

RECUEIL DES PUBLICATIONS DU CHUUCL NAMUR

N°1 - PREMIER QUADRIMESTRE 2018

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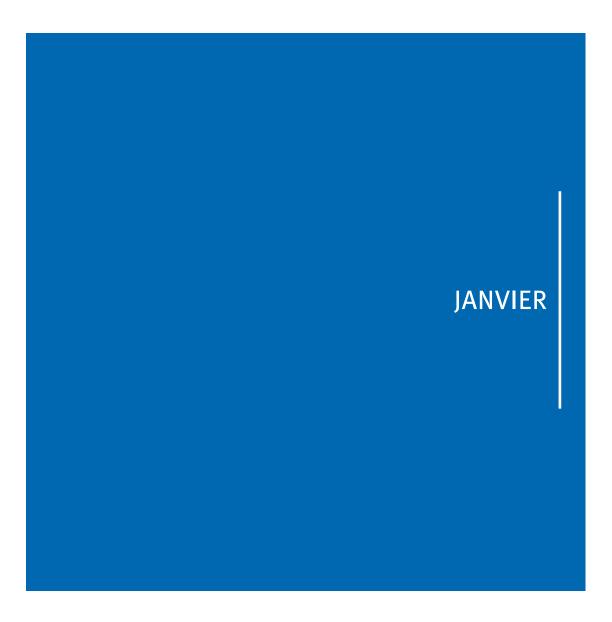
RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR N°1 - PREMIER QUADRIMESTRE 2018 Cher(e)s collègues, Madame, Monsieur,

En tant qu'hôpital universitaire depuis 1967, le CHU UCL Namur remplit les missions qui lui furent confiées par ses fondateurs : l'Excellence Clinique, l'Enseignement, la Recherche et les Services à la Société Civile. Parallèlement aux progrès de la Médecine, aux innovations technologiques et malgré les modifications permanentes de l'environnement hospitalier, les chercheurs ont toujours eu à cœur de poursuivre ces idéaux et de participer au rayonnement national et international de l'Hôpital CHU UCL Namur et de l'Université catholique de Louvain.

La publication scientifique est l'aboutissement d'un travail de recherche réalisé seul ou en équipe dont les résultats connaissent, le plus souvent, leur plus large distribution au sein d'un cénacle restreint de spécialistes du domaine. Ce premier numéro du « Recueil des publications du CHU UCL Namur » est une publication quadrimestrielle qui reprend les résumés des articles publiés par des membres du CHU UCL Namur dans des revues « peerreviewed » (évaluées par des pairs), parus durant les 4 mois précédents. Il a pour vocation de faire connaître le dynamisme de nos chercheurs à nos patients, nos collaborateurs et nos partenaires mais également aux collègues d'autres spécialités de la même institution qui méconnaissent souvent les recherches réalisées dans le service voisin.

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

> Professeur Maximilien Gourdin Directeur aux Affaires Académiques CHU UCL Namur



A new approach for diagnosing chronic myelomonocytic leukemia using structural parameters of Sysmex XNTM analyzers in routine laboratory practice.

Schillinger F, Sourdeau E, Boubaya M, Baseggio L, Clauser S, Cornet E, Debord C, Defour JP, Dubois F, Eveillard M, Galoisy AC, Geay MO, Mullier F, Nivaggioni V, Soenen V, Morel P, Garnache-Ottou F, Ronez E, Bardet V, Deconinck E.

Références	Doi	IF
Scand J Clin Lab Invest. 2018 May;78(3):159-164	10.1080/00365513.2018.1423702	1.498

Abstract

According to WHO recommendations, diagnosis of chronic myelomonocytic leukemia (CMML) beforehand requires microscopic examination of peripheral blood to identify dysplasia and/or blasts when monocytes are greater or equal to 1.0 × 109/L and 10% of leucocytes. We analyzed parameters derived from SysmexTM XN analyzers to improve the management of microscopic examination for monocytosis. We analyzed results of the complete blood count and the positioning and dispersion parameters of polymorphonuclear neutrophils and monocytes in 61 patients presenting with CMML and 635 control patients presenting with a reactive monocytosis. We used logistic regression and multivariate analysis to define a score for smear review. Three parameters were selected: neutrophil/monocyte ratio, structural neutrophil dispersion (Ne-WX) and monocyte absolute value. We established an equation in which the threshold of 0.160 guided microscopic examination in the search for CMML abnormalities with a sensitivity of 0.967 and a specificity of 0.978 in the learning cohort (696 samples) and 0.923 and 0.936 in the validation cohort (1809 samples) respectively. We created a score for microscopic smear examination of patients presenting with a monocytosis greater or equal to 1.0 × 109/L and 10% of leucocytes, improving efficiency in laboratory routine practice.

Mots-clefs

Hematology, automated blood count, chronic myelomonocytic leukemia, disease diagnostics, microscopy

Instillation oculaire accidentelle de colle forte chez un somnambule.

Levecq L, Blondeau L, Oustabassidis E.

Références	Doi	IF
Journal Français d'Ophtalmologie - (2018)		0.16

Abstract

Nous rapportons le cas d'un homme de 40 ans sans antécédent oculaire, qui se présente un matin en salle d'urgence pour ce qu'il considère être une conjonctivite purulente unilatérale apparue au réveil. L'examen clinique révèle la présence d'un matériel de consistance dure, réalisant une adhésion complète des bords libres palpébraux supérieur et inférieur (ankyloblépharon) (Fig. 1). Le patient ne sait fournir aucune explication et c'est l'interrogatoire de son épouse restée en salle d'attente qui confirme l'existence d'un somnambulisme avéré avec déplacements nocturnes. Après extraction de la colle et des cils (Fig. 2), l'examen clinique confirme l'absence de symplépharon ou de lésion cornéenne (Fig. 3). Au retour de la consultation, un flacon ouvert de colle forte liquide instantanée (cyanoacrylate d'éthyle) sera retrouvé au domicile, dans une pièce située un étage plus bas que la chambre à coucher et qui nous sera apporté le lendemain par l'épouse du patient. Le somnambulisme est une parasomnie survenant chez un sujet qui émerge de la phase 3 du sommeil. Le sujet affecté peut, notamment, se lever, déambuler dans la maison, se saisir d'objets et réaliser des tâches élaborées comme s'il était éveillé. Il peut ensuite retourner spontanément dans son lit. Cependant, l'absence de réactivité et de conscience et la difficulté à se souvenir des actes posés suggère que le patient reste partiellement endormi.

Mots-clefs

Determinants of representational and behavioral hyperactivity in patients with fibromyalgia syndrome.

Grisart J, Scaillet N, Michaux M, Masquelier E, Fantini C, Luminet O.

Références	Doi	IF
J Health Psychol. 2018 Jan 1:1359105317751616	10.1177/1359105317751616	2.039

Abstract

Fibromyalgia is associated with a premorbid hyperactivity. This study examines how contextual and personality factors contribute to premorbid hyperactivity. A total of 45 patients completed questionnaires. The results show that the number of children and the basic bodily needs neglect (and their interaction) explain nearly 50 percent of the variance of hyperactivity. The neglect toward bodily needs completely mediates the relation between self-oriented perfectionism and hyperactivity. This study suggests that hyperactivity itself would not have a pathological value, but that the neglect of basic bodily needs would represent a vulnerability factor in a hyperactive premorbid lifestyle in fibromyalgia patients.

Efficacy and safety of frontline rituximab, cyclophosphamide, doxorubicin and prednisone plus bortezomib (VR-CAP) or vincristine (R-CHOP) in a subset of newly diagnosed mantle cell lymphoma patients medically eligible for transplantation in the randomized, phase 3 LYM-3002 study.

Drach J, Huang H, Samoilova O, Belch A, Farber C, **Bosly A**, Novak J, Zaucha J, Dascalescu A, Bunworasate U, Masliak Z, Vilchevskaya K, Robak T, Pei L, Rooney B, van de Velde H, Cavalli F.

Références	Doi	IF
Leuk Lymphoma. 2018 Apr;59(4):896-903	10.1080/10428194.2017.1365855	2.644

Abstract

This post-hoc subanalysis of the LYM-3002 phase 3 study assessed the efficacy and safety of substituting vincristine in rituximab, cyclophosphamide, doxorubicin and prednisone (R-CHOP; n = 42) for bortezomib (VR-CAP; n = 38) in a subgroup of 80 mantle cell lymphoma (MCL) patients aged <60 years who did not receive stem cell transplantation (SCT) despite medical eligibility. Complete response (CR)/unconfirmed CR (CRu) rates were 67 vs. 39% (odds ratio 3.69 [95% Cl(confidence interval): 1.31, 10.41]; p = .012). After 40 months median follow-up, median progression-free survival by independent radiology committee with VR-CAP vs. R-CHOP was 32.6 vs. 12.0 months (hazard ratio (HR) 0.59 [95% Cl: 0.31, 1.13]; p = .108); median overall survival was not reached vs. 47.3 months (HR 0.81 [95% Cl: 0.33, 1.96]; p = .634). Adverse events included neutropenia (92/76%), thrombocytopenia (70/10%) and leukopenia (65/50%). VR-CAP represents a potential alternative to R-CHOP in combined and/or alternating regimens for younger, SCT-eligible MCL patients.

Mots-clefs

Bortezomib, frontline, mantle cell lymphoma, phase 3

Daratumumab: Therapeutic asset, biological trap !

Deneys V, Thiry C, Frelik A, Debry C, Martin B, Doyen C.

