RECUEIL DES PUBLICATIONS SCIENTIFIQUES DU CHU UCL NAMUR

N°2 - DEUXIÈME QUADRIMESTRE 2018

Dinant • Godinne • Sainte-Elisabeth

CHU UCL NAMUR

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Cher(e)s collègues,
Madame, Monsieur,

La parution du premier recueil des Publications Scientifiques de CHU UCL Namur nous a permis d'améliorer la collecte des travaux de nos chercheurs au sein du CHU UCL Namur. Les articles parus durant le premier quadrimestre et ne figurant pas dans le premier numéro sont tous repris en début de celui-ci.

Durant les 8 premiers mois de l'année, le CHU UCL Namur a publié près de 150 articles scientifiques dans de nombreux journaux médicaux. Ce nombre illustre la vitalité de nos chercheurs dans les différents services médicaux de notre institution.

Au-delà de la mission première de notre institution qui est de prodiguer des soins d'excellence aux patients, nous démontrons notre dynamisme et notre investissement dans les missions de Recherche, d'Enseignement et de Services à la Société qui nous sont confiées par l'Université catholique de Louvain.

Nous vous invitons à parcourir ce deuxième numéro distraitement, pour juste en prendre connaissance, ou de façon approfondie, pour y déceler des pistes de collaborations scientifiques ou pour découvrir les travaux de votre médecin, de vos collaborateurs ou de vos collègues.

Bonne lecture !

Professeur Maximilien Gourdin
Directeur aux Affaires Académiques
CHU UCL Namur

SUPPLÉMENT
PREMIER QUADRIMESTRE 2018

Genital Granulomatosis in Male and Female Patients With Crohn's Disease: Clinical Presentation and Treatment Outcomes.

Dederichs F, Iesalnieks I, Sladek M, Tzivinikos C, Hansen R, Muñoz C, Pavli P, Cavicchi M, Abitbol V, **Rahier JF**, Vavricka S, Katsanos K, Domènech E; ECCO-CONFER investigators.

Références	*Doi*	*IF*
J Crohns Colitis. 2018 Jan 24;12(2):197-203	*10.1093/ecco-jcc/jjx131*	*6,637*

Abstract

BACKGROUND: Genital granulomatosis [GG] is a metastatic form of Crohn's disease [CD], characterised by granulomatous inflammation of the genital skin without contact with the gastrointestinal tract. Little is known about GG, as most publications are case reports or small series, and only sporadic in male cases.

METHODS AND AIMS: Cases of GG were retrospectively collected through the Collaborative Network For Exceptionally Rare case reports project of the European Crohn's and Colitis Organisation.

RESULTS: A total of 43 patients [9 males, 34 females] were diagnosed as having GG, mostly as oedema and/or ulcers. Histological confirmation of granulomas was obtained in 70% of the cases. CD location was colonic or ileocolonic in 97% and perianal disease was documented in 57%. There was no significant difference between males and females in CD phenotype or genital lesions. GG was the first manifestation of inflammatory bowel disease [IBD] in one-third of the patients; these patients were younger at the time of GG occurrence and they all were non-smokers. GG occurred in the absence of gastrointestinal disease activity in 30% of the cases. Ten out of 11 patients [91%] responded to systemic corticosteroid treatment, 5/9 patients responded to immunomodulators, and 9/11 patients responded to anti-tumour necrosis factor alpha [TNF-α] agents.

CONCLUSIONS: GG is a rare extraintestinal manifestation of CD. It mainly occurs among women, in the setting of colonic involvement of CD, and perianal disease is often associated. Most cases are successfully managed with systemic corticosteroids or anti-TNF agents.

Mots-clefs

Crohn's disease; genital granulomatosis; penile; scrotal; vulvar

Centralisation des injectales et réseaux hospitaliers.

Hecq JD.

Références	*Doi*	*IF*
J Pharm Belg 2018 ;100 :16-17		

Abstract

La stabilité physico-chimique d'une préparation injectable (IV) est conditionnée par différents paramètres.

Une collaboration entre pharmacie, laboratoire de chimie et statisticiens de l'unité de support scientifique s'est installée en 1996 afin de réaliser des études de stabilité chimique à long terme d'IV couramment utilisés et de pouvoir prendre en charge leur préparation en pharmacie. En 22 ans d'activité, 29 médicaments ont été reconstitués en ambiance stérile et stockés à différentes température : 32°C, 17 à 25°C, 5±3°C, -20°C. La stabilité de la concentration a été évaluée par analyse de régression. Les résultats ont été diffusés par 51 publications et 77 posters.

Le thème de l'édition 2017 était consacré aux futurs réseaux hospitaliers.

Mots-clefs

Stability of Concentrated Solution of Vancomycin Hydrochloride in Syringes for Intensive Care Units.

Godet M, Simar J, Closset M, **Hecq JD, Braibant M, Soumoy L, Jamart J, Bihin B, Galanti L.**

Références	*Doi*	*IF*
Pharm Technol Hosp Pharm 2018 ;3(1) :23-30	*10.1515/pthp-2017-0031*	

Abstract

BACKGROUND: Vancomycin is increasingly administrated by continuous infusion. But the treatment of patient in intensive care need restricted volume to prevent fluid overload. The aim of the study was to evaluate the physical and chemical stability of solutions of a high concentration of vancomycin hydrochloride in 5% glucose or 0.9% NaCl.
METHODS: Eight syringes of 50mL, containing 41.66mg/mL of vancomycin hydrochloride four syringes in 5% glucose and four in 0.9% NaCl were prepared and stored at ambient temperature during 48 h. Immediately after preparation and during 48 h, vancomycin hydrochloride concentrations were measured by a high-performance liquid chromatography (HPLC). Spectrophotometric absorbance at different wavelengths, pH measurement and
microscopic observations were also performed..
RESULTS: All solutions were physico-chemically stable during the whole period storage at ambient temperature: no color change, turbidity, precipitation or opacity, no significant pH variations or optic densities were observed in the solutions. Any crystals were seen by microscopic analysis. Solutions are considered chemically stable as the lower limit of the 95% unilateral confidence interval on the mean remained above 90% of the initial concentration
for at least 48 h.
CONCLUSIONS: Solutions of vancomycin hydrochloride 41.66 mg/mL in syringe of 5% glucose or 0.9% NaCl are physically and chemically stable for at least 48 h when stored in syringes at ambient temperature.

Mots-clefs

Pharmacie hospitalière en Belgique : 65 ans d'histoire.

Hecq JD, Buyle F.

Références	*Doi*	*IF*
J Pharm Belg 2018 ;100 :6-10		

Abstract

En 2018, l'Association Belge des Pharmaciens d'Hôpitaux-de Belgische Vereniging van Ziekenhuis Apothekers (ABPH-BVZA) fêtera ses 65 ans d'existence. Créée en 1953, cette association professionnelle et scientifique, devenue une société royale, représente l'ensemble des pharmaciens qui travaillent dans des établissements hospitaliers, qu'ils soient privés ou publics, universitaires, généraux ou psychiatriques. Le but de ce court article est de raconter l'histoire de ce développement en quelques mots.

Mots-clefs

New insights into the clinical signs of supraventricular tachycardia: The «sign of lace-tying».

Blommaert D, Dormal F, Deceuninck O, Xhaet O, Ballant E, De Roy L.

Références	*Doi*	*IF*
Ann Noninvasive Electrocardiol. 2018 Jan;23(1)	*10.1111/anec.12471*	*1,562*

Abstract

BACKGROUND: Supraventricular tachycardias (SVT) are a common arrhythmia therefore an accurate diagnosis is of clinical importance. Although an ECG performed during tachycardia greatly aids diagnosis, patient history and predisposing factors also improve diagnostic accuracy.

METHODS: This prospective study included 100 consecutive patients undergoing electrophysiological study for SVT with the aim to reassess their clinical characteristics and describe frequent predisposing factors, such as the «sign of lace-tying» that to our knowledge has not previously been reported. Each patient completed an extensive questionnaire (70 questions) during their hospital stay.

RESULTS: Our series comprised: 67% of patients with atrioventricular nodal reentrant tachycardia (AVNRT); 24% with an accessory pathway; and 9% presented atrial tachycardia. Half of the population were male and 29% of the cohort presented hypertension. Syncope during tachycardia appeared in 15% of patients, dizziness in 52% and thoracic pain in 59%. We encountered a predisposing risk factor for SVT in 53% of cases; with 32% exhibiting an anteflexion of the trunk termed the «sign of lace-tying.» Data also showed that younger patients tended to present AVRT and regular pounding in the neck appeared only in patients with AVNRT.

CONCLUSIONS: Overall, our study has highlighted the importance of considering clinical signs and patient characteristics both before and during SVT for the precise diagnosis of paroxysmal SVT. Furthermore, 32% of patients presented the «sign of lace-tying» or body position change before SVT, implying a diagnosis of SVT.

Mots-clefs

Anamnesis; sign of lace-tying; supraventricular tachycardia; syncope

Extended adjuvant intermittent letrozole versus continuous letrozole in postmenopausal women with breast cancer (SOLE): a multicentre, open-label, randomised, phase 3 trial.

Colleoni M, Luo W, Karlsson P, Chirgwin J, Aebi S, Jerusalem G, Neven P, Hitre E, Graas MP, Simoncini E, Kamby C, Thompson A, Loibl S, Gavilá J, Kuroi K, Marth C, Müller B, O'Reilly S, Di Lauro V, Gombos A, Ruhstaller T, Burstein H, Ribi K, Bernhard J, Viale G, Maibach R, Rabaglio-Poretti M, Gelber RD, Coates AS, Di Leo A, Regan MM, Goldhirsch A; SOLE Investigators. **Vuylsteke P.**

Références	*Doi*	*IF*
Lancet Oncol. 2018 Jan;19(1):127-138	*10.1016/S1470-2045(17)30715-5*	*36,418*

Abstract

BACKGROUND: In animal models of breast cancer, resistance to continuous use of letrozole can be reversed by withdrawal and reintroduction of letrozole. We therefore hypothesised that extended intermittent use of adjuvant letrozole would improve breast cancer outcome compared with continuous use of letrozole in postmenopausal women.

METHODS: We did the multicentre, open-label, randomised, parallel, phase 3 SOLE trial in 240 centres (academic, primary, secondary, and tertiary care centres) in 22 countries. We enrolled postmenopausal women of any age with hormone receptor-positive, lymph node-positive, and operable breast cancer for which they had undergone local treatment (surgery with or without radiotherapy) and had completed 4-6 years of adjuvant endocrine therapy. They had to be clinically free of breast cancer at enrolment and without evidence of recurrent disease at any time before randomisation. We randomly assigned women (1:1) to treatment groups of either continuous use of letrozole (2.5 mg/day orally for 5 years) or intermittent use of letrozole (2.5 mg/day orally for 9 months followed by a 3-month break in years 1-4 and then 2.5 mg/day during all 12 months of year 5). Randomisation was done by principal investigators or designee at respective centres through the internet-based system of the International Breast Cancer Study Group, was stratified by type of previous endocrine therapy (aromatase inhibitors only vs selective oestrogen receptor modulators only vs both therapies), and used permuted block sizes of four and institutional balancing. No one was masked to treatment assignment. The primary endpoint was disease-free survival, analysed by the intention-to-treat principle using a stratified log-rank test. All patients in the intention-to-treat population who initiated protocol treatment during their period of trial participation were included in the safety analyses. This study is registered with ClinicalTrials.gov, number NCT00553410, and EudraCT, number 2007-001370-88; and long-term follow-up of patients is ongoing.

FINDINGS: Between Dec 5, 2007, and Oct 8, 2012, 4884 women were enrolled and randomised after exclusion of patients at a non-adherent centre, found to have inadequate documentation of informed consent, immediately withdrew consent, or randomly assigned to intervention groups in error. 4851 women comprised the intention-to-treat population that compared extended intermittent letrozole use (n=2425) with continuous letrozole use (n=2426). After a median follow-up of 60 months (IQR 53-72), disease-free survival was 85.8% (95% CI 84.2-87.2) in the intermittent letrozole group compared with 87.5% (86.0-88.8) in the continuous letrozole group (hazard ratio 1.08, 95% CI 0.93-1.26; p=0.31). Adverse events were reported as expected and were similar between the two groups. The most common grade 3-5 adverse events were hypertension (584 [24%] of 2417 in the intermittent letrozole group vs 517 [21%] of 2411 in the continuous letrozole group) and arthralgia (136 [6%] vs 151 [6%]). 54 patients (24 [1%] in the intermittent letrozole group and 30 [1%] in the continuous letrozole group) had grade 3-5 CNS cerebrovascular ischaemia, 16 (nine [<1%] vs seven [<1%]) had grade 3-5 CNS haemorrhage, and 40 (19 [1%] vs 21 [1%]) had grade 3-5 cardiac ischaemia. In total, 23 (<1%) of 4851 patients died while on trial treatment (13 [<1%] of 2417 patients in the intermittent letrozole group vs ten [<1%] of 2411 in the continuous letrozole group).

INTERPRETATION: In postmenopausal women with hormone receptor-positive breast cancer, extended use of intermittent letrozole did not improve disease-free survival compared with continuous use of letrozole. An alternative schedule of extended adjuvant endocrine therapy with letrozole, including intermittent administration, might be feasible and the results of the SOLE trial support the safety of temporary treatment breaks in selected patients who might require them.

Mots-clefs

A reminder of the place of morphology and the H-score in the diagnosis of hemophagocytic lymphohistiocytosis (HLH).

Favresse J, Lardinois B, Chatelain B, Mullier F, Jacqmin H.

Références	*Doi*	*IF*
Clin Case Rep. 2018 Feb 6;6(3):527-528	*10.1002/ccr3.1391*	

Abstract

This case report reminds the reader of the place of hemophagocytosis and the H-Score in the diagnosis of secondary hemophagocytic lymphohistiocytosis.

Mots-clefs

HLH; H-score; hemophagocytic syndrome; hemophagocytosis

Laboratory testing in patients treated with direct oral anticoagulants: a practical guide for clinicians.

Douxfils J, Ageno W, Samama CM, **Lessire S,** Ten Cate H, Verhamme P, Dogné JM, **Mullier F.**

Références	*Doi*	*IF*
J Thromb Haemost. 2018 Feb;16(2):209-219	*10.1111/jth.13912*	*4,899*

Abstract

Click to hear Dr Baglin's perspective on the role of the laboratory in treatment with new oral anticoagulants SUMMARY: One of the key benefits of the direct oral anticoagulants (DOACs) is that they do not require routine laboratory monitoring. Nevertheless, assessment of DOAC exposure and anticoagulant effects may become useful in various clinical scenarios. The five approved DOACs (apixaban, betrixaban, dabigatran etexilate, edoxaban and rivaroxaban) have different characteristics impacting assay selection and the interpretation of results. This article provides an updated overview on (i) which test to use (and their advantages and limitations), (ii) when to assay DOAC levels, (iii) how to interpret the results relating to bleeding risk, emergency situations and perioperative management, and (iv) what is the impact of DOACs on routine and specialized coagulation assays. Assays for anti-Xa or anti-IIa activity are the preferred methods when quantitative information is useful, although the situations in which to test for DOAC levels are still debated. Different reagent sensitivities and variabilities in laboratory calibrations impact assay results. International calibration standards for all specific tests for each DOAC are needed to reduce the inter-laboratory variability and allow inter-study comparisons. The impact of the DOACs on hemostasis testing may cause false-positive or false-negative results; however, these can be minimized by using specific assays and collecting blood samples at trough concentrations. Finally, prospective clinical trials are needed to validate the safety and efficacy of proposed laboratory thresholds in relation to clinical decisions. We offer recommendations on the tests to use for measuring DOACs and practical guidance on laboratory testing to help patient management and avoid diagnostic errors.

