled us to identify TSC22D1 as a potential driver gene in NSCLC.
On the other hand, the frequency of mutations in actionable genes such as EGFR and ERBB2 and of amplifications in MET were higher, while the mutation rate of TP53, which is a negative prognostic factor, was lower in never smokers compared to smokers. Together, these observations suggest a more favorable prognosis for never smokers with NSCLC. Classification of somatic mutations into six-substitution type patterns or into 96-substitution type signatures revealed distinct clusters between smokers and never smokers. Particularly, we identified in never smokers signatures related to aging, homologous recombination damage and APOBEC/AID activity as the most important underlying processes of NSCLC. This further indicates that second-hand smoking is not driving NSCLC pathogenesis in never smokers.

Mots-clefs

lung cancer; never smokers; whole-exome sequencing.

Gene Alterations in Epigenetic Modifiers and JAK-STAT Signaling Are Frequent in Breast Implant-Associated ALCL

Laurent C, Nicolae A, Laurent C, Le Bras F, Haioun C, Fataccioli V, Amara N, Adélaïde J, Guille A, Schiano JM, Tesson B, Traverse-Glehen A, Chenard MP, Mescam L, Moreau A, Chassagne-Clement C, Somja J, Escudié F, **André M**, Martin N, Lacroix L, Lemonnier F, Hamy-Petit AS, Reyal F, Bannier M, Oberic L, Prade N, Frénois FX, Beldi-Ferchiou A, Delfau-Larue MH, Bouabdallah R, Birnbaum D, Brousset P, Xerri L, Gaulard P.

Références	*Doi*	*IF*
Blood 2019; [Online ahead of print]	*10.1182/blood.2019001904*	*15.132*

Highlights

The oncogenic events involved in breast implant-associated anaplastic large cell lymphoma (BI-ALCL) remain elusive. To clarify this point, we have characterized the genomic landscape of 34 BI-ALCLs (15 tumor, 19 in situ subtypes) collected from 54 BI-ALCL patients diagnosed through the French Lymphopath network. Whole exome sequencing (n=22, with paired tumor/germline DNA) and/or targeted deep sequencing (n=24) showed recurrent mutations of epigenetic modifiers in 74% of cases, involving notably KMT2C (26%), KMT2D (9%), CHD2 (15%) and CREBBP (15%). KMT2D and KMT2C mutations correlated with a loss of H3K4 mono- and tri-methylation by immunohistochemistry. Twenty cases (59%) showed mutations in at least one member of the JAK/STAT pathway including STAT3 (38%), JAK1 (18%), STAT5B (3%) and in negative regulators like SOCS3 (6%), SOCS1 (3%) and PTPN1 (3%). These mutations were more frequent in tumor-type than in situ samples (p=0.038). All BI-ALCLs expressed pSTAT3, regardless of the mutational status of genes in JAK/STAT pathway. Mutations in EOMES gene (12%) involved in lymphocytes development, PI3K-AKT/mTOR (6%) and loss of function mutations in TP53 (12%) were also identified. Copy number aberration (CNA) analysis identified recurrent alterations including gains on chromosomes 2, 9p, 12p and 21 and losses on 4q, 8p, 15, 16 and 20. Regions of CNA encompassed genes involved in JAK/STAT pathway and epigenetic regulators. Our results show that BI-ALCL genomic landscape is not only characterized by JAK/STAT activating mutations but also loss-of-function alterations of epigenetic modifiers.

Mots-clefs

Utility of the XN-1000 Research Mode for Leukocytes Counting in Ascitic and Pleural Fluids

Favresse J, Fervaille C, Wuestenberghs F, Chatelain B, Mullier F, Jacqmin H.

Références	*Doi*	*IF*
Int J Lab Hematol 2019 [Online ahead of print]	*10.1111/ijlh.13128*	*2.073*

Abstract

Mots-clefs

Seroprevalence and factors associated with IgG anti-DENV positivity in blood donors in Burkina Faso during the 2016 dengue outbreak and implications for blood supply.

Sawadogo S, Baguiya A, Yougbare F, Bicaba BW, Nebie K, Millogo T, Kamba I, Kaba L, Sangare L, Kafando E, **Deneys V.**

Références	*Doi*	*IF*
Transfus Med. 2019 Nov 10 [Epub ahead of print]	*10.1111/tme.12646*	*1.05*

Abstract

OBJECTIVES: Our study aimed to update the seroprevalence and factors associated with anti-dengue virus (DENV) antibody positivity among blood donors and to discuss their implications for blood supply.