Références	Doi	IF
J Health Psychol. 2018 Jan 1:1359105317751616	10.1177/1359105317751616	2.039

Abstract

OBJECTIVES: Recently, daratumumab has been included in the therapeutic strategies for myeloma patients. This molecule is an antibody directed against CD38, strongly expressed on plasma cells. Nevertheless, as CD38 is also present on erythrocyte membrane, daratumumab interferes with immunohaematological tests, complicating the selection of compatible blood.

METHODS: A total of 14 patients treated by daratumumab have been followed in our transfusion laboratory. Among them, 11 have been transfused. Dithiotreitol (DTT) has been used to inhibit the daratumumab's interference, in the pre-transfusion tests (irregular antibody screening and cross-match).

RESULTS: The red blood cell treatment with DTT has been very efficacious to inhibit the daratumumab's interference in 13 patients out of 14. Some precautionary measures had to be taken into account, especially the pH and the storage conditions. An extended pheno/genotype was an additional security element in the selection of compatible blood. To simplify and to optimize the laboratory practices, a decisional flow chart has been written.

CONCLUSION: DTT red blood cell treatment is very useful and efficacious in the pretransfusion tests of patients treated with daratumumab. It allows to avoid the selection of blood bags only on the basis of an extended pheno/genotype, what is more secure and more ethical with respect to other at higher risk patients. A clear decisional flow chart allows a quality assurance gait. Collaboration with physicians is essential.

Mots-clefs

Daratumumab, Dithiotreitol, Dithiotréitol, indirect antiglobulin test, multiple myeloma, myélome multiple, réaction indirecte à l'antiglobuline

Treatment of allergic rhinitis using mobile technology with real-world data: The MASK observational pilot study

Bousquet J, Devillier P, Arnavielhe S, Bedbrook A, Alexis-Alexandre G, van Eerd M, Murray R, Canonica GW, Illario M, Menditto E, Passalacqua G, Stellato C, Triggiani M, Carreiro-Martins P, Fonseca J, Morais Almeida M, Nogueira-Silva L, Pereira AM, Todo Bom A, Bosse I, Caimmi D, Demoly P, Fontaine JF, Just J, Onorato GL, Kowalski ML, Kuna P, Samolinski B, Anto JM, Mullol J, Valero A, Tomazic PV, Bergmann KC, Keil T, Klimek L, Mösges R, Shamai S, Zuberbier T, Murphy E, McDowall P, Price D, Ryan D, Sheikh A, Chavannes NH, Fokkens WJ, Kvedariene V, Valiulis A, Bachert C, Hellings PW, Kull I, Melen E, Wickman M, Bindslev-Jensen C, Eller E, Haahtela T, Papadopoulos NG, Annesi-Maesano I, Bewick M, Bosnic-Anticevich S, Cruz AA, De Vries G, Gemicioglu B, Larenas-Linnemann D, Laune D, Mathieu-Dupas E, O'Hehir RE, Pfaar O, Portejoie F, Siroux V, Spranger O, Valovirta E, Vandenplas O, Yorgancioglu A.

Références	Doi	IF
Allergy. 2018 Jan 15. [Epub ahead of print]	10.1111/all.13406	6.048

Abstract

BACKGROUND: Large observational implementation studies are needed to triangulate the findings from randomized control trials as they reflect «real-world» everyday practice. In a pilot study, we attempted to provide additional and complementary insights on the real-life treatment of allergic rhinitis (AR) using mobile technology.

METHODS: A mobile phone app (Allergy Diary, freely available in Google Play and Apple App stores) collects the data of daily visual analog scales (VAS) for (i) overall allergic symptoms, (ii) nasal, ocular, and asthma symptoms, (iii) work, as well as (iv) medication use using a treatment scroll list including all medications (prescribed and over the counter (OTC)) for rhinitis customized for 15 countries.

RESULTS: A total of 2871 users filled in 17 091 days of VAS in 2015 and 2016. Medications were reported for 9634 days. The assessment of days appeared to be more informative than the course of the treatment as, in real life, patients do not necessarily use treatment on a daily basis; rather, they appear to increase treatment use with the loss of symptom control. The Allergy Diary allowed differentiation between treatments within or between classes (intranasal corticosteroid use containing medications and oral H1-antihistamines). The control of days differed between no [best control], single, or multiple treatments (worst control).

CONCLUSIONS: This study confirms the usefulness of the Allergy Diary in accessing and assessing everyday use and practice in AR. This pilot observational study uses a very simple assessment (VAS) on a mobile phone, shows novel findings, and generates new hypotheses.

Mots-clefs

mHealth, mobile technology, observational study, rhinitis, treatment

Early prognosis and predictor analysis for positive coronary angiography after out-of-hospital cardiac arrest (OHCA).

Higny J, Guédès A, Jamart J, Hanet C, Gabriel L, Dangoisse V, de Meester de Ravenstein C, Schroeder E.

Références	Doi	IF
Acta Cardiol. 2018 Jan 16:1-8	10.1080/00015385.2017.1415403	0.53

Abstract

BACKGROUND: Key predictors of survival after OHCA have been described in the literature. Current guidelines recommend emergency angiography in patients without an obvious extra-cardiac cause of arrest. However, the value of this strategy is debated. Moreover, diagnosis of acute coronary ischaemia after OHCA remains challenging, especially in patients without ST-segment elevation.

OBJECTIVES: The primary objective was to identify qualitative variables associated with an increased chance of 30-d survival after OHCA. The secondary objective was to identify predictors of 30-d survival among patients with ischaemic cardiomyopathy and patients without ST-segment elevation. Afterwards, we sought to identify parameters associated with acute coronary ischaemia and positive coronary angiography in patients without ST-segment elevation.

METHODS: Retrospective single-centre study including 123 patients resuscitated from OHCA. Baseline characteristics, resuscitation settings and angiographic findings were analysed.

RESULTS: The predictors of 30-d survival after OHCA included witnessed cardiac arrest, haemodynamic instability and coronary angiography. Convertible cardiac rhythm, history of coronary disease and presence of at least two cardiovascular risk factors were associated with acute coronary ischaemia. Predictors for a positive angiography in patients without ST-segment elevation included history of coronary disease, gender, diabetes, dyslipidaemia and presence of at least two cardiovascular risk factors (all p < .05).

CONCLUSIONS: We identified qualitative predictors of 30-day survival after OHCA. Our findings suggest that the recognition of acute coronary ischaemia after OHCA might be improved. The identification of risk criteria may help to select the best candidates for emergency angiography.

Mots-clefs

Out-of-hospital cardiac arrest, acute coronary syndrome, coronary angiography, prognosis, resuscitation

Refractory thyroid carcinoma: which systemic treatment to use ?

Faugeras L, Pirson A-S, Donckier J, Michel L, Lemaire J, Van der Vorst S, D'Hondt L.

Références	Doi	IF
Ther Adv Med Oncol. 2018 (23);10:1758834017752853.	10.1177/1758834017752853	3.9

Abstract

The incidence of thyroid cancer has increased markedly in recent decades, but has been stable in terms of mortality rates. For the most part, these cancers are treated with surgery, which may or may not be followed by radioactive iodine depending on the tumor subtype. Still, many of these cancers will recur and may be treated with radioactive iodine or another surgery. It is unclear what treatment is best for cases of locally advanced or metastatic thyroid cancer that are refractory to radioactive iodine. Chemotherapy has a very low response rate. However, in the past few years, several systemic therapies, primarily targeted, have emerged to improve the overall survival of these patients. Alternative treatments are also of interest, namely peptide receptor radionuclide therapy or immunotherapy.

Mots-clefs

PRRT, chemotherapy, mutations, peptide receptor radionuclide therapy, thyroid carcinoma, tyrosine kinase inhibitor

How resources determine pulmonary rehabilitation programs: A survey among Belgian chest physicians.

Janssens W, Corhay JL, **Bogaerts P**, Derom E, Frusch N, Dang DN, Kibanda J, Ruttens D, Thyrion L, Troosters T, **Marchand E**.

Références	Doi	IF
Chron Respir Dis. 2018 Jan 1:1479972318767732.	10.1177/1479972318767732	2.275

Abstract

Despite overwhelming evidence of its benefits, a widespread implementation of pulmonary rehabilitation (PR) is lacking and the landscape of multidisciplinary programs remains very scattered. The objective of this study is to assess how PR is organized in specialized care centres in Belgium and to identify which barriers may exist according to respiratory physicians. A telephone and online survey was developed by a Belgian expert panel and distributed among all active Belgian chest physicians (n = 492). Data were obtained from 200 respondents (40%). Seventy-five percentage of the chest physicians had direct access to an ambulatory rehabilitation program in their hospital. Most of these programs are organized bi or triweekly for an average period of 3-6 months. Programs focus strongly on chronic obstructive pulmonary disease patients from secondary care, have a multidisciplinary approach and provide exercise capacity and quality of life measures as main outcomes. Yet large differences were observed in process and outcome indicators between the programs of centres with standard funding and those of specialized centres with a larger allocated budget. We conclude that multidisciplinary PR programs are available in the majority of Belgian hospitals. Differences in funding determine the quality of the team, the diversity of the interventions and the monitoring of outcomes. More resources for rehabilitation will directly improve the utilization and quality of this essential treatment option in respiratory diseases.

Mots-clefs

COPD, pulmonary rehabilitation, chronic respiratory disease, outcome, resources



Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia.

Gökbuget N, Dombret H, Bonifacio M, Reichle A, Graux C, Faul C, Diedrich H, Topp MS, Brüggemann M, Horst HA, Havelange V, Stieglmaier J, Wessels H, Haddad V, Benjamin JE, Zugmaier G, Nagorsen D, Bargou RC.