Mots-clefs

apixaban; dabigatran; edoxaban; laboratory testing; practical management; rivaroxaban

European guidelines on perioperative venous thromboembolism prophylaxis: Patients with preexisting coagulation disorders and after severe perioperative bleeding.

Ahmed A, Kozek-Langenecker S, **Mullier F,** Pavord S, Hermans C; ESA VTE Guidelines Task Force.

Références	*Doi*	*IF*
Eur J Anaesthesiol. 2018 Feb;35(2):96-107	*10.1097/EJA.0000000000000725*	*3,958*

Abstract

In patients with inherited bleeding disorders undergoing surgery, we recommend assessment of individual risk for venous thromboembolism, taking into account the nature of the surgery and anaesthetic, type and severity of bleeding disorder, age, BMI, history of thrombosis, the presence of malignancy and other high-risk comorbidities. Venous thromboembolism risk should be balanced against the increased bleeding risk associated with anticoagulant use in patients with known bleeding disorders (Grade 1C). In these patients undergoing major surgery, we recommend against routine postoperative use of pharmacological thromboprophylaxis, especially for patients with haemophilia A and B (Grade 1B). Glomerular filtration rate should be assessed before initiation of each direct oral anticoagulant, and also at least once a year or more frequently as needed, such as postoperatively before the resumption of therapeutic direct oral anticoagulant administration, when it is suspected that renal function could decline or deteriorate (Grade 1C). Reduced dosages of low molecular weight heparins may be used relatively safely during transient severe (‹50×10l) thrombocytopaenia (Grade 2C). Monitoring of anti-Xa levels may be used to adjust the doses of low molecular weight heparin in patients with moderate or severe thrombocytopaenia (Grade 2C). The delay between major gastrointestinal bleeding and resuming warfarin should be at least 7 days (Grade 2C). For patients at a high risk of thromboembolism and with a high bleeding risk after surgery, we consider that administering a reduced dose of direct oral anticoagulant on the evening after surgery and on the following day (first postoperative day) after surgery is a good practice (Grade 2B).

Mots-clefs

Implementing a screening tool to improve prescribing in hospitalized older patients: a pilot study.

Sennesael AL, Dalleur O, Henrard S, Artoisenet C, Schoevaerdts D, Spinewine A.

Références	*Doi*	*IF*
Int J Clin Pharm. 2018 Feb;40(1):15-19	*10.1007/s11096-017-0563-y*	*1,508*

Abstract

Background The use of STOPP-START criteria during hospitalization reduced inappropriate medications in randomized controlled trials. Objective To evaluate whether the implementation of a screening tool (short version of STOPP-START criteria) in routine geriatric practice reduces potentially inappropriate medications (PIM) and potential prescribing omissions (PPO) at discharge. Methods We conducted a retrospective interrupted time series analysis. Four periods were selected between February and September 2013: (1) baseline situation; (2) screening tool made available to physicians; (3) 3 months later; (4) weekly meetings with junior doctors and a clinical pharmacist to review treatments according to the tool. The primary outcome was the proportion of patients with prescribing improvement from admission to discharge. Results We included 120 patients (median age 85 years). The prevalence of PIMs and PPOs on admission was 56% (67/120) and 51% (61/120) respectively. Hospitalization improved prescribing appropriateness in 49% of patients with PIMs (33/67) and 39% of patients with PPOs (24/61). The use of the screening tool by way of multidisciplinary meetings was a predictor of PIMs reduction at discharge. Conclusions The sole distribution of a screening tool in a geriatric unit did not reduce PIMs and PPOs. Multidisciplinary meetings to review treatments should be encouraged.

Mots-clefs

Belgium; Hospitalisation; Inappropriate prescribing; Older patients; STOPP/START criteria

Interprofessional Teamwork in Acute Geriatric Care: Where Are the Pharmacists ?

Spinewine A, Mouzon A, Dalleur O, **de Saint Hubert M,** Cornette P, **Schoevaerdts D.**

Références	*Doi*	*IF*
J Am Geriatr Soc. 2018 Feb;66(2):416-417	*10.1111/jgs.15177*	*4,155*

Abstract

Mots-clefs

Application of a clot-based assay to measure the procoagulant activity of stored allogeneic red blood cell concentrates.

Devalet B, Wannez A, **Bailly N,** Alpan L, **Gheldof D,** Douxfils J, **Deneys V, Bihin B, Chatelain B,** Dogné JM, **Chatelain C, Mullier F.**

Références	*Doi*	*IF*
Blood Transfus. 2018 Feb;16(2):163-172	*10.2450/2017.0230-16*	*2,138*

Abstract

BACKGROUND: Thrombotic effects are possible complications of red blood cell transfusion. The generation and accumulation of procoagulant red blood cell extracellular vesicles during storage may play an important role in these thrombotic effects. The objective of this study was to assess the value of a simple phospholipid-dependent clot-based assay (STA®-Procoag-PPL) to estimate the procoagulant activity of stored red blood cells and changes in this activity during storage of the blood component.
MATERIALS AND METHODS: Extracellular vesicles from 12 red blood cell concentrates were isolated at 13 storage time-points and characterised by quantitative and functional methods: the degree of haemolysis (direct spectrophotometry), the quantification and determination of cellular origin (flow cytometry) and the procoagulant activity (thrombin generation and STA®-Procoag-PPL assays) were assessed.
RESULTS: The mean clotting time of extracellular vesicles isolated from red blood cell concentrates decreased from 117.2±3.6 sec on the day of collection to 33.8±1.3 sec at the end of the storage period. This illustrates the phospholipid-dependent procoagulant activity of these extracellular vesicles, as confirmed by thrombin generation. Results of the peak of thrombin and the STA®-Procoag-PPL were well correlated (partial r=-0.41. p<0.001). In parallel, an exponential increase of the number of red blood cell-derived extracellular vesicles from 1,779/µL to 218,451/µL was observed.
DISCUSSION: The STA®-Procoag-PPL is a potentially useful technique for assessing the procoagulant activity of a red blood cell concentrate.

Mots-clefs

A high sense of coherence protects from the burden of caregiving in older spousal caregivers.

Potier F, Degryse JM, Henrard S, **Aubouy G, de Saint-Hubert M.**

Références	*Doi*	*IF*
Arch Gerontol Geriatr. 2018 Mar - Apr;75:76-82	*10.1016/j.archger.2017.11.013*	*2,241*

Abstract

OBJECTIVES: Caregiving is often associated with burden and chronic stress. Sense of coherence (SOC) may help the caregivers in coping with their stress and was identified as a positive factor for health outcomes and quality of life. We aimed to study the links between SOC, burden, depression and positive affects among caregivers of frail older patients.

METHODS: Seventy-nine spousal caregivers were recruited via the geriatric outpatient clinic.

DATA COLLECTED: Zarit Burden Inventory, SOC-13, Geriatric Depression Scale, Caregiver Reaction Assessment (CRA), sleep, time of supervision, Katz Index, Global Deterioration Scale and Neuropsychiatric Inventory.

ANALYSES: Caregiver's characteristics were analyzed by burden severity and SOC level. Multivariable logistic regressions were used in order to identify the variable that best predict caregiver burden and high SOC.

RESULTS: The mean age was 79.4±5.3; 53% were women. Among care-recipient, 82% had cognitive impairment and the median Katz Index was 3. Caregivers with a high SOC and an older age reported a lower burden (Odds Ratio (OR) 0.18, 95% confidence interval (CI) 0.04-0.65 and OR 0.87, 95% CI 0.76-0.98, respectively). A higher burden was associated with patient functional limitations (OR 8.69, 95% CI 2.28-40.46).

DISCUSSION: Having a high sense of coherence seems to be a protective factor against the burden. To support caregivers, health providers should recognize the expertise of the caregivers and the meaningfulness of this care situation.

Mots-clefs

Informal care; Meaningfulness; Salutogenesis; Self-fulfillment

Pertuzumab and trastuzumab with or without metronomic chemotherapy for older patients with HER2-positive metastatic breast cancer (EORTC 75111-10114): an open-label, randomised, phase 2 trial from the Elderly Task Force/Breast Cancer Group.

Wildiers H, Tryfonidis K, Dal Lago L, **Vuylsteke P,** Curigliano G, Waters S, Brouwers B, Altintas S, Touati N, Cardoso F, Brain E.

Références	*Doi*	*IF*
Lancet Oncol. 2018 Mar;19(3):323-336	*10.1016/S1470-2045(18)30083-4*	*36,418*

Abstract

BACKGROUND: Despite the high incidence of metastatic breast cancer and its related mortality in the elderly population, our knowledge about optimal treatment for older patients with cancer is far from adequate. We aimed to evaluate the efficacy of dual anti-HER2 treatment with or without metronomic chemotherapy in older patients with HER2-positive metastatic breast cancer.

METHODS: We did a multicentre, open-label, randomised, phase 2 trial in 30 centres from eight countries in Europe, in patients with histologically proven, HER2-positive metastatic breast cancer, without previous chemotherapy for metastatic disease, who were 70 years or older, or 60 years or older with confirmed functional restrictions defined by protocol, and had a life expectancy of more than 12 weeks and a performance status according to WHO scale of 0-3. Eligible patients were randomly assigned (1:1) by an online randomisation system based on the minimisation method to receive metronomic oral cyclophosphamide 50 mg per day plus trastuzumab and pertuzumab, or trastuzumab and pertuzumab alone. Trastuzumab was given intravenously with a loading dose of 8 mg/kg, followed by 6 mg/kg every 3 weeks. Pertuzumab was given intravenously with a loading dose of 840 mg, followed by 420 mg every 3 weeks. Patients were stratified by hormone receptor positivity, previous HER2 treatment, and baseline geriatric screening. The primary endpoint was investigator-assessed progression-free survival at 6 months as per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. A difference of 10% or greater between the two groups was sought. Efficacy analyses were by intention to treat; safety was assessed in all patients who received at least one dose of study treatment. In case of progression, all patients were offered trastuzumab emtansine. This trial is registered with ClinicalTrials.gov, number NCT01597414, and is completed.

FINDINGS: Between July 2, 2013, and May 10, 2016, 80 patients, of whom 56 (70%) had a potential frailty profile according to the geriatric screening G8 score (≤14), were randomly assigned to receive trastuzumab and pertuzumab (n=39) or trastuzumab and pertuzumab plus metronomic oral cyclophosphamide (n=41). Estimated progression-free survival at 6 months was 46.2% (95% CI 30.2-60.7) with trastuzumab and pertuzumab versus 73.4% (56.6-84.6) with trastuzumab and pertuzumab plus metronomic oral cyclophosphamide (hazard ratio [HR] 0.65 [95% CI 0.37-1.12], p=0.12). At a median follow-up of 20.7 months (IQR 12.5-30.4), the median progression-free survival was 5.6 months (95% CI 3.6-16.8) with trastuzumab and pertuzumab versus 12.7 months (6.7-24.8) with the addition of metronomic oral cyclophosphamide. The most frequent grade 3-4 adverse events were hypertension (in six [15%] of 39 patients in the trastuzumab and pertuzumab group vs five [12%] of 41 in the trastuzumab and pertuzumab plus metronomic oral cyclophosphamide group), diarrhoea (four [10%] vs five [12%]), dyspnoea (two [5%] vs four [10%]), fatigue (three [8%] vs two [5%]), pain (two [5%] vs two [5%]), and a thromboembolic event (0 [0%] vs four [10%]). Severe cardiac toxicities were occasionally observed in both groups. In the trastuzumab and pertuzumab group four patients died without progression, due to cardiac arrest during treatment (n=1), peritoneal infection (n=1), respiratory failure (n=1), and sudden death without a specified cause (n=1). In the trastuzumab and pertuzumab plus metronomic oral cyclophosphamide group, one patient died from heart failure.

INTERPRETATION: Addition of metronomic oral cyclophosphamide to trastuzumab plus pertuzumab in older and frail patients with HER2-positive metastatic breast cancer increased median progression-free survival by 7 months compared with dual HER2 blockade alone, with an acceptable safety profile. Trastuzumab and pertuzumab plus metronomic oral cyclophosphamide, followed by trastuzumab emtansine after disease progression, might delay or supersede the need for taxane chemotherapy in this population.

FUNDING: F Hoffmann-La Roche.

Mots-clefs

Comparison of 36 Gy, 20 Gy, or No Radiation Therapy After 6 Cycles of EBVP Chemotherapy and Complete Remission in Early-Stage Hodgkin Lymphoma Without Risk Factors: Results of the EORT-GELA H9-F Intergroup Randomized Trial.

Thomas J, Fermé C, Noordijk EM, Morschhauser F, Girinsky T, Gaillard I, Lugtenburg PJ, **André M**, Lybeert MLM, Stamatoullas A, Beijert M, Hélias P, Eghbali H, Gabarre J, van der Maazen RWM, Jaubert J, Bouabdallah K, Boulat O, Roesink JM, Christian B, Ong F, Bordessoule D, Tertian G, Gonzalez H, Vranovsky A, Quittet P, Tirelli U, de Jong D, Audouin J, Aleman BMP, Henry-Amar M.

Références	*Doi*	*IF*
Int J Radiat Oncol Biol Phys. 2018 Apr 1;100(5):1133-1145	*10.1016/j.ijrobp.2017.10.015*	*5,554*

Abstract

PURPOSE: While patients with early-stage Hodgkin lymphoma (HL) have an excellent outcome with combined treatment, the radiation therapy (RT) dose and treatment with chemotherapy alone remain questionable. This noninferiority trial evaluates the feasibility of reducing the dose or omitting RT after chemotherapy.

METHODS AND MATERIALS: Patients with untreated supradiaphragmatic HL without risk factors (age ≥ 50 years, 4 to 5 nodal areas involved, mediastinum-thoracic ratio ≥ 0.35, and erythrocyte sedimentation rate ≥ 50 mm in first hour without B symptoms or erythrocyte sedimentation rate ≥ 30 mm in first hour with B symptoms) were eligible for the trial. Patients in complete remission after chemotherapy were randomized to no RT, low-dose RT (20 Gy in 10 fractions), or standard-dose involved-field RT (36 Gy in 18 fractions). The limit of noninferiority was 10% for the difference between 5-year relapse-free survival (RFS) estimates. From September 1998 to May 2004, 783 patients received 6 cycles of epirubicin, bleomycin, vinblastine, and prednisone; 592 achieved complete remission or unconfirmed complete remission, of whom 578 were randomized to receive 36 Gy (n=239), 20 Gy of involved-field RT (n=209), or no RT (n=130).

RESULTS: Randomization to the no-RT arm was prematurely stopped (≥20% rate of inacceptable events: toxicity, treatment modification, early relapse, or death). Results in the 20-Gy arm (5-year RFS, 84.2%) were not inferior to those in the 36-Gy arm (5-year RFS, 88.6%) (difference, 4.4%; 90% confidence interval [CI] -1.2% to 9.9%). A difference of 16.5% (90% CI 8.0%-25.0%) in 5-year RFS estimates was observed between the no-RT arm (69.8%) and the 36-Gy arm (86.3%); the hazard ratio was 2.55 (95% CI 1.44-4.53; P<.001). The 5-year overall survival estimates ranged from 97% to 99%.

CONCLUSIONS: In adult patients with early-stage HL without risk factors in complete remission after epirubicin, bleomycin, vinblastine, and prednisone chemotherapy, the RT dose may be limited to 20 Gy without compromising disease control. Omitting RT in these patients may jeopardize the treatment outcome.

Mots-clefs

Risk factors of perioperative morbimortality after laparoscopic sleeve gastrectomy: a club coelio multicenter study.