BACKGROUND: Questions on the potential transmission of DENV by transfusion increased after the documentation of the risk of transmission of the West Nile virus. This risk was estimated after transfusion of DENV RNA-positive blood units of up to 37•5%. In Burkina Faso, very few studies on DENV in blood donors have been conducted. As a result, there were no reliable data on DENV to allow the implementation of appropriate measures to control the risk of transmission of the dengue virus by blood transfusion.

METHODS: We conducted a 4-week cross-sectional study from December 4 to 30, 2016. Blood donors of both genders, aged 18-60 years, accepted for blood donation after medical selection were consecutively enrolled.

RESULTS: Our study included a total of 1007 blood donors, in which donors living in urban areas represented 78•2%. The mean age was 26•1 ± 8•1 years. After adjustment in a multiple regression logistic model, the odds of having IgG anti-DENV increased as age increased. The odds of DENV was 53% lower in rural areas (OR = 0•47; P = 0•000) compared to urban settings and 42% lower in mobile sites (OR = 0•58; P = 0•03) compared to fixed ones.

CONCLUSION: Our study provides new and useful insights for future research on the risk of TT-DENV throughout blood transfusion.

Mots-clefs

anti-DENV antibodies; blood donation; dengue; transfusion-transmitted infections

Real life safety and effectiveness of nivolumab in older patients with non-small cell lung cancer: Results from the Belgian compassionate use program.

Joris S, Pieters T, Sibille A, Bustin F, Jacqmin L, Kalantari HR, Surmont V, **Goeminne JC**, Clinckart F, Pat K, Demey W, Deschepper K, Lambrechts M, Holbrechts S, Schallier D, Decoster L.

Références	*Doi*	*IF*
J Geriatr Oncol. 2019 Nov 29. [Epub ahead of print]	*10.1016/j.jgo.2019.09.011*	*3.164*

Abstract

OBJECTIVES: To compare real life effectiveness and safety of nivolumab in patients with non-small cell lung cancer (NSCLC), according to age and Eastern Cooperative Group performance status (ECOG-PS).

METHODS: We performed a retrospective analysis of patients treated with nivolumab for NSCLC within a Belgian compassionate use program from July 2015 until December 2016. Safety and effectiveness were compared between patients aged ≥70 years and < 70 years and between ECOG-PS 0/1 and ≥ 2.

RESULTS: A total of 324 patients with NSCLC were included. There was no significant difference between older (≥70) and younger (<70 years) patients with regards to progression free survival (PFS) (4 months (95%CI 2.6;4.8) versus 3.7 months (95%CI 1;7), p = 0.483) and overall survival (OS) (9.3 months (95% CI 5.5;13.1 months) versus 8.4 months (95%CI 6.3; 10.5), p = 0,638). Patients with an ECOG-PS ≥2 had a significant lower median PFS and OS compared to patients with an ECOG-PS 0-1 (2.2 (95%CI 1.4; 2.9) versus 5.6 months (95%CI 4.1; 7.1), p = 0.001 and 3.4 (95%CI 2.3; 4.5) versus 11.1 months (95%CI 8.9; 13.2), p < 0.001 respectively). No significant difference in all grades or grade 3/4 adverse events (AEs) were observed between the different age groups (p = 0.526 and p = 0.603 respectively). Patients with an ECOG-PS 0/1 had significantly more all grades AEs (p = 0.009) but no difference in grade 3/4 AEs was observed (p = 0.406) compared to ECOG-PS ≥2.

CONCLUSION: This real life retrospective study confirms that safety and effectiveness of nivolumab is similar between different age groups, but that effectiveness is driven by performance status.

Mots-clefs

Nivolumab; Non-small cell lung cancer; Older; Performance status

Increased CD8+CD28- circulating T cells and high blood interferon score characterize the systemic inflammation of amyopathic dermatomyositis.

Cassius C, Branchtein M, Battistella M, Amode R, Lepelletier C, Jachiet M, de Masson A, Frumholtz L, Chasset F, Monfort JB, Bachmeyer C, Bengoufa D, Cordoliani F, Bagot M, Bensussan A, Le Buanec H, Bouaziz JD.