Références	Doi	IF
Blood. 2018 Apr 5;131(14):1522-1531	10.1182/blood-2017-08-798322	13.164

Abstract

Approximately 30% to 50% of adults with acute lymphoblastic leukemia (ALL) in hematologic complete remission after multiagent therapy exhibit minimal residual disease (MRD) by reverse transcriptase-polymerase chain reaction or flow cytometry. MRD is the strongest predictor of relapse in ALL. In this open-label, single-arm study, adults with B-cell precursor ALL in hematologic complete remission with MRD (≥10-3) received blinatumomab 15 μ g/m2 per day by continuous IV infusion for up to 4 cycles. Patients could undergo allogeneic hematopoietic stem-cell transplantation any time after cycle 1. The primary end point was complete MRD response status after 1 cycle of blinatumomab. One hundred sixteen patients received blinatumomab. Eighty-eight (78%) of 113 evaluable patients achieved a complete MRD response. In the subgroup of 110 patients with Ph-negative ALL in hematologic remission, the Kaplan-Meier estimate of relapsefree survival (RFS) at 18 months was 54%. Median overall survival (OS) was 36.5 months. In landmark analyses, complete MRD responders had longer RFS (23.6 vs 5.7 months; P = .002) and OS (38.9 vs 12.5 months; P = .002) compared with MRD nonresponders. Adverse events were consistent with previous studies of blinatumomab. Twelve (10%) and 3 patients (3%) had grade 3 or 4 neurologic events, respectively. Four patients (3%) had cytokine release syndrome grade 1, n = 2; grade 3, n = 2), all during cycle 1. After treatment with blinatumomab in a population of patients with MRD-positive B-cell precursor ALL, a majority achieved a complete MRD response, which was associated with significantly longer RFS and OS compared with MRD nonresponders. This study is registered at www.clinicaltrials.gov as #NCT01207388.

Mots-clefs

A phase II study of the oral JAK1/JAK2 inhibitor ruxolitinib in advanced relapsed/refractory Hodgkin lymphoma.

Van Den Neste E, André M, Gastinne T, Stamatoullas A, Haioun C, Belhabri A, Reman O, Casasnovas O, Ghesquieres H, Verhoef G, Claessen MJ, Poirel HA, Copin MC, Dubois R, Vandenberghe P, Stoian IA, Cottereau AS, Bailly S, Knoops L, Morschhauser F.

Références	Doi	IF
Haematologica. 2018 May;103(5):840-848.	10.3324/haematol.2017.180554	9.090

Abstract

JAK2 constitutive activation/overexpression is common in classical Hodgkin lymphoma, and several cytokines stimulate Hodgkin lymphoma cells by recognizing JAK1-/JAK2bound receptors. JAK blockade may thus be therapeutically beneficial in Hodgkin lymphoma. In this phase II study we assessed the safety and efficacy of ruxolitinib, an oral JAK1/2 inhibitor, in patients with relapsed/refractory Hodgkin lymphoma. The primary objective was overall response rate according to the International Harmonization Project 2007 criteria. Thirty-three patients with advanced disease (median number of prior lines of treatment: 5; refractory: 82%) were included; nine (27.3%) received at least six cycles of ruxolitinib and six (18.2%) received more than six cycles. The overall response rate after six cycles was 9.4% (3/32 patients). All three responders had partial responses; another 11 patients had transient stable disease. Best overall response rate was 18.8% (6/32 patients). Rapid alleviation of B-symptoms was common. The median duration of response was 7.7 months, median progression-free survival 3.5 months (95% CI: 1.9-4.6), and the median overall survival 27.1 months (95% CI: 14.4-27.1). Forty adverse events were reported in 14/33 patients (42.4%). One event led to treatment discontinuation, while 87.5% of patients recovered without sequelae. Twentyfive adverse events were grade 3 or higher. These events were mostly anemia (n=11), all considered related to ruxolitinib. Other main causes of grade 3 or higher adverse events included lymphopenia and infections. Of note, no cases of grade 4 neutropenia or thrombocytopenia were observed. Ruxolitinib shows signs of activity, albeit shortlived, beyond a simple anti-inflammatory effect. Its limited toxicity suggests that it has the potential to be combined with other therapeutic modalities. ClinicalTrials.gov: NCT01877005.

Mots-clefs

Effectiveness of a single session of dual-transcranial direct current stimulation in combination with upper limb roboticassisted rehabilitation in chronic stroke patients: a randomized, double-blind, cross-over study.

Dehem S, Gilliaux M, Lejeune T, Delaunois E, Mbonda P, Vandermeeren Y, Detrembleur C, Stoquart G.

Références	Doi	IF
Int J Rehabil Res. 2018 Jun;41(2):138-145	10.1097/RR.000000000000274	1.432

Abstract

The impact of transcranial direct current stimulation (tDCS) is controversial in the neurorehabilitation literature. It has been suggested that tDCS should be combined with other therapy to improve their efficacy. To assess the effectiveness of a single session of upper limb robotic-assisted therapy (RAT) combined with real or sham-tDCS in chronic stroke patients. Twenty-one hemiparetic chronic stroke patients were included in a randomized, controlled, cross-over double-blind study. Each patient underwent two sessions 7 days apart in a randomized order: (a) 20 min of real dual-tDCS associated with RAT (REAL+RAT) and (b) 20 min of sham dual-tDCS associated with RAT (SHAM+RAT). Patient dexterity (Box and Block and Purdue Pegboard tests) and upper limb kinematics were evaluated before and just after each intervention. The assistance provided by the robot during the intervention was also recorded. Gross manual dexterity (1.8±0.7 blocks, P=0.008) and straightness of movement (0.01±0.03, P<0.05) improved slightly after REAL+RAT compared with before the intervention. There was no improvement after SHAM+RAT. The post-hoc analyses did not indicate any difference between interventions: REAL+RAT and SHAM+RAT (P>0.05). The assistance provided by the robot was similar during both interventions (P>0.05). The results showed a slight improvement in hand dexterity and arm movement after the REAL+RAT tDCS intervention. The observed effect after a single session was small and not clinically relevant. Repetitive sessions could increase the benefits of this combined approach.

Mots-clefs

Addressing Molecular Diagnosis of Occupational Allergies.

13

Raulf M, Quirce S, Vandenplas O.

Références	Doi	IF
Curr Allergy Asthma Rep. 2018 Feb 14;18(1):6	10.1007/s11882-018-0759-9	3.449

Abstract

PURPOSE OF REVIEW: Numerous clinically relevant allergenic molecules enhance the performance of specific (s) IgE tests and improve the specificity of allergy diagnosis. This review aimed to summarize our current knowledge of the high-molecular-weight allergens involved in the development of occupational asthma and rhinitis and to critically analyze the contribution of component-resolved diagnosis in the management of these conditions.

RECENT FINDINGS: There is a lack of standardization and validation for most available extracts of occupational agents, and assessment of sIgE reactivity to occupational allergen components has been poorly investigated, with the notable exception of natural rubber latex (NRL) and wheat flour. In the case of NRL, the application of recombinant single allergens and amplification of natural extracts with stable recombinant allergens improved the test sensitivity. IgE-sensitization profile in patients with baker's asthma showed great interindividual variation, and extract-based diagnostic is still recommended. For other occupational allergens, it remains necessary to evaluate the relevance of single allergen molecules for the sensitization induced by occupational exposure. Progress has been made to characterize occupational allergens especially NRL and wheat, although there is still an unmet need to increase the knowledge of occupational allergens, to include standardized tools into routine diagnostic, and to evaluate their usefulness in clinical practice.

Mots-clefs

Baker's asthma, component-resolved diagnosis, IgE determination, natural rubber latex, occupational allergy, wheat allergens

Prognostic value of baseline metabolic tumor volume in earlystage Hodgkin lymphoma in the standard arm of the H10 trial.

Cottereau AS, Versari A, Loft A, Casasnovas O, Bellei M, Ricci R, Bardet S, Castagnoli A, Brice P, Raemaekers J, Deau B, Fortpied C, Raveloarivahy T, Van Zele E, Chartier L, Vander Borght T, Federico M, Hutchings M, Ricardi U, Andre M, Meignan M.

Références	Doi	IF
Blood. 2018 Mar 29;131(13):1456-1463	10.1182/blood-2017-07-795476	13.164

Abstract

We tested baseline positron emission tomography (PET)/computed tomography (CT) as a measure of total tumor burden to better identify high-risk patients with earlystage Hodgkin lymphoma (HL). Patients with stage I-II HL enrolled in the standard arm (combined modality treatment) of the H10 trial (NCT00433433) with available baseline PET and interim PET (iPET2) after 2 cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine were included. Total metabolic tumor volume (TMTV) was measured on baseline PET. iPET2 findings were reported negative (DS1-3) or positive (DS4-5) with the Deauville scale (DS). The prognostic value of TMTV was evaluated and compared with baseline characteristics, staging classifications, and iPET2. A total of 258 patients were eligible: 101 favorable and 157 unfavorable. The median follow-up was 55 months, with 27 progression-free survival (PFS) and 12 overall survival (OS) events. TMTV was a prognosticator of PFS (P < .0001) and OS (P = .0001), with 86% and 84% specificity, respectively. Five-year PFS and OS were 71% and 83% in the high-TMTV (>147 cm3) group (n = 46), respectively, vs 92% and 98% in the low-TMTV group (≤ 147 cm3). In multivariable analysis including iPET₂, TMTV was the only baseline prognosticator compared with the current staging systems proposed by the European Organization for Research and Treatment of Cancer/Groupe d'Etude des Lymphomes de l'Adulte, German Hodgkin Study Group, or National Comprehensive Cancer Network. TMTV and iPET2 were independently prognostic and, combined, identified 4 risk groups: low (TMTV≤147+DS1-3; 5-year PFS, 95%), low-intermediate (TMTV>147+DS1-3; 5-year PFS, 81.6%), high-intermediate (TMTV≤147+DS4-5; 5-year PFS, 50%), and high (TMTV>147+DS4-5; 5-year PFS, 25%). TMTV improves baseline risk stratification of patients with early-stage HL compared with current staging systems and the predictive value of early PET response as well.