Tulelli B, Loi P, van Vyve E, Johanet H, Fromont G, Dabrowski A, Piquart A, Delaunay T, Ledaguenel P, Navez B, Maisonnette F, Lepere M, Dugué T, **Demoor V**, Bokobza B, Staudt J, Hauters P, Malvaux P, Closset J.

Références	*Doi*	*IF*
Acta Chir Belg. 2018 Apr;118(2):94-98	*10.1080/00015458.2017.1379804*	*0,42*

Abstract

OBJECTIVES: Postoperative complications after Laparoscopic sleeve gastrectomy (LSG) can dramatically compromise patient's outcome. The aim of this study is to analyze the per- and postoperative short-term outcomes after LSG and to assess predictive risk factors of complications.

METHODS: The study group consisted of 790 patients (610 women and 180 men) who underwent LSG In 2014. All interventions were performed by 18 experienced surgeons members of the Club Coelio. Data about preoperative work-up, surgical techniques, 30-days postoperative morbidity and mortality were collected. Endpoints were perioperative morbidity and mortality and assessment of potential risk factors for complications.

RESULTS: Mean age and body mass index were respectively 39 years and 41.5kg/m2. Ninety-one patients (11.5%) had previous bariatric surgery. Morbidity rate was 4.7% (37/790) including 16 leaks (2.0%) and 9 bleedings (1.1%) and no deaths. Risk factors for leak were: previous adjustable banding ($p = .0051$), with no difference between removal of the banding and LSG in 1 or 2 steps, and type of endostapler ($p = .0129$).

CONCLUSIONS: Leakage after Sleeve was rare but still observed even in experienced hands. The leak rate is particularly high when LSG is performed after adjustable gastric banding removal.

Mots-clefs

Bariatric surgery; postoperative morbidity; revisional surgery; sleeve gastrectomy

RECUEIL DES PUBLICATIONS SCIENTIFIQUES DU CHU UCL NAMUR

N°2 - DEUXIÈME QUADRIMESTRE 2018

MAI

1

Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines.

Arvanitakis M, Dumonceau JM, Albert J, **Badaoui A,** Bali MA, Barthet M, Besselink M, Deviere J, Oliveira Ferreira A, Gyökeres T, Hritz I, Hucl T, Milashka M, Papanikolaou IS, Poley JW, Seewald S, Vanbiervliet G, van Lienden K, van Santvoort H, Voermans R, Delhaye M, van Hooft J.

Références	*Doi*	*IF*
Endoscopy. 2018 May;50(5):524-546	*10.1055/a-0588-5365*	*6,629*

Abstract

1: ESGE suggests using contrast-enhanced computed tomography (CT) as the first-line imaging modality on admission when indicated and up to the 4th week from onset in the absence of contraindications. Magnetic resonance imaging (MRI) may be used instead of CT in patients with contraindications to contrast-enhanced CT, and after the 4th week from onset when invasive intervention is considered because the contents (liquid vs. solid) of pancreatic collections are better characterized by MRI and evaluation of pancreatic duct integrity is possible. Weak recommendation, low quality evidence.
2: ESGE recommends against routine percutaneous fine needle aspiration (FNA) of (peri)pancreatic collections. Strong recommendation, moderate quality evidence. FNA should be performed only if there is suspicion of infection and clinical/imaging signs are unclear. Weak recommendation, low quality evidence.
3: ESGE recommends initial goal-directed intravenous fluid therapy with Ringer's lactate (e.g. 5-10mL/kg/h) at onset. Fluid requirements should be patient-tailored and reassessed at frequent intervals. Strong recommendation, moderate quality evidence.
4: ESGE recommends against antibiotic or probiotic prophylaxis of infectious complications in acute necrotizing pancreatitis. Strong recommendation, high quality evidence.
5: ESGE recommends invasive intervention for patients with acute necrotizing pancreatitis and clinically suspected or proven infected necrosis. Strong recommendation, low quality evidence.ESGE suggests that the first intervention for infected necrosis should be delayed for 4 weeks if tolerated by the patient. Weak recommendation, low quality evidence.
6: ESGE recommends performing endoscopic or percutaneous drainage of (suspected) infected walled-off necrosis as the first interventional method, taking into account the location of the walled-off necrosis and local expertise. Strong recommendation, moderate quality evidence.
7: ESGE suggests that, in the absence of improvement following endoscopic transmural drainage of walled-off necrosis, endoscopic necrosectomy or minimally invasive surgery (if percutaneous drainage has already been performed) is to be preferred over open surgery as the next therapeutic step, taking into account the location of the walled-off necrosis and local expertise. Weak recommendation, low quality evidence.
8: ESGE recommends long-term indwelling of transluminal plastic stents in patients with disconnected pancreatic duct syndrome. Strong recommendation, low quality evidence. Lumen-apposing metal stents should be retrieved within 4 weeks to avoid stent-related adverse effects.Strong recommendation, low quality evidence.

Mots-clefs

2

A Retrospective Belgian Multi-Center MRI Biomarker Study in Alzheimer's Disease (REMEMBER).

Niemantsverdriet E, Ribbens A, Bastin C, Benoit F, Bergmans B, Bier JC, Bladt R, Claes L, De Deyn PP, Deryck O, Hanseeuw B, Ivanoiu A, Lemper JC, **Mormont E,** Picard G, Salmon E, Segers K, Sieben A, Smeets D, Struyfs H, Thiery E, Tournoy J, Triau E, Vanbinst AM, Versijpt J, Bjerke M, Engelborghs S.

Références	*Doi*	*IF*
J Alzheimers Dis. 2018;63(4):1509-1522	*10.3233/JAD-171140*	*3.476*

Abstract

BACKGROUND: Magnetic resonance imaging (MRI) acquisition/processing techniques assess brain volumes to explore neurodegeneration in Alzheimer's disease (AD).
OBJECTIVE: We examined the clinical utility of MSmetrix and investigated if automated MRI volumes could discriminate between groups covering the AD continuum and could be used as a predictor for clinical progression.
METHODS: The Belgian Dementia Council initiated a retrospective, multi-center study and analyzed whole brain (WB), grey matter (GM), white matter (WM), cerebrospinal fluid (CSF), cortical GM (CGM) volumes, and WM hyperintensities (WMH) using MSmetrix in the AD continuum. Baseline (n=887) and follow-up (FU, n=95) T1-weighted brain MRIs and time-linked neuropsychological data were available.
RESULTS: The cohort consisted of cognitively healthy controls (HC, n=93), subjective cognitive decline (n=102), mild cognitive impairment (MCI, n=379), and AD dementia (n=313). Baseline WB and GM volumes could accurately discriminate between clinical diagnostic groups and were significantly decreased with increasing cognitive impairment. MCI patients had a significantly larger change in WB, GM, and CGM volumes based on two MRIs (n=95) compared to HC (FU›24months, p=0.020). Linear regression models showed that baseline atrophy of WB, GM, CGM, and increased CSF volumes predicted cognitive impairment.
CONCLUSION: WB and GM volumes extracted by MSmetrix could be used to define the clinical spectrum of AD accurately and along with CGM, they are able to predict cognitive impairment based on (decline in) MMSE scores. Therefore, MSmetrix can support clinicians in their diagnostic decisions, is able to detect clinical disease progression, and is of help to stratify populations for clinical trials.

Mots-clefs

Alzheimer's disease; MSmetrix; biomarkers; magnetic resonance image; volumetry

3

Impact of a clinical decision support system for drug dosage in patients with renal failure.

Desmedt S, **Spinewine A,** Jadoul M, Henrard S, Wouters D, Dalleur O.

Références	*Doi*	*IF*
Int J Clin Pharm. 2018 May 21 [Epub ahead of print]	*10.1007/s11096-018-0612-1*	*1,508*

Abstract

BACKGROUND: A clinical decision support system (CDSS) linked to the computerized physician order entry may help improve prescription appropriateness in inpatients with renal insufficiency. Objective To evaluate the impact on prescription appropriateness of a CDSS prescriber alert for 85 drugs in renal failure patients.

SETTING: Before-after study in a 975-bed academic hospital. Method Prescriptions of patients with renal failure were reviewed during two comparable periods of 6 days each, before and after the implementation of the CDSS (September 2009 and 2010). Main outcome measure The proportion of inappropriate dosages of 85 drugs included in the CDSS was compared in the pre- and post-implementation group.

RESULTS: Six hundred and fifteen patients were included in the study (301 in pre- and 314 in post-implementation periods). In the pre- and post-implementation period, respectively 2882 and 3485 prescriptions were evaluated, of which 14.9 and 16.6% triggered an alert. Among these, the dosage was inappropriate in respectively 25.4 and 24.6% of prescriptions in the pre- and post-implementation periods (OR 0.97; 95% CI 0.72-1.29). The most frequently involved drugs were paracetamol, perindopril, tramadol and allopurinol.

CONCLUSIONS: The implementation of a CDSS did not significantly reduce the proportion of inappropriate drug dosages in patients with renal failure. Further research is required to investigate the reasons why prescribers override alerts. Collaboration with clinical pharmacists might improve compliance with the CDSS recommendations.

Mots-clefs

Decision support systems; Inappropriate prescribing; Medication error; Physician order entry system; Prescription alerts; Renal insufficiency

Radiographic analysis of the listhesis associated with lumbar isthmic spondylolysis.

Legaye J.

Références	*Doi*	*IF*
Orthop Traumatol Surg Res. 2018 Sep;104(5):569-573	*10.1016/j.otsr.2018.02.017*	*1,413*

Abstract

BACKGROUND: In cases of spondylolysis, hypoplasia of L5 mimicking spondylolisthesis has been described, mainly based on MRI; however, the treatment implications have not been analyzed specifically.
OBJECTIVE: Assess the impact of hypoplasia of the L5 vertebral body in the constitution of the spondylolisthesis associated with isthmic spondylolysis.
MATERIAL AND METHODS: A retrospective radiographic study in the standing position was performed with 104 patients with L5 isthmic spondylolysis and 24 control subjects.
RESULTS: Measurements of vertebral endplate length showed that the standard apparent posterior listhesis (APL) is made up of true listhesis (TL) and false listhesis (FL). FL is induced by hypoplasia of the L5 vertebral body relative to the S1 endplate. TL results from disk failure and leads to anterior listhesis (AL), which alters the balance of spinal curvatures.
CONCLUSIONS: By integrating the potential for false listhesis into the classification systems for spondylolisthesis, we can adapt the treatment algorithms.
TYPE OF STUDY: Retrospective radiography study.
LEVEL OF EVIDENCE: IV Retrospective review of cases.

Mots-clefs

Dysplasia; Hypoplasia; Spondylolisthesis; Spondylolysis; Vertebral body

Hodgkin lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.

Eichenauer DA, Aleman BMP, **André M,** Federico M, Hutchings M, Illidge T, Engert A, Ladetto M; ESMO Guidelines Committee.

Références	*Doi*	*IF*
Ann Oncol. 2018 May 23	*10.1093/annonc/mdy080*	*13,926*

Abstract

The crude incidence of Hodgkin lymphoma (HL) in the European Union is 2.3, the mortality 0.4 cases/100 000/year. Young adults aged 20–40 years are most often affected. Slightly more men than women are diagnosed with HL. Histologically, classical HL (cHL) accounting for ~95% of all HL cases is distinguished from nodular lymphocyte-predominant HL (NLPHL) representing ~5% of all HL cases.

These guidelines present Guidelines for diagnosis, treatment and follow-up.

Mots-clefs

Resolved versus confirmed ARDS after 24 h: insights from the LUNG SAFE study.

Madotto F, Pham T, Bellani G, Bos LD, Simonis FD, Fan E, Artigas A, Brochard L, Schultz MJ, Laffey JG; LUNG SAFE Investigators and the ESICM Trials Group.

Références	*Doi*	*IF*
Intensive Care Med. 2018 May;44(5):564-577	*10.1007/s00134-018-5152-6*	*15,008*

Abstract

PURPOSE: To evaluate patients with resolved versus confirmed ARDS, identify subgroups with substantial mortality risk, and to determine the utility of day 2 ARDS reclassification.
METHODS: Our primary objective, in this secondary LUNG SAFE analysis, was to compare outcome in patients with resolved versus confirmed ARDS after 24 h. Secondary objectives included identifying factors associated with ARDS persistence and mortality, and the utility of day 2 ARDS reclassification.
RESULTS: Of 2377 patients fulfilling the ARDS definition on the first day of ARDS (day 1) and receiving invasive mechanical ventilation, 503 (24%) no longer fulfilled the ARDS definition the next day, 52% of whom initially had moderate or severe ARDS. Higher tidal volume on day 1 of ARDS was associated with confirmed ARDS [OR 1.07 (CI 1.01-1.13), P = 0.035]. Hospital mortality was 38% overall, ranging from 31% in resolved ARDS to 41% in confirmed ARDS, and 57% in confirmed severe ARDS at day 2. In both resolved and confirmed ARDS, age, non-respiratory SOFA score, lower PEEP and P/F ratio, higher peak pressure and respiratory rate were each associated with mortality. In confirmed ARDS, pH and the presence of immunosuppression or neoplasm were also associated with mortality. The increase in area under the receiver operating curve for ARDS reclassification on day 2 was marginal.
CONCLUSIONS: ARDS, whether resolved or confirmed at day 2, has a high mortality rate. ARDS reclassification at day 2 has limited predictive value for mortality. The substantial mortality risk in severe confirmed ARDS suggests that complex interventions might best be tested in this population.
TRIAL REGISTRATION: ClinicalTrials.gov NCT02010073.

Mots-clefs

ARDS Survival; ARDS reassessment; Berlin criteria ARDS; Persisting ARDS

Le PET/CT au FDG: une imagerie prometteuse du myélome multiple.

Krug B, Vander Borght T.

Références	*Doi*	*IF*
Rev multidisciplinaire Oncol Hémato 2018;2(2):34-38		

Abstract

Le myélome multiple (MM) est le 2e cancer hématologique en termes de fréquence, avec plus de 700 nouveaux cas chaque année en Belgique. Des données de plus en plus nombreuses suggèrent que la tomographie par émission de positons couplée à la tomodensitométrie au fluorodésoxyglucose marqué au fluor-18 (PET/CT au FDG) a un rôle important à jouer, non seulement au moment du diagnostic du myélome, mais également dans le suivi. Dans le bilan initial d'un MM symptomatique, il permettrait de visualiser entre 40 et 60% de nouvelles lésions, même si le bilan radiologique squelettique est négatif. Le PET/CT au FDG a une sensibilité comparable à l'IRM conventionnelle, mais ne détecte pas nécessairement les mêmes localisations. Pour le pronostic initial, le PET/CT au FDG semble plus performant que l'IRM classique. La mise en évidence de plus de 3 lésions focales ou la présence de lésions extra-médullaires hypermétaboliques est associée à un taux de survie moindre ou à une survie sans progression diminuée. Dans le cadre du suivi, il permet de prédire certaines populations à risque de progression vers un MM, de surveiller des MM non sécrétants et de distinguer les lésions actives des lésions séquellaires. Pour faciliter l'utilisation clinique du PET/CT au FDG dans le MM, un travail de standardisation de son interprétation est cependant nécessaire.

Mots-clefs

Corrigendum to «Fully Covered Metallic Stents for the Treatment of Benign Airway Stenosis».

Dahlqvist C, Ocak S, Gourdin M, Dincq AS, Putz L, d'Odémont JP.

Références	*Doi*	*IF*
Can Respir J. 2018 May 22;2018:6202750	*10.1155/2018/6202750*	*1,132*

Abstract

This corrects the article DOI: 10.1155/2016/8085216.].

ERRATUM FOR

Fully Covered Metallic Stents for the Treatment of Benign Airway Stenosis. [Can Respir J. 2016]

Mots-clefs

Tamoxifen Metabolism and Efficacy in Breast Cancer: A Prospective Multicenter Trial.