Références	*Doi*	*IF*
J Am Acad Dermatol. 2019 Nov 22 [Epub ahead of print]	*10.1016/j.jaad.2019.11.036*	*2.35*

Abstract

Mots-clefs
CD28- lymphocytes; adaptive immune system; amyopathic dermatomyositis; dermatomyositis; flowcytometry; type I interferon

Prédiction du risque de déclin fonctionnel sur base de marqueurs transcriptomiques chez des patients hospitalisés âgés de 75 ans et plus.

Gomrée N, de Saint-Hubert M, Chainiaux F, **Bihin B.**

Références	*Doi*	*IF*
Louv Med 2019 ;138(09) :565-566		*0.010*

Abstract

L'objectif de l'étude SENEGENE 2 était d'identifier des marqueurs transcriptomiques permettant de prédire le risque de déclin fonctionnel chez des patients hospitalises âgés de 75 ans et plus.

Mots-clefs

Biomarqueurs, transcriptomique, PCR en temps réel, déclin fonctionnel, échelle de Katz

Mucoviscidose - 2019 : mise en place du dépistage néonatal en Belgique

Lebecque P, **Lebecque O**, Proesmans M, Leal T.

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):509-518		*0.010*

Abstract

En 2019, la Belgique met enfin en place un programme de dépistage néonatal de la mucoviscidose, proche de celui implémenté par la France dès 2002. L'algorithme retenu part du taux sanguin de trypsine entre 3 et 5 jours de vie. S'il est élevé, 12 variants du gène CFTR sont recherchés. R117H n'en fait pas partie parce que la pénétrance de ce variant fréquent est faible dans les 2 pays. L'article décrit de manière critique les étapes du programme, ses objectifs et ses limitations et souligne en particulier les rôles du médecin de proximité.

Mots-clefs

Mucoviscidose, dépistage néonatal

Utilisation d'une médication à base d'extrait sec de Passiflora incarnata L. dans la prise en charge du sevrage des benzodiazépines

Dubois T, Reynaert C, Zdanowicz N, Denis J, Janssens I, Dierckxsens Y, **Lepiece B.**

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):519-530		*0.010*

Abstract

INTRODUCTION: La prise en charge du sevrage des benzodiazépines est souvent accompagnée d'anxiété menant à un risque de rechute entrainant la prescription de médicaments supplémentaires. Un traitement à base d'extrait sec de Passiflora incarnata L. a déjà démontré un intérêt dans le traitement de première ligne des symptômes anxieux.

MATÉRIELS ET MÉTHODES: Nous avons réalisé une étude longitudinale d'une durée de trois mois. Une médication à base de Passiflora incarnata L. est instaurée à des patients effectuant le sevrage d'une benzodiazépine. Les patients inclus dans l'étude sont tous suffisamment stables et suivis depuis au moins trois mois en consultation. La diminution de la benzodiazépine se fait à raison de 25% de la dose initiale toutes les deux semaines. Aucune technique d'entretien spécifique n'est utilisée, ni avant ni pendant l'étude. L'évolution du score d'anxiété et du nombre de rapports sexuels est évaluée dans le décours du sevrage.

RÉSULTATS: 91 personnes ont participé à cette étude dont 27 hommes (36.5%) et 47 femmes (63.5%) d'un âge moyen de 44.1 ± 11.0 ans. Le taux de succès du sevrage est de 78.4% (IC 95% : 69.0-87.8%). On observe une diminution nette et hautement significative du score d'anxiété d'Hamilton. La fréquence mensuelle des rapports sexuels a légèrement mais significativement augmenté. Le traitement à base de Passiflora incarnata L. est poursuivi chez 70.3% des patients après le sevrage ou la diminution de la benzodiazépine.

CONCLUSIONS: Une médication à base d'extrait sec de Passiflora incarnata L., de par sa sécurité d'emploi et son effet déjà démontré sur l'anxiété, semble améliorer le sevrage des benzodiazépines.

Mots-clefs

Benzodiazépine, sevrage, passiflore, anxiété, sexualité

La bithérapie antirétrovirale comme traitement initial pour les personnes vivant avec le VIH-1?

Dupont E, Yombi JC.