Mots-clefs

International core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy.

Beuscart JB, Knol W, Cullinan S, Schneider C, Dalleur O, Boland B, Thevelin S, Jansen PAF, O'Mahony D, Rodondi N, Spinewine A.

Références	Doi	IF
BMC Med. 2018 Feb 13;16(1):21	10.1186/512916-018-1007-9	2.168

Abstract

BACKGROUND: Comparisons of clinical trial findings in systematic reviews can be hindered by the heterogeneity of the outcomes reported. Moreover, the outcomes that matter most to patients might be underreported. A core outcome set can address these issues, as it defines a minimum set of outcomes that should be reported in all clinical trials in a particular area of research. The objective in this study was to develop a core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy.

METHODS: Firstly, eligible outcomes were identified through a systematic review of trials of medication review in older patients (\geq 65 years) and interviews with 15 older patients. Secondly, an international three-round Delphi survey in four countries involving patients, healthcare professionals, and experts was conducted to validate outcomes to be included in the core outcome set. Consensus meetings were conducted to validate the results. **RESULTS:** Of the 164 participants invited to take part in the Delphi survey, 150 completed Round 1, including 55 patients or family caregivers, 55 healthcare professionals, and 40 experts. A total of 129 participants completed all three rounds. Sixty-four eligible outcomes were extracted from 47 articles, 32 clinical trial protocols, and patient interviews. Thirty outcomes were removed and one added after Round 1, 18 outcomes were removed after Round 2, and seven after Round 3. Results were discussed during consensus meetings. Consensus was reached on seven outcomes, which constitute the core outcome set: drug-related hospital admissions; drug overuse; drug underuse; potentially inappropriate medications; clinically significant drug-drug interactions; health-related quality of life; pain relief.

CONCLUSIONS: We developed a core outcome set of seven outcomes which should be used in future trials of medication review in multi-morbid older patients with polypharmacy.

Mots-clefs

Consensus, core outcome set, delphi survey, medication review, multi-morbidity, older patients, polypharmacy

The integrated stress response system in cardiovascular disease.

Santos-Ribeiro D, Godinas L, Pilette C, Perros F.

Références	Doi	IF
Drug Discov Today. 2018 Apr;23(4):920-929	10.1016/j.drudis.2018.02.008	6.848

Abstract

The integrated stress response system represents an ancillary, extremely conserved signalling pathway present in virtually all eukaryotic cells, which plays an important part in the pathophysiology of several disorders such as cancer and neurodegeneration. However, its role in the cardiovascular system remains largely elusive. Hence, this review aims to acknowledge recent findings regarding the action of the eIF2 α kinases in the cardiovascular system and their role in the pathophysiology of related disorders.

Mots-clefs

 Références
 Doi
 IF

 JAMA. 2018 Feb 27;319(8):829
 10.1001/jama.2017.20846
 47.7

 Abstract
 Comment on: Association Between Use of Non-Vitamin K Oral Anticoagulants With and Without Concurrent Medications and Risk of Major Bleeding in Nonvalvular Atrial Fibrillation. [JAMA. 2017]

17

Mots-clefs

Anti-streptavidin antibodies mimicking heterophilic antibodies in thyroid function tests. Favresse J, Lardinois B, Nassogne MC, Preumont V, Maiter D, Gruson D. Références Doi IF Clin Chem Lab Med. 2018 Jun 27;56(7):e160-e163 10.1515/cclm-2017-1027 3.556 Abstract Mots-clefs Antibodies, blocking tubes, heterophile, interference, streptavidin, thyroid

Myocardial infarction stabilization by cell-based expression of controlled Vascular Endothelial Growth Factor levels.

19

Melly L, Cerino G, Frobert A, Cook S, Giraud MN, Carrel T, Tevaearai Stahel HT, Eckstein F, Rondelet B, Marsano A, Banfi A.

Références	Doi	IF
J Cell Mol Med. 2018 May;22(5):2580-2591	10.1111/jcmm.13511	4.302

Abstract

Vascular Endothelial Growth Factor (VEGF) can induce normal or aberrant angiogenesis depending on the amount secreted in the microenvironment around each cell. Towards a possible clinical translation, we developed a Fluorescence Activated Cell Sorting (FACS)based technique to rapidly purify transduced progenitors that homogeneously express a desired specific VEGF level from heterogeneous primary populations. Here, we sought to induce safe and functional angiogenesis in ischaemic myocardium by cell-based expression of controlled VEGF levels. Human adipose stromal cells (ASC) were transduced with retroviral vectors and FACS purified to generate two populations producing similar total VEGF doses, but with different distributions: one with cells homogeneously producing a specific VEGF level (SPEC), and one with cells heterogeneously producing widespread VEGF levels (ALL), but with an average similar to that of the SPEC population. A total of 70 nude rats underwent myocardial infarction by coronary artery ligation and 2 weeks later VEGF-expressing or control cells, or saline were injected at the infarction border. Four weeks later, ventricular ejection fraction was significantly worsened with all treatments except for SPEC cells. Further, only SPEC cells significantly increased the density of homogeneously normal and mature microvascular networks. This was accompanied by a positive remodelling effect, with significantly reduced fibrosis in the infarcted area. We conclude that controlled homogeneous VEGF delivery by FACS-purified transduced ASC is a promising strategy to achieve safe and functional angiogenesis in myocardial ischaemia.

Mots-clefs

Vascular endothelial growth factor, adipose stem cells, angiogenesis, cell therapy, myocardial infarction

The Use of a β-lactamase-based Conductimetric Biosensor Assay to Detect Biomolecular Interactions.

Vandevenne M, Dondelinger M, Yunus S, Freischels A, Freischels R, Crasson O, Rhazi N, Bogaerts P, Galleni M, Filée P.

Références	Doi	IF
J Vis Exp. 2018 Feb 1;(132)	10.3791/55414	1.24

Abstract

Biosensors are becoming increasingly important and implemented in various fields such as pathogen detection, molecular diagnosis, environmental monitoring, and food safety control. In this context, we used β -lactamases as efficient reporter enzymes in several protein-protein interaction studies. Furthermore, their ability to accept insertions of peptides or structured proteins/domains strongly encourages the use of these enzymes to generate chimeric proteins. In a recent study, we inserted a singledomain antibody fragment into the Bacillus licheniformis BlaP β -lactamase. These small domains, also called nanobodies, are defined as the antigen-binding domains of single chain antibodies from camelids. Like common double chain antibodies, they show high affinities and specificities for their targets. The resulting chimeric protein exhibited a high affinity against its target while retaining the β-lactamase activity. This suggests that the nanobody and β -lactamase moieties remain functional. In the present work, we report a detailed protocol that combines our hybrid β-lactamase system to the biosensor technology. The specific binding of the nanobody to its target can be detected thanks to a conductimetric measurement of the protons released by the catalytic activity of the enzyme.

Mots-clefs

Case report: Purulent transformation of granulocytic sarcoma: An unusual pattern of differentiation in acute promyelocytic leukemia.

Collinge E, Tigaud I, Balme B, Gerland LM, Sujobert P, Carlioz V, Salles G, Thomas X, Paubelle E.

Références	Doi	IF
Medicine (Baltimore). 2018 Feb;97(8):e9657	10.1097/MD.000000000009657	1.63

Abstract

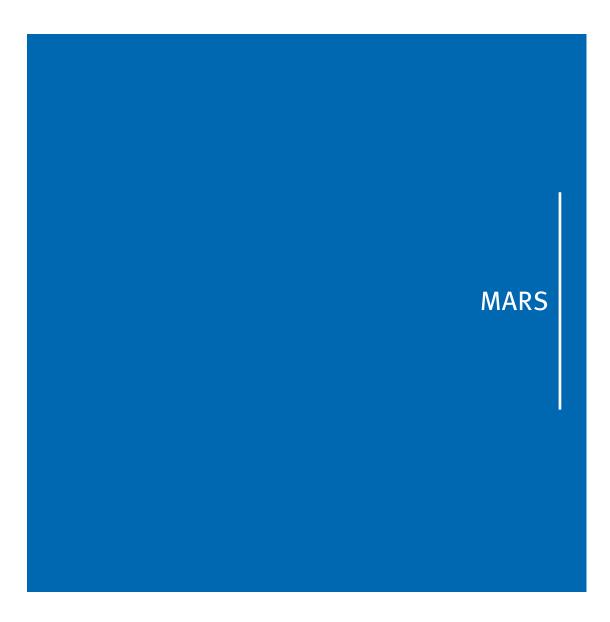
RATIONALE: Acute promyelocytic leukemia (APL) is a curable subtype of acute myeloid leukemia. APL is currently treated with combination of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) resulting in the induction of apoptosis and differentiation of the leukemic cells. Differentiation syndrome (so-called ATRA syndrome) is the main life-threatening complication of induction therapy with these differentiating agents. **PATIENT CONCERNS:** Herein, we report the case of a 49-year-old woman diagnosed with APL with, concomitantly, a bulky cutaneous lesion of 10 cm diameter with a red-to-purple background and a necrotic center, localized on her abdomen.

DIAGNOSES: After 10 days of treatment, the cutaneous lesion became purulent. Fluorescence in situ hybridization (FISH) analysis performed on this pus confirmed the presence of malignant features in the involved granulocytes proving their origin from the differentiation of leukemic APL cells, as all the analyzed nuclei showed 2 promyelocytic leukemia (PML)-retinoic acid receptor-a (RARA) fusions signals.