Neven P, Jongen L, Lintermans A, Van Asten K, Blomme C, Lambrechts D, Poppe A, Wildiers H, Dieudonné AS, Brouckaert O, Decloedt J, Berteloot P, Verhoeven D, Joerger M, **Vuylsteke P**, Wynendaele W, Casteels M, Van Huffel S, Lybaert W, Van Ginderachter J, Paridaens R, Vergote I, Dezentjé VO, Van Calster B, Guchelaar HJ.

Références	*Doi*	*IF*
Clin Cancer Res. 2018 May 15;24(10):2312-2318	*10.1158/1078-0432.CCR-17-3028*	*10,199*

Abstract

PURPOSE: Levels of endoxifen, the most active metabolite of tamoxifen, vary by the highly polymorphic cytochrome P450 (CYP) 2D6 enzyme. We prospectively investigated tamoxifen efficacy by serum endoxifen levels and the tamoxifen activity score (TAS).

EXPERIMENTAL DESIGN: A prospective observational multicenter study included postmenopausal women with an estrogen receptor-positive breast cancer receiving first-line tamoxifen, 20 mg daily in the neoadjuvant or metastatic setting, recruited between February 2009 and May 2014. The primary endpoint was the objective response rate (ORR) using RECIST criteria 1.0. Secondary endpoints were clinical benefit (CB), progression-free survival (PFS), and tolerability of tamoxifen. The main analysis used logistic regression to relate ORR to serum endoxifen levels after 3 months. Endpoints were also related to other tamoxifen metabolites and to TAS.

RESULTS: Endoxifen levels were available for 247 of all 297 patients (83%), of which 209 with target lesions (85%). Median follow-up time for PFS was 32.5 months, and 62% progressed. ORR and CB were 45% and 84%, respectively. ORR was not related to endoxifen, and the OR of ORR was 1.008 per μg/L increase in endoxifen (95% confidence interval, 0.971-1.046; P = 0.56). In general, none of the endpoints was associated with endoxifen levels, tamoxifen metabolites, or TAS.

CONCLUSIONS: Under the prespecified assumptions, the results from this prospective clinical trial do not suggest therapeutic drug monitoring of endoxifen to be of clinical value in postmenopausal women treated with tamoxifen for breast cancer in the neoadjuvant or metastatic setting.

Mots-clefs

Elderly Patients (Age 70 Years or Older) With Secondary Acute Myeloid Leukemia or Acute Myeloid Leukemia Developed Concurrently to Another Malignant Disease.

Collinge E, Loron S, Larcher MV, Elhamri M, Heiblig M, Deloire A, Ducastelle S, Labussière H, Barraco F, Wattel E, Salles G, Paubelle E, Thomas X.

Références	*Doi*	*IF*
Clin Lymphoma Myeloma Leuk. 2018 May;18(5):e211-e218	*10.1016/j.clml.2018.02.018*	*2,308*

Abstract

INTRODUCTION: Secondary acute myeloid leukemia (sAML) remains a therapeutic challenge. In elderly patients with AML, it is unclear whether sAML displays an inferior outcome compared with de novo AML.

PATIENTS AND METHODS: We studied AML with an antecedent of hematologic disease, treatment-related AML, or AML occurring concurrently to another malignancy in a single-center cohort of patients aged 70 and older with AML. The study included 169 patients who were compared with a cohort of patients with de novo AML, without any prior history of malignant disorders, seen during the same period of time.

RESULTS: Hematologic antecedents or presence of prior/concurrent solid malignancy did not impact complete remission rates and overall survival. In multivariate analysis, sAML appeared without independent prognostic value in the elderly.

CONCLUSION: Our results support that sAML and de novo AML in elderly patients are not prognostically distinct entities. They should therefore not be considered separately when investigating outcomes and new treatment strategies.

Mots-clefs

Chemotherapy; Hypomethylating agents; Prognosis; Treatment; Treatment-related leukemia

JUIN

Genetic and Biochemical Characterization of OXA-519, a Novel OXA-48-Like β-Lactamase.

Dabos L, **Bogaerts P,** Bonnin RA, Zavala A, **Sacré P,** Iorga BI, Huang DT, **Glupczynski Y,** Naas T.

Références	*Doi*	*IF*
Antimicrob Agents Chemother. 2018 Jul 27;62(8). pii: e00469-18	*10.1128/AAC.00469-18*	*4,255*

Abstract

A multidrug-resistant Klebsiella pneumoniae 1210 isolate with reduced carbapenem susceptibility revealed the presence of a novel plasmid-encoded blaOXA-48-like gene, named blaOXA-519 The 60.7-kb plasmid (pOXA-519) was similar to the IncL-OXA-48 prototypical plasmid except for a ca. 2-kb deletion due to an IS1R insertion. OXA-519 differed from OXA-48 by a Val120Leu substitution, which resulted in an overall reduced β-lactam-hydrolysis profile, except those for ertapenem and meropenem, which were increased. Thus, detection of OXA-519 producers using biochemical tests that monitor imipenem hydrolysis will be difficult.

Mots-clefs

OXA-48 like; carbapenemase; detection; mutant; steady-state kinetics

The eGVHD App has the potential to improve the accuracy of graft versus host disease assessment: a multicenter randomized controlled trial.

Haguet H, Douxfils J, **Chatelain C, Graux C, Mullier F,** Dogné J-M.

Références	*Doi*	*IF*
TH Open 2018 ;2(2) :e68-e88		

Abstract

Imatinib, the first-in-class BCR-ABL tyrosine kinase inhibitor (TKI), had been a revolution for the treatment of chronic myeloid leukemia (CML) and had greatly enhanced patient survival. Second- (dasatinib, nilotinib, and bosutinib) and third-generation (ponatinib) TKIs have been developed to be effective against BCR-ABL mutations making imatinib less effective. However, these treatments have been associated with arterial occlusive events. This review gathers clinical data and experiments about the pathophysiology of these arterial occlusive events with BCR-ABL TKIs. Imatinib is associated with very low rates of thrombosis, suggesting a potentially protecting cardiovascular effect of this treatment in patients with BCR-ABL CML. This protective effect might be mediated by decreased platelet secretion and activation, decreased leukocyte recruitment, and anti-inflammatory or antifibrotic effects. Clinical data have guided mechanistic studies toward alteration of platelet functions and atherosclerosis development, which might be secondary to metabolism impairment. Dasatinib, nilotinib, and ponatinib affect endothelial cells and might induce atherogenesis through increased vascular permeability. Nilotinib also impairs platelet functions and induces hyperglycemia and dyslipidemia that might contribute to atherosclerosis development. Description of the pathophysiology of arterial thrombotic events is necessary to implement risk minimization strategies.

Mots-clefs

BCR-ABL ; arterial thrombotic events ; tyrosine kinase inhibitors ; chronic myeloid leukemia

Standardization of extracellular vesicle measurements by flow cytometry through vesicle diameter approximation.

van der Pol E, Sturk A, van Leeuwen T, Nieuwland R, Coumans F; ISTH-SSC-VB Working group. **Mullier F.**

Références	*Doi*	*IF*
J Thromb Haemost. 2018 Jun;16(6):1236-1245	*10.1111/jth.14009*	*4,899*

Abstract

BACKGROUND: Detection of extracellular vesicles (EVs) by flow cytometry has poor interlaboratory comparability, owing to differences in flow cytometer (FCM) sensitivity. Previous workshops distributed polystyrene beads to set a scatter-based diameter gate in order to improve the comparability of EV concentration measurements. However, polystyrene beads provide limited insights into the diameter of detected EVs. Objectives To evaluate gates based on the estimated diameter of EVs instead of beads.
METHODS: A calibration bead mixture and platelet EV samples were distributed to 33 participants. Beads and a light scattering model were used to set EV diameter gates in order to measure the concentration of CD61-phycoerythrin-positive platelet EVs.
RESULTS: Of the 46 evaluated FCMs, 21 FCMs detected the 600-1200-nm EV diameter gate. The 1200-3000-nm EV diameter gate was detected by 31 FCMs, with a measured EV concentration interlaboratory variability of 81% as compared with 139% with the bead diameter gate. Part of the variation in both approaches is caused by precipitation in some of the provided platelet EV samples. Flow rate calibration proved essential because systems configured to 60 μL min-1 differed six-fold in measured flow rates between instruments.
CONCLUSIONS: EV diameter gates improve the interlaboratory variability as compared with previous approaches. Of the evaluated FCMs, 24% could not detect 400-nm polystyrene beads, and such instruments have limited utility for EV research. Finally, considerable differences were observed in sensitivity between optically similar instruments, indicating that maintenance and training affect the sensitivity.

Mots-clefs

Blood platelets; cell-derived microparticles; exosomes; extracellular vesicles; flow cytometry; standardization

Betrixaban: Impact on Routine and Specific Coagulation Assays-A Practical Laboratory Guide.

Siriez R, Evrard J, Dogné JM, Pochet L, Gheldof D, **Chatelain B, Mullier F,** Douxfils J.

Références	*Doi*	*IF*
Thromb Haemost. 2018 Jul;118(7):1203-1214	*10.1055/s-0038-1657772*	*4,952*

Abstract

INTRODUCTION: Betrixaban is a novel direct oral factor Xa inhibitor approved by the Food and Drug Administration for prophylaxis of venous thromboembolism in adult patients hospitalized for an acute illness at risk for thromboembolic complications. Assessment of the anti-coagulant effect of betrixaban may be useful in some situations. Also, clinicians need to know how routine coagulation assays are influenced.

OBJECTIVE: The aim of this study is to determine which coagulation assay(s) should be used to assess the impact of betrixaban on haemostasis and provide laboratory guidance for their interpretation.

MATERIALS AND METHODS: Betrixaban was spiked at final concentrations ranging from 0 to 250 ng/mL in platelet-poor plasma. Different reagents from several manufacturers were tested and the impact of betrixaban on pro-thrombin time (PT), activated partial thromboplastin time (aPTT), dilute Russel viper venom time (dRVV-T), chromogenic anti-Xa assays, thrombin generation assay (TGA), and a large panel of haemostasis diagnostic tests has been assessed.

RESULTS: A concentration-dependent prolongation of aPTT, PT and dRVV-T is observed. The sensitivity mainly depends on the reagent. Chromogenic anti-Xa assays show high sensitivity depending on the reagent and/or the methodology. These assays applicable for other direct factor Xa inhibitors have to be adapted to obtain a relevant range of measurement. TGA may also be attractive to assess the anti-coagulant activity of betrixaban.

CONCLUSION: Adapted chromogenic anti-Xa assays are the most appropriate assays to estimate the concentration of betrixaban. Betrixaban significantly affects several haemostasis diagnostic tests and this needs to be taken into consideration when requesting and interpreting such tests.

Mots-clefs

Evaluation of the DOAC-Stop® Procedure to Overcome the Effect of DOACs on Several Thrombophilia Screening Tests.

Favresse J, Lardinois B, Sabor L, Devalet B, Vandepapelière J, Braibant M, **Lessire S, Chatelain B, Jacqmin H,** Douxfils J, **Mullier F.**

Références	*Doi*	*IF*
TH Open 2018 ;2(2) :e202-e209		

Abstract

The impact of direct oral anticoagulants (DOACs) on laboratory assays used for thrombophilia testing (e.g., antithrombin, protein S, protein C, lupus anticoagulant and activated protein-C resistance) is a well-known issue and may cause false-positive and -negative results. Therefore, the correct interpretation of tests that are performed in patients taking DOACs is mandatory to prevent misclassification and the subsequent clinical consequences. We aimed at evaluating the efficiency of a new and simple procedure (DOAC-Stop®; Haematex Research, Hornsby, Australia) to overcome the effect of all DOACs in real- life settings and to assess the percentage of erroneous results due to the presence of DOACs on thrombophilia screening tests. For this purpose, 135 DOAC-treated patients (38 apixaban, 40 dabigatran, 15 edoxaban, and 42 rivaroxaban) and 20 control patients were enrolled. A significant drop in apixaban, dabigatran, edoxaban, and rivaroxaban plasma concentrations following the DOAC-Stop® treatment was observed (74.8– 8.2 ng/mL [p ‹ 0.0001], 95.9–4.7 ng/mL [p ‹ 0.0001], 102.1–8.8 ng/mL [p ¼ 0.001],and 111.3–7.0 ng/mL [p ‹ 0.0001], respectively). The DOAC-Stop® treatment was mostly effective to overcome the effect of DOACs on PTT-LA, dilute Russell's viper venom time (dRVVT) screen, and dRVVT confirm tests. Using our procedures, false-positive results due to DOACs were observed only with lupus anticoagulant tests (up to 75%) and fell to zero after the DOAC-Stop® procedure, regardless of the DOAC considered. In conclusion, the DOAC-Stop® adsorbent procedure appeared to be an effective and simple way to overcome the interference of DOAC on coagulation tests and should facilitate the interpretation of thrombophilia screening tests in patients taking DOACs.

Mots-clefs

Thrombophilia ; direct oral anticoagulants ; interference

The eGVHD App has the potential to improve the accuracy of graft versus host disease assessment: a multicenter randomized controlled trial.

Schoemans HM, Goris K, Van Durm R, Fieuws S, De Geest S, Pavletic SZ, Im A, Wolff D, Lee SJ, Greinix H, Duarte RF, Poiré X, Selleslag D, Lewalle P, Kerre T, **Graux C,** Baron F, Maertens JA, Dobbels F; EBMT Transplantation Complications Working Party.

Références	*Doi*	*IF*
Haematologica. 2018 Jun 14. haematol.2018.190777.	*10.3324/haematol.2018.190777*	*9,09*

Abstract

Graft-versus-host disease assessment has been shown to be a challenge for healthcare professionals, leading to the development of the eGVHD App (www.uzleuven.be/egvhd). In this study, we formally evaluated the accuracy of using the App compared to traditional assessment methods to assess graft-versus-host disease. Our national multicenter randomized controlled trial involved seven Belgian transplantation centers and 78 healthcare professionals selected using a two-stage convenience sampling approach between January and April 2017. Using a 1:1 randomization stratified by profession, healthcare professionals were assigned to use either the App («APP&») or their usual graft-versus-host disease assessment aids («No APP») to assess the diagnosis and severity score of ten expert-validated clinical vignettes. Our main outcome measure was the difference in accuracy for graft-versus-host disease severity scoring between both groups. The odds of being correct were 6.14 (95% CI: 2.83-13.34) and 6.29 (95% CI: 4.32-9.15) times higher in favor of the «APP» group for diagnosis and scoring, respectively (p<0.001). App-assisted graft-versus-host disease severity scoring was significantly superior for both acute and chronic graft-versus-host disease, with an Odds Ratio of 17.89 and 4.34 respectively (p<0.001) and showed a significantly increased inter-observer agreement compared to standard practice. Despite a mean increase of 24 minutes (95% CI: 20.45-26.97) in time needed to score the whole graft-versus-host disease test package in the»APP» group (p<0.001), usability feedback was positive. The eGVHD App showed superior graft-versus-host disease assessment accuracy compared to standard practice and has the potential to improve the quality of outcome data registration in allogeneic stem cell transplantation.

Mots-clefs

Stem Cell Transplantation; eHealth; graft versus host disease; mobile application

Reduction of the turn-around time for the measurement of rivaroxaban and apixaban: Assessment of the performance of a rapid centrifugation method.

Dincq AS, Lessire S, Pirard G, Siriez R, **Guldenpfennig M, Baudar J, Favresse J,** Douxfils J, **Mullier F.**

Références	*Doi*	*IF*
Int J Lab Hematol. 2018 Jun 19. [Epub ahead of print]	*10.1111/ijlh.12870*	*1,919*

Abstract

Mots-clefs

Are high- and low-molecular-weight sensitizing agents associated with different clinical phenotypes of occupational asthma ?