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):531-538		*0.010*

Abstract

L'utilisation des thérapies antirétrovirales combinées (TARc) a considérablement amélioré le pronostic et l'espérance de vie des personnes vivant avec le VIH (PVVIH). Les directives internationales ont ces dernières années en matière de traitement recommander une trithérapie qui consiste par convention à associer à deux inhibiteurs nucléosidiques/ nucléotidiques de la transcriptase inverse (INTI), un troisième agent qui est soit un inhibiteur de protéase (IP) boosté par du ritonavir (r) ou du cobicistat (c), soit un inhibiteur non nucléosidique de la transcriptase inverse (INNTI), soit un inhibiteur de l'intégrase (INI) boosté ou non boosté. Cependant, en raison de la toxicité des INTIs, des schémas thérapeutiques alternatifs les excluant ont longtemps connu un succès mitigé en raison d'une faible efficacité (en particulier chez les patients avec une charge virale élevée et un faible taux de lymphocytes T CD4) par rapport à la trithérapie standard.

Mots-clefs

Bithérapie antirétrovirale ; personnes vivant avec HIV (PLHIV) ; traitement initial

Etude rétrospective de l'utilisation concomitante de médicaments aux propriétés anticholinergiques et d'inhibiteurs d'acétylcholinestérase dans la maladie d'Alzheimer et de leurs associations avec l'évolution du déclin cognitif

Cambier E, **Spinewine A, Bihin B, Schoevaerdts D.**

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):567-568		*0.010*

Abstract

Mots-clefs
Maladie d 'Alzheimer, anticholinergiques , inhibiteurs d'acétylcholinestérase

Évaluation du PET/CT en fin de traitement à l'ère du PET/CT précoce dans le lymphome de Hodgkin classique en traitement de première ligne

Bodart F, Andre M, Bosly A.

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):569-570		*0.010*

Abstract

Le lymphome de Hodgkin classique est une hemopathie maligne curable, en traitement de premiere ligne, dans plus de 90% des cas aux stades localises et 80% des cas aux stades avances. Le PET/CT est devenu la technique d'imagerie essentielle dans la prise en charge des patients atteints d'un lymphome de Hodgkin classique aux stades localises et aux stades avances. La reponse metabolique au PET/CT precoce, evaluee par l'echelle en 5 points de Deauville, est un facteur pronostique puissant et independant de la survie sans progression et est recemment apparue comme le facteur decisionnel principal pour adapter la strategie therapeutique au risque d'echec therapeutique. Dans ce contexte, notre etude clinique retrospective avait pour objectif principal d'evaluer le PET/CT en fin de traitement a l'ere du PET/CT precoce et pour objectif secondaire d'evaluer si la realisation d'un PET/CT en fin du traitement peut etre omise en cas de resultat negatif au PET/CT precoce (score de Deauville I-III).

Mots-clefs

Lymphome de Hodgkin classique, PET/CT précoce, PET/CT en fin de traitement, Échelle en 5 points de Deauville, Score de Deauville, [18F]-Fluorodéoxyglucose, Survie globale, Survie sans progression

Étude du profil lymphocytaire en situation de rechute précoce et tardive après allogreffe de cellules souches hématopoïétiques

Sansen PY, **Graux C.**

Références	*Doi*	*IF*
Louv Med 2019 ;138(09):571-572		*0.010*

Abstract

Le risque de rechute post-allogreffe de moelle dans un contexte de leucémie myéloïde aigue (AML) varie entre 35 et 45% selon différentes variables considérées, et dépasse 50% dans le cas des syndromes myélodysplasiques (MDS). Une immunité anti-tumorale défective, au coeur d'interactions immunologiques complexes, en constitue l'une des causes majeures. Nous nous sommes intéressés au profil lymphocytaire de patients ayant rechuté après allogreffe de moelle dans un contexte d'AML ou de MDS ainsi qu'à des variables cliniques précises afin d'établir d'éventuelles corrélations clinico-biologiques. Cette analyse fait suite au protocole « DLI-Vidaza » ayant testé l'efficacité du Vidaza + DLI chez des patients rechuteurs, dont elle constitue en partie l'objectif tertiaire.

Mots-clefs

Leucémie myéloïde aiguë (LMA) ; syndrome myélodysplasique ; immunité anti-tumorale ; cytométrie de flux ; greffe de moelle osseuse

DECEMBRE

Puumala hantavirus: an imaging review.

Lebecque O, Dupont M.