INTERVENTION: The association by ATRA and ATO was continued.

OUTCOME: Eventually, the evolution was favorable with healing in three weeks. **LESSONS:** This case report therefore highlights the differentiation phenomenon of promyelocytic blasts within promyelocytic sarcoma with the ATRA-ATO combination and the efficacy of this drug association in resolving both the malignant sarcoma and a secondary local infection.

Mots-clefs



In Regard to Bibault et al.		
Daisne J-F, Nuyts S, Duprez F, <mark>Bihin B.</mark>		
Références	Doi	IF
Int J Radiat Oncol Biol Phys. 2018 (1);100(3):807-808	10.1016/j.ijrobp.2017.11.039	5.554

Tailored Y-stent on the Secondary Carina for Recurrent Nonanastomotic Posttransplant Left Bronchial Stenosis.		
Pirard L, Dahlqvist C, Ocak S, Putz L, Dincq A-S, d'Odémont J-P.		
Références	Doi	IF
Transplantation. 2018 Jun;102(6):e253		
nunsplaination. 2010 juli,102(0):8253	10.1097/TP.0000000000002166	3.960
Mots-clefs		

Idiopathic pericardial cyst causing heart failure. Valschaerts AS, Dupont M, Seldrum S. Références IF Doi Acta Cardiol. 2018 Mar 23:1-20 10.1080/00015385.2018.1453450 0.808 Abstract Mots-clefs

Physical therapy in patients with disorders of consciousness: Impact on spasticity and muscle contracture.

Thibaut A, Wannez S, **Deltombe T**, Martens G, Laureys S, Chatelle C.

Références	Doi	IF
NeuroRehabilitation. 2018;42(2):199-205	10.3233/NRE-172229	0.84

Abstract

BACKGROUND: Spasticity is a frequent complication after severe brain injury, which may prevent the rehabilitation process and worsen the patients' quality of life. In this study, we investigated the correlation between spasticity, muscle contracture, and the frequency of physical therapy (PT) in subacute and chronic patients with disorders of consciousness (DOC).

METHODS: 109 patients with subacute and chronic disorders of consciousness (Vegetative state/Unresponsive wakefulness syndrome - VS/UWS; minimally conscious state - MCS and patients who emerged from MCS - EMCS) were included in the study (39 female; mean age: 40±13.5y; 60 with traumatic etiology; 35 VS/UWS, 68 MCS, 6 EMCS; time since insult: 38±42months). The number of PT sessions (i.e., 20 to 30 minutes of conventional stretching of the four limbs) was collected based on patients' medical record and varied between 0 to 6 times per week (low PT=0-3 and high PT=4-6 sessions per week). Spasticity was measured with the Modified Ashworth Scale (MAS) on every segment for both upper (UL) and lower limbs (LL). The presence of muscle contracture was assessed in every joint. We tested the relationship between spasticity and muscle contracture with the frequency of PT as well as other potential confounders such as time since injury or anti-spastic medication intake.

RESULTS: We identified a negative correlation between the frequency of PT and MAS scores as well as the presence of muscle contracture. We also identified that patients who received less than four sessions per week were more likely to be spastic and suffer from muscle contracture than patients receiving 4 sessions or more. When separating subacute (3 to 12 months post-insult) and chronic (>12months post-insult) patients, these negative correlations were only observed in chronic patients. A logit regression model showed that frequency of PT influenced spasticity, whereas neither time since insult nor medication had a significant impact on the presence of spasticity. On the other hand, PT, time since injury and medication seemed to be associated with the presence of muscle contracture.

CONCLUSION: Our results suggest that, in subacute and chronic patients with DOC, PT could have an impact on patients' spasticity and muscles contractures. Beside PT, other factors such as time since onset and medication seem to influence the development of muscle contractures. These findings support the need for frequent PT sessions and regular re-evaluation of the overall spastic treatment for patients with DOC.

Mots-clefs

Spasticity, disorders of consciousness, hypertonicity, minimally conscious state, muscle contracture, non-pharmacological treatment, physical therapy, upper motor neuron, vegetative state/unresponsive wakefulness syndrome

Long-Term Safety of In Utero Exposure to Anti-TNFα Drugs for the Treatment of Inflammatory Bowel Disease: Results from the Multicenter European TEDDY Study.

Chaparro M, Verreth A, Lobaton T, Gravito-Soares E, Julsgaard M, Savarino E, Magro F, Avni Biron I, Lopez-Serrano P, Casanova MJ, Gompertz M, Vitor S, Arroyo M, Pugliese D, Zabana Y, Vicente R, Aguas M, Bar-Gil Shitrit A, Gutierrez A, Doherty GA, Fernandez-Salazar L, Martínez Cadilla J, Huguet JM, O'Toole A, Stasi E, Manceñido Marcos N, Villoria A, Karmiris K, **Rahier J-F,** Rodriguez C, Diz-Lois Palomares M, Fiorino G, Benitez JM, Principi M, Naftali T, Taxonera C, Mantzaris G, Sebkova L, Iade B, Lissner D, Ferrer Bradley I, Lopez-San Roman A, Marin-Jimenez I, Merino O, Sierra M, Van Domselaar M, Caprioli F, Guerra I, Peixe P, Piqueras M, Rodriguez-Lago I, Ber Y, van Hoeve K, Torres P, Gravito-Soares M, Rudbeck-Resdal D, Bartolo O, Peixoto A, Martin G, Armuzzi A, Garre A, Donday MG, Martín de Carpi FJ, Gisbert JP.

Références	Doi	IF
Am J Gastroenterol. 2018 Mar;113(3):396-403	10.1038/ajg.2017.501	

Abstract

OBJECTIVES: The long-term safety of exposure to anti-tumor necrosis factor (anti-TNF α) drugs during pregnancy has received little attention. We aimed to compare the relative risk of severe infections in children of mothers with inflammatory bowel disease (IBD) who were exposed to anti-TNF α drugs in utero with that of children who were not exposed to the drugs.

METHODS: Retrospective multicenter cohort study. Exposed cohort: children from mothers with IBD receiving anti-TNF α medication (with or without thiopurines) at any time during pregnancy or during the 3 months before conception. Non-exposed cohort: children from mothers with IBD not treated with anti-TNF α agents or thiopurines at any time during pregnancy or the 3 months before conception. The cumulative incidence of severe infections after birth was estimated using Kaplan-Meier curves, which were compared using the log-rank test. Cox-regression analysis was performed to identify potential predictive factors for severe infections in the offspring.

RESULTS: The study population comprised 841 children, of whom 388 (46%) had been exposed to anti-TNF α agents. Median follow-up after delivery was 47 months in the exposed group and 68 months in the non-exposed group. Both univariate and multivariate analysis showed the incidence rate of severe infections to be similar in nonexposed and exposed children (1.6% vs. 2.8% per person-year, hazard ratio 1.2 (95% confidence interval 0.8-1.8)). In the multivariate analysis, preterm delivery was the only variable associated with a higher risk of severe infection (2.5% (1.5-4.3)).

CONCLUSIONS: In utero exposure to anti-TNF α drugs does not seem to be associated with increased short-term or long-term risk of severe infections in children.

Mots-clefs

Central nervous system relapse in patients over 80 years with diffuse large B-cell lymphoma: an analysis of two LYSA studies.

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Cabannes-Hamy A, Peyrade F, Jardin F, Emile JF, Delwail V, Mounier N, Haioun C, Perrot A, Fitoussi O, Lara D, Delarue R, **André M**, Offner F, Ghesquières H, Pascal L, Soussain C, Lazarovici J, Schiano JM, Gaulard P, Tilly H, Thieblemont C; LYSA; lymphoma study association.

Références	Doi	IF
Cancer Med. 2018 Mar;7(3):539-548	10.1002/cam4.1139	3.362

Abstract

CNS relapse is reported in 2-5% of diffuse large B-cell lymphoma (DLBCL) patients, dramatically decreasing overall survival (OS). Very few studies address incidence and risk factors of CNS relapse in very elderly patients, a challenging population to treat given their commonly associated comorbidities. A retrospective analysis was performed of 270 DLBCL patients >80 years treated between 2004 and 2013 in two multicentre phase II LYSA trials (LNH03-7B, LNH09-7B) evaluating the addition of rituximab or of atumumab to mini-CHOP as front-line therapy. No patients received CNS prophylaxis. CNS relapse was evaluated according to cumulative incidence, patient characteristics, risk factors, and survival. Median age was 83 years (range: 79-95). After a median follow-up of 28.7 months, eight patients had CNS relapse (3.0%). Median time between inclusion and CNS relapse was 19.2 months (range: 3.2-32.6). Patients survived a median of 1.5 months after CNS relapse (range: 0.4-4.1). Median OS from relapse was significantly lower in CNS relapse patients (1.5 months, 95% CI: 0.4-3.5) compared to patients with non-CNS relapse (6.6 months; 95% CI: 4.6-11.9). No baseline characteristics were associated with CNS relapse. The proportion of patients with CNS disease did not differ significantly between patients with low-intermediate risk according to CNS-IPI and patients with high risk (3% vs. 2.8%, P = 1.00). CNS relapse cumulative incidence in very elderly treatment-naive patients is 1.8% at 2 years and is associated with poor survival. This population had a long median time to CNS relapse. Absence of prophylaxis did not strongly impact CNS relapse incidence.

Preventability of serious thromboembolic and bleeding events related to the use of oral anticoagulants: a prospective study.

Sennesael AL, Larock A-S, Devalet B, Mathieux V, Verschuren F, Muschart X, Dalleur O, Dogné J-M, Spinewine A.