Vandenplas O, Godet J, Hurdubaea L, **Rifflart C,** Suojalehto H, Wiszniewska M, Munoz X, Sastre J, Klusackova P, Moore V, Merget R, Talini D, Svanes C, Mason P, dell'Omo M, Cullinan P, Moscato G, Quirce S, Hoyle J, Sherson D, Kauppi P, Preisser A, Meyer N, de Blay F; European network for the PHenotyping of OCcupational ASthma (E-PHOCAS) investigators.

Références	*Doi*	*IF*
Allergy. 2018 Jun 28. [Epub ahead of print]	*10.1111/all.13542*	*6,048*

Abstract

BACKGROUND: High-molecular-weight (HMW) proteins and low-molecular-weight (LMW) chemicals can cause occupational asthma (OA) although few studies have thoroughly compared the clinical, physiological, and inflammatory patterns associated with these different types of agents. The aim of this study was to determine whether OA induced by HMW and LMW agents show distinct phenotypic profiles.

METHODS: 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 response to HMW (n=544) and LMW (n=635) agents.

RESULTS: Multivariate logistic regression analysis showed significant associations between OA caused by HMW agents and work-related rhinitis (OR [95% CI]: 4.79 [3.28-7.12]), conjunctivitis (2.13 [1.52-2.98]), atopy (1.49 [1.09-2.05]), and early asthmatic reactions (2.86 [1.98-4.16]). By contrast, OA due to LMW agents was associated with chest tightness at work (2.22 [1.59-3.03]), daily sputum (1.69 [1.19-2.38]), and late asthmatic reactions (1.52 [1.09-2.08]). Furthermore, OA caused by HMW agents showed a higher risk of airflow limitation (1.76 [1.07-2.91]) whereas OA due to LMW agents exhibited a higher risk of severe exacerbations (1.32 [1.01-1.69]). There were no differences between the two types of agents in the baseline sputum inflammatory profiles, but OA caused by HMW agents showed higher baseline blood eosinophilia and a greater post-challenge increase in fractional nitric oxide.

CONCLUSION: This large cohort study describes distinct phenotypic profiles in OA caused by HMW and LMW agents, There is a need to further explore differences in underlying pathophysiological pathways and outcome after environmental interventions. This article is protected by copyright. All rights reserved.

Mots-clefs

Asthma; bronchial provocation tests; occupational diseases; phenotype

Dental caries and diabetes: A Belgian survey of patients with type 1 and type 2 diabetes.

Buysschaert M, Buysschaert B, **Jamart J.**

Références	*Doi*	*IF*
Diabetes Metab. 2018 Jun 14. pii: S1262-3636(18)30117-4. [Epub ahead of print]	*10.1016/j.diabet.2018.06.002*	*3,744*

Abstract

Mots-clefs

Circulating MicroRNAs as Biomarkers in Diffuse Large B-cell Lymphoma: A Pilot Prospective Longitudinal Clinical Study.

Bouvy C, **Wannez A, George F, Graux C, Chatelain C,** Dogné JM.

Références	*Doi*	*IF*
Biomark Cancer. 2018 Jun 18;10:1179299X18781095. eCollection 2018	*10.1177/1179299X18781095*	*2,392*

Abstract

OBJECTIVES: Diffuse large B-cell lymphoma (DLBCL) is highly heterogeneous in terms of phenotype and treatment response in patients. These characteristics make the prognosis difficult to establish and hinder the use of new personalized treatments in clinical practice. In this context, there is currently a need to define new biomarkers enabling a better definition of DLBCL subtypes, prognosis evaluation, and an overview of the resistance to chemotherapeutics. The aim of this study was to evaluate the use of microRNAs found in plasma from patients with DLBCL as biomarkers of tumor evolution in these patients.

METHOD: For this purpose, a plasma biobank was created with samples from patients with DLBCL. The evolution of the level of selected microRNAs during treatment has been studied. A total of 19 patients with DLBCL were included in this pilot mono-centered study and a total of 68 samples were analyzed.

RESULTS: The first step of this study was the selection of the microRNAs to be quantified in all the samples of the biobank and that could potentially be used as biomarkers. To this end, quantification of 377 microRNAs was performed on the plasma samples of 2 selected patients with DLBCL and 1 healthy donor with no history of cancer. Among the 377 microRNAs evaluated, 7 were selected and analyzed in the entire biobank.

CONCLUSIONS: This study highlighted 5 circulating microRNAs whose plasma levels would be worth further investigating for the characterization of DLBCL evolution in patients. MiR-21 and miR-197 had a significant higher plasmatic level in patients with tumors unresponsive to treatment. With a higher plasma level in patients with complete remission, miR-19b, miR-20a, and miR-451 could enable to differentiate, at the remission review, patients with residual tumor, from patients with complete remission.

Mots-clefs

Diffuse large B-cell lymphoma; biomarkers; circulating microRNAs; plasma

Occurrence and persistence of carbapenemases genes in hospital and wastewater treatment plants and propagation in the receiving river.

Proia L, Anzil A, Borrego C, Farrè M, Llorca M, Sanchis J, **Bogaerts P,** Balcázar JL, Servais P.

Références	*Doi*	*IF*
J Hazard Mater. 2018 Sep 15;358:33-43	*10.1016/j.jhazmat.2018.06.058*	*6,434*

Abstract

This study aims to investigate the prevalence of clinically relevant carbapenemases genes (blaKPC, blaNDM and blaOXA-48) in water samples collected over one-year period from hospital (H), raw and treated wastewater of two wastewater treatment plants (WWTPs) as well as along the Zenne River (Belgium). The genes were quantified in both particle-attached (PAB) and free-living (FLB) bacteria. Our results showed that absolute abundances were the highest in H waters. Although absolute abundances were significantly reduced in WWTP effluents, the relative abundance (normalized per 16S rRNA) was never lowered through wastewater treatment. Particularly, for the PAB the relative abundances were significantly higher in the effluents respect to the influents of both WWTPs for all the genes. The absolute abundances along the Zenne River increased from upstream to downstream, peaking after the release of WWTPs effluents, in both fractions. Our results demonstrated that blaKPC, blaNDM and blaOXA-48 are widely distributed in the Zenne as a consequence of chronic discharge from WWTPs. To conclude, the levels of carbapenemases genes are significantly lower than other genes conferring resistance to more widely used antibiotics (analyzed in previous studies carried out at the same sites), but could raise up to the levels of high prevalent resistance genes.

Mots-clefs

ARGs; Carbapenemases genes; Hospital; Urban River; Wastewaters

Temocillin dosing in haemodialysis patients based on population pharmacokinetics of total and unbound concentrations and Monte Carlo simulations.

Miranda Bastos AC, Vandecasteele SJ, **Spinewine A,** Tulkens PM, Van Bambeke F.

Références	*Doi*	*IF*
J Antimicrob Chemother. 2018 Jun 1;73(6):1630-1638	*10.1093/jac/dky078*	*5,217*

Abstract

OBJECTIVES: To develop a population model describing temocillin pharmacokinetics (PK) in patients undergoing haemodialysis and investigate how pharmacokinetic/pharmacodynamic (PD) targets can be met with different dosage regimens.

MATERIAL AND METHOD: Patients and methods: Sixteen patients received the currently licenced dosing of 1, 2 or 3 g of temocillin (total of 61 doses) corresponding to an inter-dialytic period of 20, 44 or 68 h, respectively, and a dialysis period of 4 h. A non-linear mixed-effects model was developed jointly for total and unbound temocillin serum concentrations. The performance of clinically feasible dosing regimens was evaluated using a 5000-subject Monte Carlo (MC) simulation for determining the highest MIC for which the PK/PD target of 40%ƒT>MIC would be reached in 90% of patients [probability of target attainment (PTA)]. This PK study was registered at ClinicalTrials.gov (NCT02285075).

RESULTS: Temocillin unbound and total serum concentrations (429 samples) were used to fit an open two-compartment model with non-linear albumin binding and first-order elimination. In addition to total body clearance, dialysis clearance was modelled using the Michaels function. The currently licenced dosing achieved a 90% PTA for an MIC up to 8 mg/L. A new temocillin dosage regimen was designed that would achieve a 90% PTA for an MIC of 16 mg/L (MIC90 of target organisms) adjusted to patient weight and inter-dialytic period.

CONCLUSIONS: Currently licensed dosage regimen is suboptimal for MICs >8 mg/L (frequently found in clinical isolates). Model-based simulations allowed suggestion of a new dosage regimen with improved probability of microbiological success, applicability in routine clinical practice and more appropriate for empirical therapy.

Mots-clefs

Immunocompromised patients with acute respiratory distress syndrome: secondary analysis of the LUNG SAFE database.

Cortegiani A, Madotto F, Gregoretti C, Bellani G, Laffey JG, Pham T, Van Haren F, Giarratano A, Antonelli M, Pesenti A, Grasselli G; LUNG SAFE Investigators and the ESICM Trials Group.

Références	*Doi*	*IF*
Crit Care. 2018 Jun 12;22(1):157	*10.1186/s13054-018-2079-9*	*6,425*

Abstract

BACKGROUND: The aim of this study was to describe data on epidemiology, ventilatory management, and outcome of acute respiratory distress syndrome (ARDS) in immunocompromised patients.

METHODS: We performed a post hoc analysis on the cohort of immunocompromised patients enrolled in the Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNG SAFE) study. The LUNG SAFE study was an international, prospective study including hypoxemic patients in 459 ICUs from 50 countries across 5 continents.

RESULTS: Of 2813 patients with ARDS, 584 (20.8%) were immunocompromised, 38.9% of whom had an unspecified cause. Pneumonia, nonpulmonary sepsis, and noncardiogenic shock were their most common risk factors for ARDS. Hospital mortality was higher in immunocompromised than in immunocompetent patients (52.4% vs 36.2%; $p < 0.0001$), despite similar severity of ARDS. Decisions regarding limiting life-sustaining measures were significantly more frequent in immunocompromised patients (27.1% vs 18.6%; $p < 0.0001$). Use of noninvasive ventilation (NIV) as first-line treatment was higher in immunocompromised patients (20.9% vs 15.9%; $p = 0.0048$), and immunodeficiency remained independently associated with the use of NIV after adjustment for confounders. Forty-eight percent of the patients treated with NIV were intubated, and their mortality was not different from that of the patients invasively ventilated ab initio.

CONCLUSIONS: **Immunosuppression is frequent in patients with ARDS, and infections are** the main risk factors for ARDS in these immunocompromised patients. Their management differs from that of immunocompetent patients, particularly the greater use of NIV as first-line ventilation strategy. Compared with immunocompetent subjects, they have higher mortality regardless of ARDS severity as well as a higher frequency of limitation of life-sustaining measures. Nonetheless, nearly half of these patients survive to hospital discharge.

Mots-clefs

ARDS; Acute respiratory failure; Immunocompromised patients; Mechanical ventilation; Noninvasive ventilation

Reduction in electrocardiographic lateral precordial voltage after subcutaneous implantable cardioverter-defibrillator implantation.

De Roy L, Blommaert D.

Références	*Doi*	*IF*
Acta Cardiol. 2018 Jun;73(3):318	*10.1080/00015385.2017.1375732*	*0,876*

Abstract

Mots-clefs

International Forum on typing and matching strategies in patients on anti-CD38 monoclonal therapy.

De Vooght KMK, Lozano M, Bueno JL, Alarcón A, Romera I, Suzuki K, Zhiburt E, Holbro A, Infanti L, Buser A, Hustinx H, **Deneys V, Frélik A, Thiry C,** Murphy M, Staves J, Selleng K, Greinacher A, Kutner JM, Bonet Bub C, Castilho L, Kaufman RM, Colling ME, Perseghin P, Incontri A, Dassi M, Brilhante D, Macédo A, Cserti-Gazdewich C, Pendergrast JM, Hawes J, Lundgren MN, Storry JR, Jain A, Marwaha N, Sharma RR.

Références	*Doi*	*IF*
Vox Sang. 2018 Jun 26. [Epub ahead of print]	*10.1111/vox.12652*	*2,107*

Abstract

Mots-clefs

Mounier Kuhn syndrome presenting with recurrent atelectasis.

Quentin C, Lefevre N, **Bodart E,** Hanssens L.

Références	*Doi*	*IF*
Acta Clin Belg. 2018 Jun;73(3):233-235	*10.1080/17843286.2017.1373498*	*0,916*

Abstract

Mounier Kuhn syndrome is usually diagnosed in adulthood, and only a few cases have been described in childhood. Clinical presentation We present the case of a seven-year-old boy suffering from recurrent pneumonia and atelectasis. Intervention Previously performed chest X-rays showed bilateral hyperinflation and tracheobronchomegaly. Chest computed tomography (CT) confirmed the presence of distal enlargement of trachea and bronchi. Tracheobronchomegaly associated with recurrent respiratory tract infections is consistent with Mounier Kuhn syndrome. Pseudomonas aeruginosa was isolated from the sputum of the patient. He was then treated according to the guidelines for P. aeruginosa management in cystic fibrosis patients considering the similarities in clinical presentations and pathophysiology of both diseases. Antibiotic treatment resulted in a remarkable reduction of events of pulmonary exacerbation and hospitalizations. There are no specific guidelines for treatment options in case of pulmonary exacerbation of Mounier Kuhn syndrome. Case reports discussing the choice and efficiency of antibiotic treatment are random. Conclusion headings We share our experience of treating pulmonary exacerbation caused by P. aeruginosa in a patient with Mounier Kuhn syndrome suggesting a possible treatment option of pseudomonas infections in this syndrome.

Mots-clefs

Mounier Kuhn syndrome; Pseudomonas aeruginosa; tracheobronchomegaly

Adherence to geriatric assessment-based recommendations in older patients with cancer: a multicenter prospective cohort study in Belgium.

Kenis C, Decoster L, Flamaing J, Debruyne PR, De Groof I, Focan C, Cornelis F, Verschaeve V, Bachmann C, Bron Do, Luce S, Debugne G, Van den Bulck H, **Goeminne JC,** Schrijvers D, Geboers K, Petit B, Langenaeken C, Van Rijswijk R, Specenier P, Jerusalem G, Praet JP, Vandenborre K, Lobelle JP, Lycke M, Milisen K, Wildiers H.

Références	*Doi*	*IF*
Ann Oncol. 2018 Jun 14. [Epub ahead of print]	*10.1093/annonc/mdy210*	*13,926*

Abstract

BACKGROUND: In the general older population, geriatric assessment (GA)-guided treatment plans can improve overall survival, quality of life and functional status (FS). In GA-related research in geriatric oncology, studies mainly focused on geriatric screening and GA but not on geriatric recommendations, interventions and follow-up. The aim of this study was to investigate the adherence to geriatric recommendations and subsequent actions undertaken in older patients with cancer.

PATIENT AND METHODS: A prospective Belgian multicenter (N=22) cohort study included patients ≥70 years with a malignant tumor upon oncologic treatment decision. Patients with an abnormal result on the geriatric screening (G8 ≤14/17) underwent GA. Geriatric recommendations were formulated based on GA results. At follow-up the adherence to geriatric recommendations was documented including a description of actions undertaken.

RESULTS: From 11-2012 till 2-2015, G8 screening was performed in 8451 patients, of which 5838 patients had an abnormal result. Geriatric recommendations data were available for 5631 patients. Geriatric recommendations were made for 4459 patients. Geriatric interventions data were available for 4167 patients. A total of 12384 geriatric recommendations were made. At least one different geriatric recommendation was implemented in 2874 patients. A dietician, social worker and geriatrician intervened most frequently for problems detected on the nutritional, social and functional domain. A total of 7569 actions were undertaken for a total of 5725 geriatric interventions, most frequently nutritional support and supplements, extended home care and psychological support.