Références	*Doi*	*IF*
Acta Radiol. 2019 Dec 5:284185119889564 [Epub ahead of print]	*10.1177/0284185119889564*	*1.586*

Abstract

Mots-clefs
Hantavirus; Puumala virus; hemorrhagic fever with renal syndrome; review

Characterization of the role of TMEM45A in cancer cell sensitivity to cisplatin.

Schmit K, Chen JW, Ayama-Canden S, Fransolet M, Finet L, Demazy C, **D'Hondt L, Graux C**, Michiels C.

Références	*Doi*	*IF*
Cell Death Dis. 2019;10(12):919	*10.1038/s41419-019-2088-x.*	*5.959*

Abstract

TMEM45A is a transmembrane protein involved in tumor progression and cancer resistance to chemotherapeutic agents in hypoxic condition. It is correlated to a low breast cancer patient overall survival. However, little is known about this protein, in particular the mechanisms by which TMEM45A modulates cancer cell chemosensitivity. In this work, the messenger RNA expression of TMEM45A was assessed in head and neck squamous cell carcinoma (HNSCC) and renal cell carcinoma (RCC) biopsies. TMEM45A was upregulated in patients diagnosed for head and neck or renal cancer. Then, the implication of this protein in cisplatin sensitivity was explored in SQD9 and RCC4 + pVHL cells. TMEM45A inactivation decreased cell proliferation and modulated cell responses to cisplatin. Indeed, TMEM45A inactivation increased the sensitivity of SQD9 cells to cisplatin, whereas it rendered RCC4 + pVHL cells resistant to this anticancer agent. Through RNA-sequencing analysis, we identified several deregulated pathways that indicated that the impact on cisplatin sensitivity may be associated to the inhibition of DNA damage repair and to UPR pathway activation. This study demonstrated, for the first time, an anti or a pro-apoptotic role of this protein depending on the cancer type and highlighted the role of TMEM45A in modulating patient responses to treatment.

Mots-clefs

Clinique de la dépression chez la personne âgée

Sibille FX, Verreckt E, Philippot P, Agrigoroaei S, Gobiet P**, Mees L, Masse M, Schoevaerdts D.**

Références	*Doi*	*IF*
Louvain Médical 2020;138(10)		*0.010*

Abstract

Nous dressons le tableau clinique parfois trompeur de la dépression de la personne âgée et proposons des pistes de prise en charge de ce syndrome fréquent et grevé d'une lourde morbidité et mortalité. Le diagnostic peut être difficile à poser à cause de l'intrication des plaintes liées au vieillissement, aux comorbidités ou aux traitements,mais il est crucial de le poser précocement. La première étape thérapeutique indispensable est de réserver du temps de parole à nos ainés. Différentes méthodes empruntées à la revalidation cognitive peuvent ensuite être proposées. Cet article est le résumé de la vingtième journée de gériatrie organisée en mars 2017 par le Réseau Universitaire Gériatrique du Namurois.

Mots-clefs

Depression ; elderly ; older ; clinical presentation ; cognitive rehabilitation

A Case report - On-pump Coronary Artery Bypass in a Paraplegic Patient

Bohorquez Derriks X, **Dincq AS, Kalscheuer G, Michaux I, Mitchell J, Melly L.**

Références	*Doi*	*IF*
Cardiol and Cardiovascul Med 2019;03(05):286-289	*10.26502/fccm.92920077*	*3.4*

Abstract

Here, we report a 71-year-old Caucasian male with a chronic spinal cord injury at the level of T4, who underwent a coronary artery bypass grafting for a 3-vessel disease. During surgery an almost fatal hypotension took place in the presence of an autonomic dysregulation, requiring to go back on cardiopulmonary bypass. A few other episodes of hyper- and hypotension occurred perioperatively. We discuss the issues with the anesthesia and surgical cardiac procedures in the light of this acute blood pressure variability called autonomic dysreflexia.

Mots-clefs

Spinal Cord Injury; Cardiac Surgery; Autonomic Dysreflexia

Long-Term Stability of an Infusion Containing Morphine, Ketamine and Lorazepam in Syringe at 5±3°C

Colsoul ML, Hecq JD, Soumoy L, Defrene L, Goderniaux N, Bihin B, Jamart J, Galanti L

Références	*Doi*	*IF*
J Pharm and Pharm Sciences 2019;3(1)	*10.29011/2574-7711.100082*	*0.69*

Abstract

BACKGROUND AND OBJECTIVE: Patients in palliative care are injected with a sedation infusion containing morphine, ketamine and lorazepam in order to relieve pain. This infusion is prepared by the nursing staff according to demand, but the awareness of its long-term stability could allow a preparation in batch and in advance by a Centralized Intravenous Additive Services (CIVAS). The aim of this study was to evaluate the physicochemical stability in syringes at 5±3°C of the injectable with two different levels of concentration commonly used.