Références	Doi	IF
Br J Clin Pharmacol. 2018 Jul;84(7):1544-1556	10.1111/bcp.13580	3.838

Abstract

AIMS: To determine the preventability of serious adverse drug reactions (ADRs) related to the use of direct oral anticoagulants (DOACs), and to explore contributing factors to preventable ADRs. Results were compared with vitamin K antagonists (VKAs). **METHODS:** We conducted a prospective observational study in the emergency departments of two teaching hospitals from July 2015 to January 2016. Patients admitted with a thrombotic or bleeding event while under DOAC or VKA were included. Four independent reviewers assessed causality, seriousness and preventability of ADRs using pilot-tested scales. For cases of serious and potentially preventable ADRs, we performed semi-structured interviews with general practitioners to identify contributing factors to ADRs. The primary outcome was the proportion of serious ADRs that were potentially preventable.

RESULTS: The analysis included 46 DOAC and 43 VKA patients (median age 79 years). Gastrointestinal (n = 34) and intracranial (n = 16) bleedings were the most frequent ADRs. Results were that 53% of DOAC- and 61% of VKA-related serious ADRs were deemed potentially preventable. Prescribing issues and inadequate monitoring were frequent for DOAC and VKA respectively. We identified many causes of preventable ADRs that applied to all oral anticoagulants, such as pharmacodynamic drug interactions and lack of communication.

CONCLUSIONS: More than half of serious ADRs were potentially preventable for both DOACs and VKAs. Interventions focusing on prescribing, patient education and continuity of care should help improve the use of DOACs in practice.

Mots-clefs

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

29

Daily allergic multimorbidity in rhinitis using mobile technology: A novel concept of the MASK study.

Bousquet J, Devillier P, Anto JM, Bewick M, Haahtela T, Arnavielhe S, Bedbrook A, Murray R, van Eerd M, Fonseca JA, Morais Almeida M, Todo Bom A, Menditto E, Passalacqua G, Stellato C, Triggiani M, Ventura MT, Vezzani G, Annesi-Maesano I, Bourret R, Bosse I, Caimmi D, Cartier C, Demoly P, Just J, Portejoie F, Siroux V, Viart F, Bergmann KC, Keil T, Klimek L, Mösges R, Pfaar O, Shamai S, Zuberbier T, Mullol J, Valero A, Spranger O, Tomazic PV, Kowalski ML, Kuna P, Kupczyk M, Raciborski F, Samolinski B, Toppila-Salmi SK, Valovirta E, Cruz AA, Sarquis-Serpa F, da Silva J, Stelmach R, Larenas-Linnemann D, Rodriguez Gonzalez M, Burguete Cabañas MT, Kvedariene V, Valiulis A, Chavannes NH, Fokkens WJ, Ryan D, Sheikh A, Bachert C, Hellings PW, Vandenplas O, Ballardini N, Kull I, Melén E, Westman M, Wickman M, Bindslev-Jensen C, Eller E, Bosnic-Anticevich S, O'Hehir RE, Agache I, Bieber T, Casale T, Gemicioğlu B, Ivancevich JC, De Vries G, Sorensen M, Yorgancioglu A, Laune D; MACVIA working group.

Références	Doi	IF
Allergy. 2018 Aug;73(8):1622-1631	10.1111/all.13448	6.048

Abstract

BACKGROUND: Multimorbidity in allergic airway diseases is well known, but no data exist about the daily dynamics of symptoms and their impact on work. To better understand this, we aimed to assess the presence and control of daily allergic multimorbidity (asthma, conjunctivitis, rhinitis) and its impact on work productivity using a mobile technology, the Allergy Diary.

METHODS: We undertook a 1-year prospective observational study in which 4 210 users and 32 585 days were monitored in 19 countries. Five visual analogue scales (VAS) assessed the daily burden of the disease (i.e., global evaluation, nose, eyes, asthma and work). Visual analogue scale levels <20/100 were categorized as «Low» burden and VAS levels ≥50/100 as «High» burden.

RESULTS: Visual analogue scales global measured levels assessing the global control of the allergic disease were significantly associated with allergic multimorbidity. Eight hypothesis-driven patterns were defined based on «Low» and «High» VAS levels. There were <0.2% days of Rhinitis Low and Asthma High or Conjunctivitis High patterns. There were 5.9% days with a Rhinitis High-Asthma Low pattern. There were 1.7% days with a Rhinitis High-Asthma High-Conjunctivitis Low pattern. A novel Rhinitis High-Asthma High-Conjunctivitis Low pattern. A novel Rhinitis High-Asthma High-Conjunctivitis High pattern was identified in 2.9% days and had the greatest impact on uncontrolled VAS global measured and impaired work productivity. Work productivity was significantly correlated with VAS global measured levels.

CONCLUSIONS: In a novel approach examining daily symptoms with mobile technology, we found considerable intra-individual variability of allergic multimorbidity including a previously unrecognized extreme pattern of uncontrolled multimorbidity.

Mots-clefs

Asthma, conjunctivitis, multimorbidity, rhinitis, work productivity

Periprocedural management of anticoagulation for atrial fibrillation catheter ablation in direct oral anticoagulant-treated patients.

Martin AC, Lessire S, Leblanc I, Dincq A-S, Philip I, Gouin-Thibault I, Godier A.

Références	Doi	IF
Clin Cardiol. 2018 May;41(5):646-651	10.1002/clc.22944	2.733

Abstract

BACKGROUND: Guidelines recommend performing atrial fibrillation (AF) catheter ablation without interruption of a direct oral anticoagulants (DOACs) and to administer unfractionated heparin (UFH) for an activated clotting time (ACT) ≥300 seconds, by analogy with vitamin K antagonist (VKA). Nevertheless, pharmacological differences between DOACs and VKA, especially regarding ACT sensitivity and UFH response, prevent extrapolation from VKA to DOACs.

HYPOTHESIS: The level of anticoagulation at the time of the procedure in uninterrupted DOAC-treated patients is unpredictable and would complicate intraprocedural UFH administration and monitoring.

METHODS: This prospective study included interrupted DOAC-treated patients requiring AF ablation. Preprocedural DOAC concentration ([DOAC]), intraprocedural UFH administration, and ACT values were recorded. A cohort of DOAC-treated patients requiring flutter catheter ablation was considered to illustrate [DOAC] without DOAC interruption.

RESULTS: Forty-eight patients underwent AF and 14 patients underwent flutter ablation, respectively. In uninterrupted DOAC-treated patients, [DOAC] ranged from \leq 30 to 466 ng/mL. When DOAC were interrupted, from 54 to 218 hours, [DOAC] were minimal (maximum: 36 ng/mL), preventing DOAC-ACT interference. Anyway, ACT values were poorly correlated with UFH doses (R 2 = 0.2256).

CONCLUSIONS: Our data showed that uninterrupted DOAC therapy resulted in an unpredictable and highly variable initial level of anticoagulation before catheter ablation. Moreover, even with DOAC interruption preventing interference between DOAC, UFH, and ACT, intraprocedural UFH monitoring was complex. Altogether, our exploratory results call into question the appropriateness of transposing UFH dose protocols, as well as the relevance of ACT monitoring in uninterrupted DOAC-treated patients.

Mots-clefs

Activated clotting time, atrial fibrillation catheter ablation, direct oral anticoagulant, heparin, monitoring

Molecular Characterization of OXA-198 Carbapenemase-Producing Pseudomonas aeruginosa Clinical Isolates.

31

Bonnin RA, Bogaerts P, Girlich D, Huang TD, Dortet L, Glupczynski Y, Naas T.

Références	Doi	IF
Antimicrob Agents Chemother. 2018 May 25;62(6)	10.1128/AAC.02496-17	4.302

Abstract

Carbapenemase-producing Pseudomonadaceae have increasingly been reported worldwide, with an ever-increasing heterogeneity of carbapenem resistance mechanisms, depending on the bacterial species and the geographical location. OXA-198 is a plasmidencoded class D β-lactamase involved in carbapenem resistance in one Pseudomonas aeruginosa isolate from Belgium. In the setting of a multicenter survey of carbapenem resistance in P. aeruginosa strains in Belgian hospitals in 2013, three additional OXA-198producing P. aeruginosa isolates originating from patients hospitalized in one hospital were detected. To reveal the molecular mechanism underlying the reduced susceptibility to carbapenems, MIC determinations, whole-genome sequencing, and PCR analyses to confirm the genetic organization were performed. The plasmid harboring the blaOXA-198 gene was characterized, along with the genetic relatedness of the four P. aeruginosa isolates. The blaOXA-198 gene was harbored on a class 1 integron carried by an ~49kb IncP-type plasmid proposed as IncP-11. The same plasmid was present in all four P. aeruginosa isolates. Multilocus sequence typing revealed that the isolates all belonged to sequence type 446, and single-nucleotide polymorphism analysis revealed only a few differences between the isolates. This report describes the structure of a 49-kb plasmid harboring the blaOXA-198 gene and presents the first description of OXA-198-producing P. aeruginosa isolates associated with a hospital-associated cluster episode.

Mots-clefs

IncP-11, carbapenemase, integrin, outbreak, plas

Melly L, Torregrossa G, Lee T, Jansens J-L, Puskas JD.

Références	Doi	IF
J Thorac Dis. 2018 Mar;10(3):1960-1967	10.21037/jtd.2018.02.43	2.33

Abstract

Coronary artery bypass grafting (CABG) remains the most common cardiac surgery performed today worldwide. The history of this procedure can be traced back for more than 100 years, and its development has been touched by several pioneers in the field of cardiac surgery, who have contributed with both their successes and failures. With ever increasing follow up and number of patients treated, thinking regarding optimal CABG technique evolves continually. This article reviews the history of CABG from its early experimental work to recent technological advances.