CONCLUSIONS: This large scale Belgian study focuses on the adherence to geriatric recommendations and subsequent actions undertaken and contributes to the optimal management of older patients with cancer. We identified the domains for which geriatric recommendations are most frequently made and adhered to, and which referrals to other health care workers and facilities are frequently applied in the multidisciplinary approach of older patients with cancer.

Mots-clefs

JUILLET

Effect of ABCB1 genetic polymorphisms on the transport of rivaroxaban in HEK293 recombinant cell lines.

Sennesael AL, Panin N, Vancraeynest C, Pochet L, **Spinewine A,** Haufroid V, Elens L.

Références	*Doi*	*IF*
Sci Rep. 2018 Jul 12;8(1):10514	*10.1038/s41598-018-28622-4*	

Abstract

Direct oral anticoagulants (DOAC) are substrates for the ABCB1 transporter (also called P-glycoprotein), an active efflux pump. ABCB1 polymorphisms have been previously reported to influence the pharmacokinetics of several drugs such as immunosuppressants and tyrosine kinase inhibitors. Recently, in vivo studies have suggested that genetic variants might contribute to the inter-individual variability in DOAC plasma concentrations. Therefore, we evaluated the in vitro effect of the most common coding ABCB1 single nucleotide polymorphisms (SNP), 1236 C›T-2677G›T-3435C›T, and the coding ABCB1 1199 G›A SNP on the transport activity towards rivaroxaban. HEK293 cells were transfected to overexpress the ABCB1 wild-type (1236C-2677G-3435C, 1199 G) or variant proteins (1236C-2677G-3435T, 1236T-2677T-3435T or 1199 A). ABCB1 expression decreased the intracellular accumulation of rivaroxaban, when compared to control cells. This confirms the involvement of ABCB1 in the active transport of rivaroxaban. However, the ABCB1 1236 C›T-2677G›T-3435C›T and 1199 G›A SNPs had no significant influence on the intracellular accumulation of rivaroxaban when compared to the wild-type protein. These results suggest that the ABCB1 coding SNPs investigated in the present study are unlikely to contribute to the inter-individual variability in rivaroxaban plasma concentrations.

Mots-clefs

Adverse drug reactions; medication errors; oral anticoagulants; patient safety; qualitative research

Development and validation of a liquid chromatography/ tandem mass spectrometry method for the simultaneous quantification of serotonin and thromboxane B2 from activated platelets.

Minet V, Evrard J, Vancraeynest C, Dogné JM, **Mullier F,** Pochet L.

Références	*Doi*	*IF*
Int J Lab Hematol. 2018 Jul 17. [Epub ahead of print]	*10.1111/ijlh.12901*	*1,919*

Abstract

INTRODUCTION: Availability of a rapid and reliable platelet activation assay avoiding limitations of current techniques would be valuable to diagnose heparin-induced thrombocytopenia and platelet secretion disorders.
OBJECTIVES: The first aim was to develop and validate an ultra-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) method to quantify in a single run TxB2 synthesized and serotonin released from platelets. The second aim was to use our method in association with light transmission aggregometry (LTA) to select good platelet responders for the diagnosis of HIT.
METHODS: Electrospray ionization and chromatographic separation were optimized for the simultaneous dosage of serotonin and TxB2. The method was validated according to the European Medicines Agency (EMA) guideline for bioanalytical method validation. LTA was performed with monoclonal anti-CD9 (clone ALB6) as platelet activator to select good responders.
RESULTS: Detection was performed using a tandem mass spectrometer with alternated positive and negative electrospray ionization. The total run time was 6 minutes.
The method was validated for calibration curves, precision, accuracy, lower limit of quantification, carry-over, selectivity, and matrix effect. Platelet response to ALB6 was highly variable among donors.
CONCLUSION: We developed and validated a UHPLC-MS/MS method for the simultaneous quantification of TxB2 and serotonin.

Mots-clefs

Serotonin; UHPLC-MS/MS; platelet; thromboxane B2; triple quadrupole

Post-resection treatment of glioblastoma with an injectable nanomedicine-loaded photopolymerizable hydrogel induces long-term survival.

Zhao M, Danhier F, Bastiancich C, Joudiou N, Ganipineni LP, Tsakiris N, Gallez B, Rieux AD, **Jankovski A**, Bianco J, Préat V.

Références	*Doi*	*IF*
Int J Pharm. 2018 Sep 5;548(1):522-529	*10.1016/j.ijpharm.2018.07.033*	*3,862*

Abstract

Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor. Despite available therapeutic options, the prognosis for patients with GBM remains very poor. We hypothesized that the intra-operative injection of a photopolymerizable hydrogel into the tumor resection cavity could sustain the release of the anti-cancer drug paclitaxel (PTX) encapsulated in poly (lactic-co-glycolic acid) (PLGA) nanoparticles and prevent GBM recurrence. The tumor was resected 13 days after implantation and a pre-gel solution composed of polyethylene glycol dimethacrylate (PEG-DMA) polymer, a photoinitiator and PTX-loaded PLGA nanoparticles (PTX PLGA-NPs) was injected into the tumor resection cavity. A solid gel filling the whole cavity was formed immediately by photopolymerization using a 400 nm light. PTX in vitro release study showed a burst release (11%) in the first 8 h and a sustained release of 29% over a week. In vitro, U87 MG cells were sensitive to PTX PLGA-NPs with IC50 level of approximately 0.010 µg/mL. The hydrogel was well-tolerated when implanted in the brain of healthy mice for 2 and 4 months. Administration of PTX PLGA-NPs-loaded hydrogel into the resection cavity of GBM orthotopic model lead to more than 50% long-term survival mice (150 days) compared to the control groups (mean survival time 52 days). This significant delay of recurrence is very promising for the post-resection treatment of GBM.

Mots-clefs

Glioblastoma; Hydrogel; Local delivery; Orthotopic model; PLGA nanoparticles; Paclitaxel

Overuse of inhaled corticosteroids in COPD: five questions for withdrawal in daily practice.

Cataldo D, Derom E, Liistro G, **Marchand E,** Ninane V, Peché R, Slabbynck H, Vincken W, Janssens W.

Références	*Doi*	*IF*
Int J Chron Obstruct Pulmon Dis. 2018 Jul 5;13:2089-2099. eCollection 2018	*10.2147/COPD.S164259*	*2,917*

Abstract

Evidence and guidelines are becoming increasingly clear about imbalance between the risks and benefits of inhaled corticosteroids (ICSs) in patients with COPD. While selected patients may benefit from ICS-containing regimens, ICSs are often inappropriately prescribed with - according to Belgian market research data - up to 70% of patients in current practice receiving ICSs, usually as a fixed combination with a long-acting β2-adrenoreceptor agonist. Studies and recommendations support withdrawal of ICSs in a large group of patients with COPD. However, historical habits appear difficult to change even in the light of recent scientific evidence. We have built a collaborative educational platform with chest physicians and primary care physicians to increase awareness and provide guidance and support in this matter.

Mots-clefs

COPD; education; exacerbation; inhaled steroids; systematic review; withdrawal

Development of a standardized chart review method to identify drug-related hospital admissions in older people.

Thevelin S, **Spinewine A,** Beuscart JB, Boland B, Marien S, Vaillant F, Wilting I, Vondeling A, Floriani C, Schneider C, Donzé J, Rodondi N, Cullinan S, O'Mahony D, Dalleur O.

Références	*Doi*	*IF*
Br J Clin Pharmacol. 2018 Jul 14. [Epub ahead of print]	*10.1111/bcp.13716*	*3,838*

Abstract

AIMS: We aimed to develop a standardized chart review method to identify drug-related hospital admissions (DRA) in older people caused by non-preventable adverse drug reactions and preventable medication errors including overuse, underuse and misuse of medications: the DRA adjudication guide.

METHODS: The DRA adjudication guide was developed based on design and test iterations with international and multidisciplinary input in four subsequent steps: literature review; evaluation of content validity using a Delphi consensus technique; a pilot test; and a reliability study.

RESULTS: The DRA adjudication guide provides definitions, examples and step-by-step instructions to measure DRA. A three-step standardized chart review method was elaborated including: (i) data abstraction; (ii) explicit screening with a newly developed trigger tool for DRA in older people; and (iii) consensus adjudication for causality by a pharmacist and a physician using the World Health Organization-Uppsala Monitoring Centre and Hallas criteria. A 15-member international Delphi panel reached consensus agreement on 26 triggers for DRA in older people. The DRA adjudication guide showed good feasibility of use and achieved moderate inter-rater reliability for the evaluation of 16 cases by four European adjudication pairs (71% agreement, $\alpha = 0.41$). Disagreements arose mainly for cases with potential underuse.

CONCLUSIONS: The DRA adjudication guide is the first standardized chart review method to identify DRA in older persons. Content validity, feasibility of use and inter-rater reliability were found to be satisfactory. The method can be used as an outcome measure for interventions targeted at improving quality and safety of medication use in older people.

Mots-clefs

Adverse drug reactions; elderly; medication errors; medication safety; patient safety

Development of the Multi-Dimensional Analysis of Patient Outcome Predictions (MD.POP) during medical encounters.

Ménard C, Libert Y, Canivet D, Van Achte L, Farvacques C, Liénard A, Merckaert I, **Reynaert C**, Slachmuylder JL, Durieux JF, Klastersky J, Razavi D.

Références	*Doi*	*IF*
Patient Educ Couns. 2018 Jan;101(1):52-58	*10.1016/j.pec.2017.07.004*	*2,785*

Abstract

OBJECTIVE: Our first objective was to develop the Multi-Dimensional analysis of Patient Outcome Predictions (MD.POP), an interaction analysis system that assesses how HCPs discuss precisely and exclusively patient outcomes during medical encounters. The second objective was to study its interrater reliability.
METHOD: The MD.POP was developed by consensus meetings. Forty simulated medical encounters between physicians and an actress portraying a patient were analysed. Interrater reliability analysis was conducted on 20 of those simulated encounters.
RESULTS: The MD.POP includes six dimensions: object, framing, value, domain, probability and form of POP. The coding method includes four steps: 1) transcription of the encounter, 2) POP identification, 3) POP dimension coding and 4) POP scoring. Descriptive analyses show that the MD.POP is able to describe verbal expressions addressing the patient's outcomes. Statistical analyses show excellent interrater reliability (Cohen's Kappa ranging from 0.92 to 0.94).
CONCLUSION: The MD.POP is a reliable interaction analysis system that assesses how HCPs discuss patient medical, psychological or social outcomes during medical encounters.
PRACTICAL IMPLICATION: The MD.POP provides a measure for researchers to study how HCPs communicate with patients about potential outcomes. Results of such studies will allow to provide recommendations to improve HCP's communication about patients' outcomes.

Mots-clefs

Communication; Healthcare professionals; Interaction analysis system; Patient outcome; Patient-centeredness; Uncertainty

Role of FDG PET-CT in the treatment management of Hodgkin lymphoma.

Berriolo-Riedinger A, Becker S, Casasnovas O, **Vander Borght T,** Édeline V.

Références	*Doi*	*IF*
Cancer Radiother. 2018 Sep;22(5):393-400	*10.1016/j.canrad.2018.06.001*	*1,128*

Abstract

Fluorodeoxyglucose (FDG) positons emission tomography (PET)-computed tomography (CT) is used in many ways at baseline and during the treatment of patients with Hodgkin lymphoma. Many properties of the technique are used in the different steps of patient's management. Initial staging with PET-CT is more accurate than conventional imaging and PET-CT also became the gold standard imaging at the end of treatment with a negative PET-CT mandatory for reaching a complete remission. Early assessment of response by PET-CT is one of the most powerful prognostic factors for progression-free survival of patients with localized and advanced stages and allows guiding treatment. Conversely, previous studies showed that there is no role of FDG PET-CT for the patient's follow-up.

Mots-clefs

Hodgkin lymphoma; Imagerie; Interim PET; Lymphome de Hogkin; PET-CT; TEP-scanographie

An outpatient clinic as a potential site of transmission for an outbreak of NDM-producing Klebsiella pneumoniae ST716: a study using whole-genome sequencing.

Heinrichs A, Argudín MA, De Mendonça R, Deplano A, Roisin S, Dodémont M, Coussement J, Filippin L, Dombrecht J, De Bruyne K, **Huang TD,** Supply P, Byl B, **Glupczynski Y,** Denis O.

Références	*Doi*	*IF*
Clin Infect Dis. 2018 Jul 18. [Epub ahead of print]	*10.1093/cid/ciy581*	*9,117*

Abstract

BACKGROUND: The incidence of nosocomial infections due to carbapenem-resistant Klebsiella pneumoniae is increasing worldwide. Whole genome sequencing (WGS) can help elucidate the transmission route of nosocomial pathogens.

METHODS: We combined WGS and epidemiological data to analyze an outbreak of NDM-producing K. pneumoniae that occurred in two Belgian hospitals situated about 50 miles apart. We characterized 74 NDM-producing K. pneumoniae isolates [Hospital A (n=9); Hospital B (n=24) and 41 contemporary isolates from 15 other Belgian hospitals] using pulsed-field gel electrophoresis and WGS.

RESULTS: A K. pneumoniae ST716 clone was identified as being responsible for the outbreak with 9/9 strains from Hospital A and 20/24 strains from Hospital B sharing a unique pulsotype and being clustered together on WGS (compared with 1/41 isolates from other Belgian hospitals). We identified the outpatient clinic of Hospital B as the probable bridging site between the hospitals after combining epidemiological, phylogenetic and resistome data. We also identified the patient who probably caused the transmission. In fact, all but one strain from Hospital A carried a Tn1331-like transposon, whereas none of the Hospital B isolates did. The patient from Hospital A who did not have the Tn1331-like transposon was treated at the outpatient clinic of Hospital B on the same day as the first NDM-producing K. pneumoniae positive patient from Hospital B.

CONCLUSIONS: The results from our WGS-guided investigation highlight the importance of implementing adequate infection control measures in outpatient settings, especially when healthcare delivery moves from acute care facilities to outpatient clinics.

Mots-clefs

Imagerie moléculaire des affections neurodégénératives.

Vander Borght T.

Références	*Doi*	*IF*
Asbl Focus on Medical Imaging 7-13		

Abstract

L'évaluation du fonctionnement cérébral par l'imagerie moléculaire, tant la tomographie à émission de positrons (PET) que la tomographie par émission monophotonique (SPECT),contribuent de plus en plus au diagnostic positif des maladies neurodégénératives, principalement des démences et des syndromes parkinsoniens.
En l'absence actuelle de traitement modifiant l'évolution de la maladie, la plupart des patients sont souvent diagnostiqués cliniquement, sans recourir à l'imagerie moléculaire. Ceci explique que leur prescription, hormis l'étude de la perfusion cérébrale au SPECT, soit réservée aux médecins spécialistes: neurologues, neuropsychiatres ou gériatres. Les examens d'imagerie moléculaire possèdent une importante valeur prédictive,tant positive que négative, qui les aide dans les cas difficiles.

Mots-clefs

Long-term Physicochemical Stability of Concentrated Solutions of Noradrenaline Bitartrate in Polypropylene Syringes for Administration in the Intensive Care Unit.

Lardinois B, Pector J, Delcave C, Soumoy L, Jamart J, Bihin B, Hecq JD, Galanti LM.