METHOD: Five syringes were prepared under aseptic conditions for each level of concentration (low concentration: morphine 1.5 mg/ml, ketamine 1.5 mg/ml and lorazepam 0.1 mg/ml; high concentration: morphine 6 mg/ml, ketamine 5 mg/ml and lorazepam 0.3 mg/ml). Solutions were stored at 5±3°C for 25 days and the stability was periodically investigated (each day the first week, then 3 times a week). Particle appearance or colour change were checked by visual inspection while crystals were searched under the microscope. pH was measured to assess its stability and absorbance at 350, 410 and 550 nm were monitored to estimate the solution turbidity. The molecules concentrations were measured by Ultra-High Performance Liquid Chromatography (UHPLC) – diode array detection.

RESULTS: Crystals were visible to the naked eye after 23 days in syringes of low concentration and after 11 days in syringes of high concentration. Some crystals were already observed under the microscope after 7 days in high concentration solutions. pH and absorbance at 410 and 550 nm were stable. Absorbance at 350 nm showed a decrease after 11 and 7 days in low and high concentration infusion respectively, suggesting the degradation of a compound absorbing at this wavelength. Solutions were considered chemically stable while the lower one-sided prediction limit at 95% remains superior to 90% of the initial concentration. Morphine and ketamine were stable for 25 days while lorazepam was unstable from day 0.

CONCLUSION: Infusions containing morphine, ketamine and lorazepam used in palliative care are unstable at 5±3°C immediately after preparation. Consequently, the mixture of these three components should be prevented, even extemporaneously.

Mots-clefs

Gestion des agents antiplaquettaires en cas de procédure invasive non programmée ou d'hémorragie. Propositions du Groupe d'intérêt en hémostase périopératoire (GIHP) et du Groupe français d'études sur l'hémostase et la thrombose (GFHT) en collaboration avec la Société française d'anesthésie et de réanimation (SFAR)

Godier A, Garrigue D, Lasne D, Fontana P, Bonhomme F, Collet JP, de Maistre E, Ickx B, Gruel Y, Mazighi M, Nguyen P, Vincentelli A, Albaladejo P, Lecompte T, Belisle S, Blais N, Borel-Derlon A, Borg JY, Bosson JL, Cohen A, Faraoni D, Garrigue Huet D, Guay J, Hardy JF, Huet Y, Laporte S, Levy JH, Llau J, Le Gal G, **Lessire S,** Longrois D, Madi-Jebara S, Marret E, Mas JL, Meyer G, Mismetti P, Morange PE, Motte S, **Mullier F,** Nathan N, Ozier Y, Pernod G, Rosencher N, Roullet S, Roy PM, Samama CM, Schlumberger S, Schved JF, Sié P, Steib A, Susen S, van Belle E, van Der Linden P, Zufferey P

Références	*Doi*	*IF*
Anesthésie & Réanimation 2019;5(3) :218-237	*10.1016/j.anrea.2018.10.003*	

Abstract

Le Groupe d'intérêt en hémostase périopératoire (GIHP) et le Groupe français d'études sur l'hémostase et la thrombose (GFHT), en collaboration avec la Société française d'anesthésie et de réanimation (SFAR) ont fait des propositions de gestion des agents antiplaquettaires (AAP) pour une procédure invasive programmée. Ces propositions ont été discutées et validées par vote ; toutes sauf une ont fait l'objet d'un accord fort. La gestion des AAP dépend de leur indication et de la procédure considérée. Le risque hémorragique lié à la procédure invasive peut être divisé en bas, intermédiaire ou élevé, selon la possibilité ou non de réaliser la procédure sous traitement (sous respectivement bithérapie antiplaquettaire, aspirine en monothérapie ou aucun AAP). Si une interruption des AAP est indiquée avant la procédure, une dernière prise d'aspirine, clopidogrel, ticagrélor et prasugrel 3, 5, 5 et 7 jours avant la procédure est proposée. Le risque thrombotique associé à l'interruption des AAP doit être évalué en fonction de l'indication des AAP. Il est plus élevé chez les patients traités par bithérapie pour un stent coronaire que chez ceux traités par monothérapie pour une prévention cardiovasculaire, un antécédent d'accident vasculaire cérébral ischémique ou une artériopathie oblitérante des membres inférieurs. Ces propositions concernent aussi le rôle potentiel des tests fonctionnels plaquettaires, la gestion des AAP pour l'anesthésie locorégionale, centrale et périphérique, et pour la chirurgie cardiaque coronair