Mots-clefs

Coronary artery bypass grafting (CABG), coronary revascularization, history

32

Fifty years of coronary artery bypass grafting.

Management of antiplatelet therapy in patients undergoing elective invasive procedures : Proposals from the French Working Group on perioperative hemostasis (GIHP) and the French Study Group on thrombosis and hemostasis (GFHT). In collaboration with the French Society for Anesthesia and Intensive Care (SFAR).

Godier A, Fontana P, Motte S, Steib A, Bonhomme F, Schlumberger S, Lecompte T, Rosencher N, Susen S, Vincentelli A, Gruel Y, Albaladejo P, Collet JP; French Working Group on perioperative hemostasis (GIHP).

Références	Doi	IF
Arch Cardiovasc Dis. 2018 Mar;111(3):210-223	10.1016/j.acvd.2017.12.004	0.48

Abstract

Mots-clefs

Agent antiplaquettaire, anesthésie loco-régionale, antiplatelet therapy, chirurgie, haemorrhage, hémorragie, local anaesthesia, surgery, thrombose, thrombosis

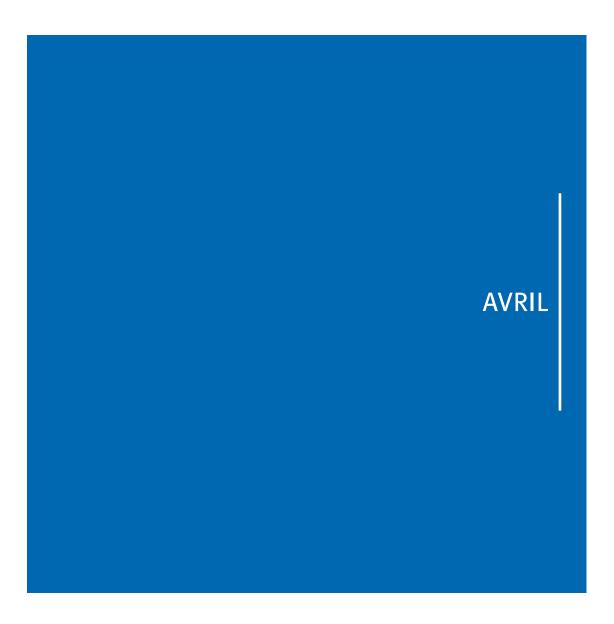
Assessment of the risk of alcohol relapse following liver transplantation for alcoholic hepatitis using a meta-analysis approach.

Deltenre P, Marot A, Dubois M, Trépo E, Moreno C.

Références	Doi	IF
J Hepatol. 2018 Jun;68(6):1322-1323	10.1016/j.jhep.2018.02.020	12.486

Abstract

Mots-clefs



Very long-term Voice Handicap Index Voice Outcomes after Montgomery Thyroplasty: A cross-sectional study.

Desuter G, Zapater E, Van der Vorst S, Henrard S, van Lith-Bijl JT, van Benthem PP, Sjögren EV.

Références	Doi	IF
Clin Otolaryngol. 2018 Apr 6. doi: 10.1111/coa.13113	10.1111/coa.13113	2.696

Abstract

OBJECTIVE: The aim of this multicentric cross-sectional study was to examine the permanency of Montgomery thyroplasty (MTIS) results from a patient's perspective. **DESIGN:** The study consisted of collecting Voice Handicap Index (VHI-30) questionnaires from patients who had previously been operated with MTIS between 2 and 12 years before. Very long-term (>2 years) postoperative data were compared with the previously acquired preoperative and early postoperative VHI results. Influence of factors such as age, gender, size/side of the prosthesis and length of the follow-up were also analysed. **SETTING:** Multicentric study involving three tertiary European voice centres.

PARTICIPANTS: Forty-nine unilateral vocal fold paralysis (UVFP) patients, treated by MTIS, were included in the study.

MAIN OUTCOME MEASURES: The Voice Handicap Index-30 score.

RESULTS & CONCLUSIONS: The median VHI was significantly different over time-points (Friedman's test P < .001), with a significant difference between preoperative and early postoperative time-points (median VHI: 70 vs 21, respectively; P < .001) and between preoperative and very long-term postoperative time-points (median VHI: 70 vs 16, respectively; P < .001). The median VHI did not differ for the early and very long-term postoperative time-points (median VHI: 21 vs 16; P = .470). Age differences, gender differences and size/side differences of the prostheses, centres where surgery took place and length of the follow-up showed no significant influence. Medialisation thyroplasty (MT) overall and MTIS, in particular, should be considered as a possible standard of care for UVFP when permanency of voice results is sought.

Mots-clefs

Dysphonia, medical education, outcomes quality of life, phoniatrics, voice

Evaluation of the Fully Automated HemosIL Acustar ADAMTS13 Activity Assay. Favresse J, Lardinois B, Chatelain B, Jacqmin H, Mullier F. Références IF Doi Thromb Haemost. 2018 May;118(5):942-944 10.1055/s-0038-1641151 4.899 Abstract Mots-clefs

Doi 10.1007/\$13760-018-0916-x	IF 2.072
10.1007/\$13760-018-0916-x	2.072

Lung allocation score: the Eurotransplant model versus the revised US model - a cross-sectional study.

Smits JM, Nossent G, **Evrard P**, Lang G, Knoop C, Kwakkel-van Erp JM, Langer F, Schramm R, van de Graaf E, Vos R, Verleden G, **Rondelet B**, Hoefer D, Hoek R, Hoetzenecker K, Deuse T, Strelniece A, Green D, de Vries E, Samuel U, Laufer G, Buhl R, Witt C, Gottlieb J.

Références	Doi	IF
Transpl Int. 2018 Aug;31(8):930-937	10.1111/tri.13262	3.196

Abstract

Both Eurotransplant (ET) and the US use the lung allocation score (LAS) to allocate donor lungs. In 2015, the US implemented a new algorithm for calculating the score while ET has fine-tuned the original model using business rules. A comparison of both models in a contemporary patient cohort was performed. The rank positions and the correlation between both scores were calculated for all patients on the active waiting list in ET. On February 6th 2017, 581 patients were actively listed on the lung transplant waiting list. The median LAS values were 32.56 and 32.70 in ET and the US, respectively. The overall correlation coefficient between both scores was o.71. Forty-three per cent of the patients had a < 2 point change in their LAS. US LAS was more than two points lower for 41% and more than two points higher for 16% of the patients. Median ranks and the 90th percentiles for all diagnosis groups did not differ between both scores. Implementing the 2015 US LAS model would not significantly alter the current waiting list in ET.

Development of clinical pharmacy in Belgian hospitals through pilot projects funded by the government.

Somers A, **Spinewine A**, Spriet I, Steurbaut S, Tulkens P, **Hecq J-D**, Willems L, Robays H, Dhoore M, Yaras H, Vanden Bremt I, Haelterman M.

Références	Doi	IF
Acta Clin Belg. 2018 Apr 30:1-7	10.1080/17843286.2018.1462877	0.916

Abstract

Objectives The goal is to develop clinical pharmacy in the Belgian hospitals to improve drug efficacy and to reduce drug-related problems. Methods From 2007 to 2014, financial support was provided by the Belgian federal government for the development of clinical pharmacy in Belgian hospitals. This project was guided by a national Advisory Working Group. Each funded hospital was obliged to describe yearly its clinical pharmacy activities. Results In 2007, 20 pharmacists were funded in 28 pilot hospitals; this number was doubled in 2009 to 40 pharmacists over 54 institutions, representing more than half of all acute Belgian hospitals. Most projects (72%) considered patient-related activities, whereas some projects (28%) had a hospital-wide approach. The projects targeted patients at admission (30%), during hospital stay (52%) or at discharge (18%). During hospital stay, actions were mainly focused on geriatric patients (20%), surgical patients (15%), and oncology patients (9%). Experiences, methods, and tools were shared during meetings and workshops. Structure, process, and outcome indicators were reported and strengths, weaknesses, opportunities, and threats were described. The yearly reports revealed that the hospital board was engaged in the project in 87% of the cases, and developed a vision on clinical pharmacy in 75% of the hospitals. In 2014, the pilot phase was replaced by structural financing for clinical pharmacy in all acute Belgian hospitals. Conclusion The pilot projects in clinical pharmacy funded by the federal government provided a unique opportunity to launch clinical pharmacy activities on a broad scale in Belgium. The results of the pilot projects showed clear implementation through case reports, time registrations, and indicators. Tools for clinical pharmacy activities were developed to overcome identified barriers. The engagement of hospital boards and the results of clinical pharmacy activities persuaded the government to start structural financing of clinical pharmacy.

Mots-clefs

Clinical pharmacy, hospital pharmacist, indicators, national pilot project, patient safety

Circulating tumor DNA in early response assessment and monitoring of advanced colorectal cancer treated with a multi-kinase inhibitor.

Vandeputte C, Kehagias P, El Housni H, Ameye L, Laes JF, Desmedt C, Sotiriou C, Deleporte A, Puleo F, Geboes K, Delaunoit T, Demolin G, Peeters M, D'Hondt L, Janssens J, Carrasco J, Marechal R, Galdon MG, Heimann P, Paesmans M, Flamen P, Hendlisz A.