Références	*Doi*	*IF*
Int J Pharm Compd. 2018 Jul-Aug;22(4):335-339		

Abstract

Intensive care units use drug solutions within higher concentrations to avoid fluid overload. The purpose of this study was to evaluate the physicochemical stability of concentrated solutions of noradrenaline bitartrate in polypropylene syringes during 30 days of storage at 5°C ± 3°C. Five 50-mL syringes containing 0.240 mg/mL of noradrenaline bitartrate in 0.9% sodium chloride were prepared and stored at 5°C ± 3°C during 30 days. Immediately after preparation and periodically during the storage, noradrenaline concentrations were measured by high-performance liquid chromatography. Spectrophotometric absorbance at different wavelengths, pH measurement, and microscopic observations were also performed. The results showed that all solutions were physicochemically stable during the entire storage period at 5°C ± 3°C, and no color change, turbidity, precipitation, opacity, significant pH variations, nor optic densities were observed. Microscopic analysis was used to determine if there was any formation of crystals. The concentration of noradrenaline was not found to decrease during the 30 days of storage. Solutions of noradrenaline bitartrate 0.240 mg/mL in syringes of 0.9% sodium chloride were physically and chemically stable for at least 30 days when stored in syringes at 5°C ± 3°C and may be prepared in advanced by a centralized intravenous additive service.

Mots-clefs

Multimodality imaging using PET/CT (18F)-fluorodeoxyglucose for radiotherapy field delineation of localized Hodgkin lymphoma.

Édeline V, **Remouchamps V,** Isnardi V, **Vander Borght T.**

Références	*Doi*	*IF*
Cancer Radiother. 2018 Sep;22(5):384-392	*10.1016/j.canrad.2018.07.008*	*1,128*

Abstract

It is now well demonstrated that (18F)-fluorodeoxyglucose PET/CT is the most accurate imaging method for determining disease extent in Hodgkin lymphoma. Thus, up-front PET/CT is mandatory for involved node radiation therapy design. For a proper use of this new imaging modality for radiotherapy, some adaptations should be made to the PET/CT acquisition as well as to the report. Initial PET/CT should be performed in the radiotherapy treatment position. Nuclear medicine physicians should report to the radiation oncologist the precise location of each involved lymph node, for which the use of a common atlas of upper diaphragmatic nodal stations could be useful. All these new procedures have to be implemented in close collaboration among the different medical specialists providing care to Hodgkin lymphoma patients. We report here the usual procedures of PET/CT acquisition in the radiotherapy environment and propose a more sophisticated description of the different lymph nodes for a more efficient nuclear medicine report to the radiation oncologist.

Mots-clefs

Conformal radiotherapy; Hodgkin lymphoma; INRT; Imagerie multimodale; Lymphome de Hodgkin; Multimodal imaging

Individualized prediction of hepatocellular carcinoma occurrence in a large cohort of patients with cirrhosis.

Marot A, Henrion J, Knebel JF, Deltenre P.

Références	*Doi*	*IF*
J Hepatol. 2018 Jul 23. pii: S0168-8278(18)32160-3. [Epub ahead of print]	*10.1016/j.jhep.2018.06.007*	*14,911*

Abstract

Mots-clefs

Long-Term Stability Comparaison between an Original and a Generic Version of Piperacillin/Tazobactam in Dextrose 5% Infusion Polyolefin Bags at 5 ± 3°C after Microwave Freeze-Thaw Treatment.

Huvelle S, Godet M, Galanti L, Closset M, Bihin B, Jamart J, Hecq JD.

Références	*Doi*	*IF*
«Pharmaceutical Technology in Hospital Pharmacy» [Epub ahead of print]	*10.1515/pthp-2018-0014*	

Abstract

BACKGROUND: Piperacillin-Tazobactam is frequently infused in hospitals. The use of a generic version was considered after the out of stock of the brand name Tazocin®. The stability of 4 g of Tazocin® in 120mL of dextrose 5% (D5)was demonstrated during 35 days at 5 °C ± 3 °C after freezing (–20 °C) and microwave thawing (FMT). The aim of the study was to investigate and compare the long-term stability of Tazocin® and a generic product in the same conditions.

METHODS: Five polyolefin bags of 4 g of Piperacillin/Tazobactam® Sandoz and 5 bags of 4 g of Tazocin® were prepared under aseptic conditions in 120mL of D5 and stored 3 months at 20 °C then thawed and stored 58 days at 5 ± 3 °C. Spectrophotometric absorbance at different wavelengths, pH measurement, visual and microscopic observations were also performed. The concentrations were measured by HPLC, at 211nm for tazobactam and 230nm for piperacilline.

RESULTS: No significant change in pH values or optic densities, no crystals were detected. The lower confidence limit at 95% of the concentration for the solutions remains superior to 90% of the initial concentration until 58 days of storage at 5 ± 3 °C.

Mots-clefs

Piperacillin ; tazobactam infusion ; physicochemical stability ; high performance liquid chromatography; microwave freeze-thaw treatment ; centralized intravenous admixture services ; hospital pharmacy

Factitious hypoglycemia: «A never-ending story» ?

Bayart JL, **Closset M,** Coulon A, Furnica RM, Gruson D.

Références	*Doi*	*IF*
Ann Biol Clin (Paris). 2018 Aug 1;76(4):439-444	*10.1684/abc.2018.1362.*	*0,401*

Abstract

Our team of diabetologist is challenged by the case of a 41 year-old woman with recurrent hypoglycaemic episodes. Her clinical background was complex with, among others, a neuroendocrine tumor, a nonalcoholic steatohepatitis and an adrenal insufficiency; these conditions require the exploration of several potential causes. After excluding an endogenous etiology, a factitious hypoglycemia was quicky suspected by clinicians. However, several venous samples showed normal insulinemia and a moderately decreased C-peptide. After multidisciplinary team discussion and facing a strong clinical suspicion, samples were sent to another laboratory to confirm the insulin results. Substantially supratherapeutics insulin concentrations were highlighted. This confirms the previous suspicion of surreptitious insulin administration with a recombinant form unrecognized by our routinely used analyzer. This observation leads us to briefly discuss the lack of cross-reactivities observed with many different insulin assays.

Mots-clefs

cross-reactivity; diabetes; hypoglycemia; immunoassay; insulin

Spousal Caregiving Is Associated with an Increased Risk of Frailty: A Case-Control Study.

Potier F, Degryse JM, Aubouy G, Henrard S, **Bihin B,** Debacq-Chainiaux F, Martens H, **de Saint-Hubert M.**

Références	*Doi*	*IF*
J Frailty Aging. 2018;7(3):170-175.	*10.14283/jfa.2018.11.*	

Abstract

BACKGROUND: Evidence suggests that providing care for a disabled elderly person may have implications for the caregiver's own health (decreased immunity, hypertension, and depression).
OBJECTIVE: Explore if older spousal caregivers are at greater risks of frailty compared to older people without a load of care.
DESIGN: Case-control study.
SETTING: Participants were assessed at home in Wallonia, Belgium.
PARTICIPANTS: Cases: community-dwelling spousal caregivers of older patients, recruited mainly by the geriatric outpatient clinic.
CONTROLS: People living at home with an independent spouse at the functional and cognitive level matched for age, gender and comorbidities.
MEASUREMENTS: Mini nutritional assessment-short form (MNA-SF), short physical performance battery (SPPB), frailty phenotype (Fried), geriatric depression scale (GDS-15), clock drawing test, sleep quality, and medications. The multivariable analysis used a conditional logistic regression.
RESULTS: Among 79 caregivers, 42 were women; mean age and Charlson comorbidity index were 79.4±5.3 and 4.0±1.2, respectively. Among care-receivers (mean age 81.4±5.2), 82% had cognitive impairment. Caregiving was associated with a risk of frailty (Odd Ratio (OR) 6.66; 95% confidence interval (CI) 2.20-20.16), the consumption of antidepressants (OR 4.74; 95% CI 1.32 -17.01), shorter nights of sleep (OR 3.53; 95% CI 1.37-9.13) and more difficulties maintaining a social network (OR 5.25; 95% CI 1.68-16.40).
CONCLUSIONS: Spousal caregivers were at an increased risk of being frail, having shorter nights of sleep, taking antidepressants and having difficulties maintaining their social network, compared to non-caregiver controls. Older spousal caregivers deserve the full attention of professionals to prevent functional decline and anticipate a care breakdown

Mots-clefs

Caregiving; depression; frailty; nutrition

Potentially Inappropriate Prescribing in Belgian Nursing Homes: Prevalence and Associated Factors.

Anrys PMS, Strauven GC, Foulon V, Degryse JM, Henrard S, **Spinewine A.**

Références	*Doi*	*IF*
J Am Med Dir Assoc. 2018 Jul 25. pii: S1525-8610(18)30330-X. [Epub ahead of print]	*10.1016/j.jamda.2018.06.010*	*5,325*

Abstract

BACKGROUND/OBJECTIVES: Our aim was to describe the prevalence of potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs) in Belgian nursing homes and to identify characteristics of residents, general practitioners (GPs), and nursing homes (NHs) that are associated with the number of PIMs and PPOs.
DESIGN: A cross-sectional study.
SETTING: Nursing home residents (NHRs), aged ≥65 years, not in palliative care were included in 54 Belgian NHs participating in the COME-ON study.
MEASURES: Instances of PIMs were detected using a combination of the STOPP v2 and AGS 2015 Beers criteria. Instances of PPOs were detected using START v2. To assess factors associated with the number of PIMs and PPOs, a multivariate binomial negative regression analysis was performed.
RESULTS: A total of 1410 residents, with a median age of 87 years, was included. The median number of medications taken was 9. PIMs were detected in 88.3% of NHRs and PPOs in 85.0%. Use of benzodiazepines (46.7%) and omission of vitamin D (51.5%) were the most common PIM and PPO, respectively. The factor most strongly associated with increased PIMs was the use of 5 to 9 drugs or ≥10 drugs [relative risk (RR) (95% confidence interval [CI]: 2.27 (1.89, 2.76) and 4.04 (3.37, 4.89), respectively]. The resident's age was associated with both decreased PIMs and increased PPOs. PIMs and PPOs were also associated with some NH characteristics, but not with GP characteristics.
CONCLUSION: Implications: The high prevalence of PIMs and PPOs remains a major challenge for the NH setting. Future interventions should target in priority residents taking at least 10 medications and/or those taking psychotropic drugs. Future studies should explore factors related to organizational and prescribing culture. Moreover, special attention must be paid to the criteria used to measure inappropriate prescribing, including criteria relative to underuse.

Mots-clefs

Beers criteria; Inappropriate prescribing; STOPP/START; nursing homes

Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach.

Hoste P, Hoste E, Ferdinande P, Vandewoude K, Vogelaers D, Van Hecke A, Rogiers X, Eeckloo K, Vanhaecht K; Donation after Brain Death Study Group, **Evrard P.**

Références	*Doi*	*IF*
BMC Health Serv Res. 2018 Jul 24;18(1):580	*10.1186/s12913-018-3386-1*	*1,843*

Abstract

BACKGROUND: A substantial degree of variability in practices exists amongst donor hospitals regarding the donor detection, determination of brain death, application of donor management techniques or achievement of donor management goals. A possible strategy to standardize the donation process and to optimize outcomes could lie in the implementation of a care pathway. The aim of the study was to identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact.

METHODS: A RAND modified three-round Delphi approach was used to build consensus within a single country about potential key interventions and quality indicators identified in existing guidelines, review articles, process flow diagrams and the results of the Organ Donation European Quality System (ODEQUS) project. Comments and additional key interventions and quality indicators, identified in the first round, were evaluated in the following rounds and a subsequent physical meeting. The study was conducted over a 4-month time period in 2016.

RESULTS: A multidisciplinary panel of 18 Belgian experts with different relevant backgrounds completed the three Delphi rounds. Out of a total of 80 key interventions assessed throughout the Delphi process, 65 were considered to contribute to the quality of care for the management of a potential donor after brain death; 11 out of 12 quality indicators were validated for relevance and feasibility. Detection of all potential donors after brain death in the intensive care unit and documentation of cause of no donation were rated as the most important quality indicators.

CONCLUSIONS: Using a RAND modified Delphi approach, consensus was reached for a set of 65 key interventions and 11 quality indicators for the management of a potential donor after brain death. This set is considered to be applicable in quality improvement programs for the care of potential donors after brain death, while taking into account each country's legislation and regulations regarding organ donation and transplantation.

Mots-clefs

Critical care; Deceased donation; Delphi technique; Donation after brain death; Key interventions; Quality indicators

In Regard to Maguire et al.

Nevens D, **Duprez F, Daisne JF,** De Neve W, Nuyts S.

Références	*Doi*	*IF*
Int J Radiat Oncol Biol Phys. 2018 Jul 1;101(3):746-747	*10.1016/j.ijrobp.2018.03.031*	*5,554*

Abstract

Mots-clefs

AOÛT

Bendamustine and rituximab in elderly patients with low-tumour burden follicular lymphoma. Results of the LYSA phase II BRIEF study.

Gyan E, **Sonet A,** Brice P, Anglaret B, Laribi K, Fruchart C, Tilly H, Araujo C, Soubeyran P, Gonzalez H, Morineau N, Nicolas-Virelizier E, Ghesquières H, Salles B, Bouabdallah R, Orfeuvre H, Fahri J, Couturier O, Xerri L, Feugier P; Lymphoma Study Association (LYSA).

Références	*Doi*	*IF*
Br J Haematol. 2018 Aug 16. [Epub ahead of print]	*10.1111/bjh.15513*	*5,128*

Abstract

The treatment of low-tumour burden follicular lymphoma (LTBFL) remains a challenge. Rituximab-based strategies may be improved by adding chemotherapy. This Lymphoma Study Association multicentre phase II study assessed rituximab and bendamustine in 63 patients with untreated LTBFL who were aged over 60 years old and had a follicular lymphoma International Prognostic Index (FLIPI) score ≥2. Induction comprised 4 weekly cycles of rituximab 375 mg/m2 intravenously combined with 2 cycles of bendamustine 90 mg/m2 days 1-2 with a 28-day interval, followed by twelve cycles of 375 mg/m2 rituximab maintenance therapy every 8 weeks. The primary endpoint was complete response (CR)/unconfirmed CR (CRu), at 12 weeks. Median age was 67.4 years and median FLIPI was 3. Ultimately, 18 patients (29%) had high tumour burden according to Groupe d'Etude des Lymphomes Folliculaires criteria. The 12-week CR/CRu rate was 54.0% and the overall response rate was 93.7%. Surprisingly, 3 patients died during maintenance (2 sepsis, 1 neoplasm). Progression-free survival was 85.4% at 24 months. In LTBFL patients with FLIPI ≥2, two cycles of rituximab and bendamustine result in a CR rate of 54.0%. However, the treatment-related deaths observed do not allow this regimen to be recommended for LTBFL patients aged over 60 years. EudraCT: 2010-020757-14; ClinicalTrials.gov: NCT01313611.

Mots-clefs

Bendamustine; efficacy; follicular lymphoma; rituximab; tolerance

Launching Global Lung Function Initiative reference values in Belgium: tips and tricks.

Derom E, Liistro G, Oostveen E, **Marchand E,** Bedert L, Peché R, Janssens W;
Pulmonary Function Working Group of the Belgian Thoracic Society.

Références	*Doi*	*IF*
Eur Respir J. 2018 Aug 2;52(2)	*10.1183/13993003.00922-2018*	*12,242*

Abstract

Mots-clefs

Botulinum toxin type A or selective neurotomy for treating focal spastic muscle overactivity ?