Mots-clefs

Agent antiplaquettaire Chirurgie Hémorragie Thrombose Anesthésie locorégionale

Implementation of a classification strategy of Raman data collected in different clinical conditions: application to the diagnosis of chronic lymphocytic leukemia.

Féré M, Gobinet C, Liu LH, Beljebbar A, Untereiner V, Gheldof D, Chollat M, Klossa J, **Chatelain B**, Piot O.

Références	*Doi*	*IF*
Anal Bioanal Chem. 2019 Dec 18 [Epub ahead of print]	*10.1007/s00216-019-02321-z*	*3.286*

Abstract

The literature is rich in proof of concept studies demonstrating the potential of Raman spectroscopy for disease diagnosis. However, few studies are conducted in a clinical context to demonstrate its applicability in current clinical practice and workflow. Indeed, this translational research remains far from the patient's bedside for several reasons. First, samples are often cultured cell lines. Second, they are prepared on non-standard substrates for clinical routine. Third, a unique supervised classification model is usually constructed using inadequate cross-validation strategy. Finally, the implemented models maximize classification accuracy without taking into account the clinician's needs. In this paper, we address these issues through a diagnosis problem in real clinical conditions, i.e., the diagnosis of chronic lymphocytic leukemia from fresh unstained blood smears spread on glass slides. From Raman data acquired in different experimental conditions, a repeated double cross-validation strategy was combined with different cross-validation approaches, a consensus label strategy and adaptive thresholds able to adapt to the clinician's needs. Combined with validation at the patient level, classification results were improved compared to traditional strategies

Mots-clefs

Chronic lymphocytic leukemia; Clinical practice; Label consensus; Pre-processing; Raman spectroscopy; Supervised classification algorithms

Process evaluation of a complex intervention to optimize quality of prescribing in nursing homes (COME-ON study)

Anrys P, Strauven G, Roussel S, Vande Ginste M, De Lepeleire J, Foulon V, **Spinewine A.**

Références	*Doi*	*IF*
Implement Sci. 2019 Dec 11;14(1):104.	*10.1186/s13012-019-0945-8.*	*4.345*

Abstract

BACKGROUND: The COME-ON study was a cluster-controlled trial of a complex intervention that consisted of a blended training program, local interdisciplinary meetings, and interdisciplinary case conferences in Belgian nursing homes. The intervention was associated with significant improvements in the appropriateness of prescribing. The aims of this study were to describe the implementation of the intervention and to explore the experiences of participants, for the purpose of identifying factors associated with implementation and perceived impact and to draw lessons for future implementation.

METHODS: We performed a mixed-method process evaluation. Questionnaires and reports were used to collect quantitative data on implementation and experiences from the 24 NHs and participating healthcare professionals (coordinating physicians, general practitioners, pharmacists, and nurses) in the intervention group. Multidisciplinary focus groups focusing on factors associated with implementation and perceived impact were conducted in 11 NHs.

RESULTS: Overall, the rate of implementation and the satisfaction of participants were good, despite some variability between NHs and HCPs. Although perceived impact on nursing home residents varied, most participants perceived a positive impact for themselves. Factors associated with implementation and perceived impact were identified at different levels: intervention, healthcare professionals, organization, and external context. The interdisciplinary and face-to-face approaches were recognized as key elements for the success of the intervention, despite organizational constraints. The attitude of general practitioners was identified both as a barrier to and a facilitator for implementation and its success. The professional role and competency of the pharmacist influenced perceived impact. The pre-existing relationships between HCPs and the presence of a leader facilitated implementation and perceived impact. Remuneration was deemed necessary for the study and for future implementation.