Deltombe T, Lejeune T, **Gustin T.**

Références	*Doi*	*IF*
Ann Phys Rehabil Med. 2018 Aug 11. pii: S1877-0657(18)31439-8 [Epub ahead of print]	*10.1016/j.rehab.2018.07.008*	

Abstract

OBJECTIVE: To discuss the effectiveness, indications, limitations and side effects of botulinum toxin type A and selective neurotomy for treating focal spastic muscle overactivity to help clinicians choose the most appropriate treatment.
METHODS: Expert opinion based on scientific evidence and personal experience.
RESULTS: Botulinum toxin type A can decrease muscle tone in different types of spastic muscle overactivity, which allows for treating a large variety of spastic patterns with several etiologies. The toxin effect is sometimes insufficient to improve functional outcome and is transient, thereby requiring repeated injections. Selective neurotomy is a permanent surgical treatment of the reflex component of the spastic muscle overactivity (spasticity) that is effective for spastic equinovarus foot. The neurotomy provides a greater and more constant reduction in spasticity. However, the long-lasting effect on the non-reflex muscle overactivity, especially dystonia, is doubted. The effectiveness, clinical indications, advantages, side effects and limitations of both techniques are discussed.
CONCLUSION: Botulinum toxin type A has the highest level of evidence and the largest range of indications. However, the botulinum toxin effect is reversible and seems less effective, which supports a permanent surgical treatment such as selective neurotomy, especially for the spastic foot. Further research is needed to compare the effect of botulinum toxin type A and selective neurotomy for the different types of spastic muscle overactivity and clinical patterns.

Mots-clefs

Equinovarus foot; Hemiplegia; Motor nerve block; Muscle spasticity; Neurotomy

The impact of breast MRI workup on tumor size assessment and surgical planning in patients with early breast cancer.

Pop CF, **Stanciu-Pop C,** Drisis S, Radermeker M, Vandemerckt C, Noterman D, Moreau M, Larsimont D, Nogaret JM, Veys I.

Références	*Doi*	*IF*
Breast J. 2018 Aug 3. [Epub ahead of print]	*10.1111/tbj.13104*	*2,424*

Abstract

BACKGROUND: The size and focality of the primary tumor in breast cancer (BC) influence therapeutic decision making. The purpose of this study was to evaluate whether preoperative breast magnetic resonance imaging (MRI) is helpful for the assessment of tumor size and surgical planning in early BC.

METHODS: We performed a retrospective review of a prospectively collected database of 174 patients treated at a single institution for invasive BC who had complete documentation of the tumor size from mammography (MMG), ultrasonography (US), and MRI.

RESULTS: A total of 186 breast tumors were analyzed. Mean tumor size varied by imaging method: 14.7 mm by MMG, 13.8 mm by US, and 17.9 mm by MRI. The concordance between breast imaging techniques (BIT) and final pathology with a cutoff ≤ 2 mm was 34.8% for MRI, 32.1% for US, and 27.2% for MMG. US and MMG underestimated while MRI and MMG overestimated the real tumor size. Concordance was the same in premenopausal women for MRI and US at 35%, while concordance was higher in postmenopausal women for MRI. Correlations between size determined by BIT and histopathological size were best with MRI (0.59), compared to US (0.56) or MMG (0.42). Intrinsic subtypes of BC had different concordances according to imaging method, but no significant associations were found. MRI examination revealed additional lesions in 13.8% of patients, 69% of these lesions were malignant. MRI changed the surgical plan in 15 patients (8.6%), and the rate of mastectomy increased by 6.9%.

CONCLUSIONS: MRI estimates BC tumor size more accurately than US or MMG, but a significant overestimation exists. Complementary MRI examination improved the concordance for tumor size between BIT and final pathology in 16.7%. MRI did not alter surgical planning for most patients and allowed more appropriate treatment for 8% of them.

Mots-clefs

MRI; breast cancer; pathology; surgical treatment; tumor size

Risk of meningioma in European patients treated with growth hormone in childhood: results from the SAGhE cohort.

Swerdlow AJ, Cooke R, **Beckers D,** Butler G, Carel JC, Cianfarani S, Clayton P, Coste J, Deodati A, Ecosse E, Hokken-Koelega ACS, Khan AJ, Kiess W, Kuehni CE, Flück CE, Pfaffle R, Sävendahl L, Sommer G, Thomas M, Tidblad A, Tollerfield S, Zandwijken GRJ.

Références	*Doi*	*IF*
J Clin Endocrinol Metab. 2018 Aug 17 [Epub ahead of print]	*10.1210/jc.2018-01133*	*5,789*

Abstract

CONTEXT: There has been concern that growth hormone (GH) treatment of children might increase meningioma risk. Results of published studies have been inconsistent and limited.

OBJECTIVE: To examine meningioma risks in relation to GH treatment.

DESIGN: Cohort study with follow-up via cancer registries and other registers.

SETTING: Population-based.

Patients: A cohort of 10,403 patients treated in childhood with recombinant GH (r-hGH) in 5 European countries since this treatment was first used in 1984. Expected rates from national cancer registration statistics.

Main Outcome Measures: Risk of meningioma incidence.

RESULTS: During follow-up 38 meningiomas occurred. Meningioma risk was greatly raised in the cohort overall (SIR=75.4; 95% confidence interval (CI) 54.9-103.6), as a consequence of high risk in subjects who had received radiotherapy for underlying malignancy (SIR= 658.4; 95% CI 460.4-941.7). Risk was not significantly raised in patients who did not receive radiotherapy. Risk in radiotherapy-treated patients was not significantly related to mean daily dose of GH, duration of GH treatment or cumulative dose of GH.

CONCLUSIONS: Our data add to evidence of very high risk of meningioma in patients treated in childhood with GH after cranial radiotherapy, but suggest that GH may not affect radiotherapy-related risk, and that there is no material raised risk of meningioma in GH-treated patients who did not receive radiotherapy.

Mots-clefs

A web application to involve patients in the medication reconciliation process: a user-centered usability and usefulness study.

Marien S, Legrand D, Ramdoyal R, Nsenga J, Ospina G, Ramon V, Boland B, **Spinewine A.**

Références	*Doi*	*IF*
J Am Med Inform Assoc. 2018 Aug 17 [Epub ahead of print]	*10.1093/jamia/ocy107*	*4,27*

Abstract

OBJECTIVE: Medication reconciliation (MedRec) can improve patient safety by resolving medication discrepancies. Because information technology (IT) and patient engagement are promising approaches to optimizing MedRec, the SEAMPAT project aims to develop a MedRec IT platform based on two applications: the «patient app» and the «MedRec app.» This study evaluates three dimensions of the usability (efficiency, satisfaction, and effectiveness) and usefulness of the patient app.

METHODS: We performed a four-month user-centered observational study. Quantitative and qualitative data were collected. Participants completed the system usability scale (SUS) questionnaire and a second questionnaire on usefulness. Effectiveness was assessed by measuring the completeness of the medication list generated by the patient application and its correctness (ie medication discrepancies between the patient list and the best possible medication history). Qualitative data were collected from semi-structured interviews, observations and comments, and questions raised by patients.

RESULTS: Forty-two patients completed the study. Sixty-nine percent of patients considered the patient app to be acceptable (SUS Score ≥ 70) and usefulness was high. The medication list was complete for a quarter of the patients (7/28) and there was a discrepancy for 21.7% of medications (21/97). The qualitative data enabled the identification of several barriers (related to functional and non-functional aspects) to the optimization of usability and usefulness.

CONCLUSIONS: Our findings highlight the importance and value of user-centered usability testing of a patient application implemented in «real-world» conditions. To achieve adoption and sustained use by patients, the app should meet patients' needs while also efficiently improving the quality of MedRec.

Mots-clefs

Elderly versus nonelderly patients with invasive aspergillosis in the ICU: a comparison and risk factor analysis for mortality from the AspICU cohort.

Matthaiou DK, Dimopoulos G, Taccone FS, **Bulpa P,** Van den Abeele AM, Misset B, Meersseman W, Spapen H, Cardoso T, Charles PE, Vogelaers D, Blot S; AspICU Study Investigators

Références	*Doi*	*IF*
Med Mycol. 2018 Aug 1;56(6):668-678	*10.1093/mmy/myx117*	*2,799*

Abstract

Data regarding the epidemiology and diagnosis of invasive aspergillosis in the critically ill population are limited, with data regarding elderly patients (≥75 years old) even scarcer. We aimed to further compare the epidemiology, characteristics and outcome of elderly versus nonelderly critically ill patients with invasive aspergillosis (IA) Prospective, international, multicenter observational study (AspICU) including adult intensive care unit (ICU) patients, with a culture and/or direct examination and/or histopathological sample positive for Aspergillus spp. at any site. We compared clinical characteristics and outcome of IA in ICU patients using two different diagnostic algorithms. Elderly and nonelderly ICU patients with IA differed in a number of characteristics, including comorbidities, clinical features of the disease, mycology testing, and radiological findings. No difference regarding mortality was found. According to the clinical algorithm, elderly patients were more likely to be diagnosed with putative IA. Elderly patients had less diagnostic radiological findings and when these findings were present they were detected late in the disease course. The comparison between elderly survivors and nonsurvivors demonstrated differences in clinical characteristics of the disease, affected sites and supportive therapy needed. All patients who were diagnosed with proven IA died. Increased vigilance combined with active search for mycological laboratory evidence and radiological confirmation are necessary for the timely diagnosis of IA in the elderly patient subset. Although elderly state per se is not a particular risk factor for mortality, a high SOFA score and the decision not to administer antifungal therapy may have an impact on survival of elderly patients.

Mots-clefs

Corynebacterium Macginleyi - Associated Blebitis: A Case Report.

Qin V, Laurent T, Ledoux A.

Références	*Doi*	*IF*
J Glaucoma. 2018 Aug 14 [Epub ahead of print]	*10.1097/IJG.0000000000001051*	*1,742*

Abstract

PURPOSE: To report a rare case of post-trabeculectomy bleb-related infection associated with Corynebaterium macginleyi, a rare conjunctival pathogen.

METHODS: Case description including clinical imaging and microbiology data, and literature review of Corynebacterium macginleyi-related infections.

RESULTS: A 60-year old glaucomatous female patient presented with a bleb-related infection 6 years after trabeculectomy in her right eye, suggestive of blebitis. No bleb-related endophthalmitis was reported.

CONCLUSIONS: Corynebacterium macginleyi is a rare conjunctival pathogen which can cause conjunctivitis and, rarely, bleb-related infections.

Mots-clefs

Evaluation of the Bruker® MBT Sepsityper IVD module for the identification of polymicrobial blood cultures with MALDI-TOF MS.

Scohy A, Noël A, Boeras A, Brassinne L, **Laurent T,** Rodriguez-Villalobos H, Verroken A.

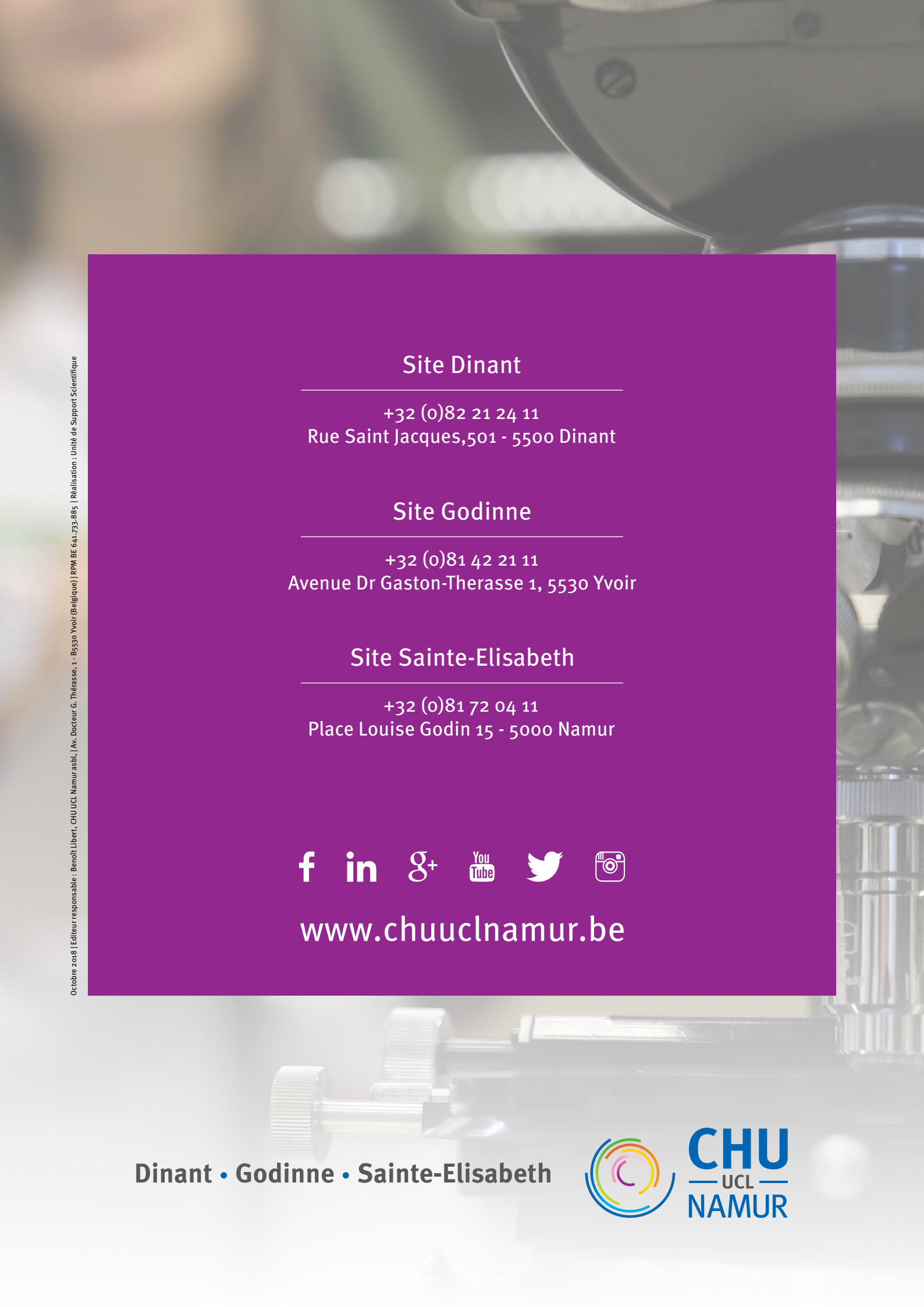
Références	*Doi*	*IF*
Eur J Clin Microbiol Infect Dis. 2018 Aug 20 [Epub ahead of print]	*10.1007/s10096-018-3351-2*	*2,537*

Abstract

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) considerably reduces timeframe required from initial blood culture positivity towards complete bacterial identification. However, rapid identification of polymicrobial blood cultures remains challenging. We evaluated the performances of the Bruker® MBT Sepsityper IVD module on MALDI-TOF MS for the direct identification of polymicrobial blood culture bottles. This module has the ability to give a strong indication that a sample contains a mixture of organisms and to identify two of them. Blood culture bottles considered as polymicrobial using routine subculture were collected and processed using the Sepsityper kit. MALDI-TOF MS identification was performed using the MBT Compass IVD software including the Sepsityper module. From 143 polymicrobial blood culture bottles tested, 34.3% (49/143) were completely identified by the module. Both microorganisms were more easily detected by the module in samples containing two pathogens than in samples containing two contaminants (36.8% vs 29.4%). Additionally, in more than half of the samples, the module detected 1 of the different microorganisms contained in the same vial. In these cases, with a pathogen and contaminant in the same sample, the module detected the pathogen in more than 80%. The Sepsityper module identified 14 microorganisms which were not recovered by conventional culture methods. The Bruker® MBT Sepsityper IVD module contributed to a valuable identification of polymicrobial blood cultures in more than a third of all cases. Conventional culture methods are still required to complete the results and to carry on susceptibility testing.

Mots-clefs

Bacteremia; Direct identification; MALDI-TOF MS; Polymicrobial blood culture



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