CONCLUSIONS: Overall, the intervention, and more specifically its interdisciplinary aspect, was well implemented and appreciated by HCPs. This probably contributed to the positive effect on the appropriateness of prescribing. Future implementation must take into account the various factors found to affect implementation and perceived impact, in order to maximize effect and sustainability. Trial registration Current Controlled Trials ISRCTN66138978; registered 18 November 2015, retrospectively registered, https://www.isrctn.com/ISRCTN66138978.

Mots-clefs

Complex intervention; Mixed methods; Nursing homes; Potentially inappropriate prescribing; Process evaluation

Pituitary neuroendocrine tumors (PitNETs): nomenclature evolution, not clinical revolution

Asa SL, AsioliS, Bozkurt S, Casar-Borota O, Chinezu L, **Delgrange E**, Yarman S, et al.

Références	*Doi*	*IF*
Pituiarty 2019	*10.1007/s11102-019-01015-0*	*3.335*

Abstract

Mots-clefs
Endocrinology ; Diabetes and Metabolism

Nasolabial Cysts: Case Series

Riahi I, **De Dorlodot C, Eloy P.**

Références	*Doi*	*IF*
Austin J Surg. 2019; 6(19): 1211		*2.1*

Abstract

Nasolabial cyst is a rare, benign soft tissue mass located in the nasolabial fold. It is submucosal and extra osseous. It affects more commonly middle aged women with coloured skin. They can be regularly infected or cause nasal obstruction and alar deformity. Clinical examination, nasal endoscopy and imaging are necessary to make the diagnosis. When symptomatic surgery is the treatment. It may consist of a complete excision via a transoral sublabial incision or a endonasal marsupialization. Both techniques have the same efficacy. We report herein a series of 6 patients treated successfully in the ENT department of the CHU UCL Namur from Belgium.

Mots-clefs

Nasolabial cyst; Case series; Imaging; Sublabial excision; Endonasal marsupialization

Complication sévère après injection de produit de contraste par voie intraosseuse

Thonon H, Gusu D, Glorieux D.

Références	*Doi*	*IF*
Ann Fr Med Urgence 2019;9(5):329-331	*10.3166/afmu-2019-0168*	

Abstract

La voie intraosseuse pour l'administration de solutions de remplissage est utilisée depuis la Seconde Guerre mondiale après le développement de la technique au début du XX e siècle. Beaucoup de publications ont remis cette technique en lumière durant la dernière décennie, particulièrement dans le domaine de l'urgence pédiatrique. Actuellement, cette technique est validée tant chez l'enfant que chez l'adulte. Cette voie d'accès est principalement utilisée chez le patient critique après l'échec des tentatives de placement de voies d'accès intravasculaires classiques. Dans certaines conditions, comme lors de la prise en charge du patient traumatisé hémodynamiquement instable, la voie d'accès intraosseuse est souvent placée sur le terrain pour permettre une perfusion rapide de solutés de remplissage ou l'administration de médicaments. Après restauration d'un équilibre hémodynamique, la question se pose de savoir si cette voie d'accès peut être utilisée pour injecter un produit de contraste avant la réalisation d'un scanner d'évaluation des lésions traumatiques. Nous décrivons ici une complication sérieuse survenue après l'usage d'un dispositif intraosseux dans ces conditions.

Mots-clefs

Les cancers thyroidiens avancés bénéficient-ils également de l'émergence des nouvelles molécules?

Faugeras L, Pirson AS, Donckier J, Michel L, Van Der Vorst S, D'Hondt L.

Références	*Doi*	*IF*
Hemato Oncol 2019;13(2):22-29		

Abstract

Depuis quelques dizaines d'années, la fréquence du cancer de la thyroïde est en nette progression; toutefois, son taux de mortalité reste stable. La plupart de ces cancers sont traités par chirurgie
suivie ou non de radio-iode en fonction du sous-type tumoral. Malgré cela, un certain nombre de patients récidiveront et pourront être traités par radio-iode ou reprise chirurgicale. Mais que
faire en cas de cancer thyroïdien localement avancé ou métastatique réfractaire au radio-iode? La chimiothérapie donne de très faibles taux de réponse. En revanche, ces dernières années, plusieurs
thérapies systémiques ont émergé et ont permis d'améliorer la survie globale de ces patients, notamment les thérapies ciblées, mais certaines pistes de recherche intéressantes sont en cours
d'étude, à savoir le traitement par Peptide Receptor Radionuclide Therapy ou bien l'immunothérapie.

Mots-clefs

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