Références	Doi	IF
Oncotarget. 2018 Apr 3;9(25):17756-17769	10.18632/oncotarget.24879	5.168

Abstract

Predictive biomarkers are eagerly awaited in advanced colorectal cancer (aCRC). Targeted sequencing performed on tumor and baseline plasma samples in 20 patients with aCRC treated with regorafenib identified 89 tumor-specific mutations of which \geq 50% are also present in baseline plasma. Droplet digital PCR (ddPCR) assays were optimized to monitor circulating tumor DNA (ctDNA) levels in plasmatic samples collected throughout the treatment course and showed the importance of using the absolute value for ctDNA rather than the mutant/wild type ratio in monitoring the therapy outcome. High baseline cell free DNA (cfDNA) levels are associated with shorter overall survival (OS) (HR 7.38, P=0.001). An early increase (D14) in mutated copies/mL is associated with a significantly worse PFS (HR 6.12, P=0.008) and OS (HR 8.02, P=0.004). These data suggest a high prognostic value for early ctDNA level changes and support the use of blood-born genomic markers as a tool for treatment.

Late diagnosis of a congenitally corrected transposition of the great arteries discovered at pacemaker implantation in a patient previously diagnosed with dextrocardia and situs solitus.

Vasiliu A, Seldrum S, Dupont M, Dormal F, Blommaert D, De Roy L.

Références	Doi	IF
Clin Case Rep. 2018 Apr 22;6(6):1112-1116	10.1002/ccr3.1541. eCollection	

Abstract

Congenitally corrected transposition of the great arteries (CCTGA) should not be missed in patients with dextrocardia and situs solitus. We report a case of a 56-year-old man with late diagnosis of CCTGA after ventricular lead replacement. Free LV wall pacing may be favorable in these patients so to prevent deterioration of the systemic RV function.

Mots-clefs CCTGA, dextrocardia, pacemaker

Prédisposition héréditaire aux hémopathies malignes.

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Dupriez S, Ferrant A, Vekemans MC, Brichard B, Michaux L, Connerotte T, Van Den Neste E, Vermylen C, Knoops L, **Graux C**, Duhoux FP, Lambert C, Poiré X, Antoine-Poirel H.

Références	Doi	IF
LouvMed 2018 ;137(4)166-173		

Abstract

Les syndromes de prédisposition héréditaire aux hémopathies malignes (SPHHM) sont encore sous-diagnostiqués. Il est pourtant important de les identifier afin de sélectionner le conditionnement pré-greffe adéquat, d'exclure la présence d'une mutation familiale chez un donneur sélectionné et d'effectuer la prévention et/ou le suivi personnel et familial. À travers un recensement rétrospectif de 252 personnes appartenant à 117 familles ayant présenté plusieurs cancers dont au moins une hémopathie maligne, une mutation dans un gène de prédisposition a été identifiée dans 8 familles différentes (GATA2 dans 2 familles, TERT, FANCA, TP53, PTCH1, BRCA1 et ATM dans une seule famille chacun). Ceci a permis une prise en charge spécifique de ces patients et un dépistage pré-symptomatique chez les apparentés. Cette étude montre l'importance d'une identification précoce des SPHHM et d'une étroite collaboration entre l'hématologue et le généticien. Enfin, nous proposons un ensemble de recommandations afin de reconnaître et de suivre de façon la plus optimale possible les SPHHM sur base de la littérature et de nos observations.

Que savons-nous à ce propos ?

La prédisposition héréditaire aux hémopathies malignes a longtemps été sous-estimée. Grâce aux nouvelles technologies de séquençage, près d'une centaine de gènes pouvant prédisposer aux hémopathies malignes ont été identifiés à ce jour. Actuellement, on estime qu'une prédisposition héréditaire serait présente chez près de 10% des individus atteints d'une hémopathie maligne, principalement myéloïde. Leur identification a des conséquences cruciales pour la prise en charge de ces patients ainsi que pour le diagnostic pré-symptomatique. De plus, il n'existe pas ou peu de consensus et de recommandations basées sur les preuves concernant le conseil oncogénétique et la prise en charge des patients atteints d'un SPHHM et de leur famille.

Que nous apporte cet article ?

Cet article est l'occasion de faire le point sur les recommandations, le conseil oncogénétique et la prise en charge des patients atteints d'un SPHHM et de leur famille. L'étude rétrospective multicentrique réalisée dans ce cadre permet de rappeler les bénéfices de l'identification de ces syndromes de prédisposition et l'importance de la collaboration entre l'onco-hématologue et le généticien.

Mots-clefs

Hémopathie maligne, prédisposition héréditaire, génétique, conseil génétique

Clinical application of targeted next-generation sequencing for colorectal cancer patients: a multicentric Belgian experience.

D'Haene N, Fontanges Q, De Nève N, Blanchard O, Melendez B, **Delos M**, Dehou MF, Maris C, Nagy N, Rousseau E, Vandenhove J, Gilles A, De Prez C, Verset L, Van Craynest MP, Demetter P, Van Laethem JL, Salmon I, Le Mercier M.

Références	Doi	IF
Oncotarget. 2018 Apr 17;9(29):20761-20768	10.18632/oncotarget.25099	5.168

Abstract

International guidelines made RAS (KRAS and NRAS) status a prerequisite for the use of anti-EGFR agents for metastatic colorectal cancer (CRC) patients. Daily, new data emerges on the theranostic and prognostic role of molecular biomarkers; this is a strong incentive for a validated, sensitive, and broadly available molecular screening test. Nextgeneration sequencing (NGS) has begun to supplant other technologies for genomic profiling. We report here our 2 years of clinical practice using NGS results to guide therapeutic decisions. The Ion Torrent AmpliSeq colon/lung cancer panel, which allows mutation detection in 22 cancer-related genes, was prospectively used in clinical practice (BELAC ISO 15189 accredited method). The DNA of 741 formalin-fixed paraffin-embedded CRC tissues, including primary tumors and metastasis, was obtained from 14 different Belgian institutions and subjected to targeted NGS. Of the tumors tested, 98% (727) were successfully sequenced and 89% (650) harbored at least one mutation. KRAS, BRAF and NRAS mutations were found in 335 (46%), 78 (11%) and 32 (4%) samples, respectively. These mutation frequencies were consistent with those reported in public databases. Moreover, mutations and amplifications in potentially actionable genes were identified in 464 samples (64%), including mutations in PIK3CA (14%), ERBB2 (0.4%), AKT1 (0.6%), and MAP2K1 (0.1%), as well as amplifications of ERBB2 (0.3%) and EGFR (0.3%). The median turnaround time between reception of the sample in the laboratory and report release was 8 calendar days. Overall, the AmpliSeg colon/lung cancer panel was successfully applied in daily practice and provided reliable clinically relevant information for CRC patients.

Mots-clefs

Colorectal cancer, next-generation sequencing

Adult Height after Growth Hormone Treatment at Pubertal Onset in Short Adolescents Born Small for Gestational Age: Results from a Belgian Registry-Based Study.

Thomas M, **Beckers D**, Brachet C, Dotremont H, Lebrethon MC, Lysy P, Massa G, Reynaert N, Rooman R, van der Straaten S, Roelants M, De Schepper J.

Références	Doi	IF
Int J Endocrinol. 2018 Apr 3;2018:6421243	10.1155/2018/6421243	2.340

Abstract

OBJECTIVES: Information on the efficacy of GH treatment in short SGA children starting their treatment in adolescence is limited. Therefore, adult height (AH), total height gain, and pubertal height gain were evaluated in short SGA children who started GH treatment at pubertal onset.

PATIENT AND METHODS: Growth data of 47 short SGA adolescents (22 boys) who started GH treatment at pubertal onset (PUB group) were compared with results from 27 short SGA patients (11 boys) who started GH therapy at least 1 year before pubertal onset (PrePUB group).

RESULTS: The PUB group achieved a mean (\pm SD) total height gain of 0.8 \pm 0.7 SDS and an AH of -2.5 \pm 0.7 SDS after 4.1 \pm 1.1 years of GH treatment with a dosage of 41.8 \pm 8.4 µg/kg/ day. These results were comparable with those in the PrePUB group, which was treated for a longer duration (5.8 \pm 2.1 years), resulting in a total height gain of 1.1 \pm 0.7 SDS and an AH of -2.1 \pm 1.0 SDS. Multiple regression analysis showed a significantly lower height gain in pubertal patients, females, and patients weighing less at start of GH treatment. An AH above -2 SDS and above the parent-specific lower limit of height was, respectively, reached in 28% and 70% of PUB and 44% and 67% of PrePUB patients (NS). AH SDS was positively correlated with the height SDS at start of GH.

CONCLUSIONS: Short SGA adolescents starting GH therapy at an early pubertal stage have a modest and variable height gain. A normal AH can be expected in one third of the patients, especially in those with a smaller height deficit at onset of GH treatment.

Mots-clefs

Granulomatose avec polyangéite, à propos de plusieurs complications rares et sévères.

Scius N, Migali G, Tintillier M, Cuvelier C, Pochet J-M.

Références	Doi	IF
Louv Med. 2018;137(4)219-223		

Abstract

La granulomatose avec polyangéite est une vascularite systémique rare avec une morbimortalité importante. Le diagnostic se base sur l'association de signes cliniques (atteinte des voies aériennes supérieures et inférieures ainsi que rénale), la présence d'anticorps spécifiques (ANCA anti-PR3) et l'examen anatomo-pathologique. Si le traitement actuel de la maladie a permis une forte diminution de la mortalité, la morbidité reste importante, liée à la maladie mais également aux effets secondaires du traitement.

Que savons-nous à ce propos ?

La GPA est une maladie sévère avec de multiples complications et un traitement contraignant et complexe.

Que nous apporte cet article ?

Malgré un traitement précoce et selon les recommandations, il n'est pas rare que le patient développe des manifestations plus ou moins sévères de la maladie.

Mots-clefs

Granulomatose avec polyangéite, complications, infarctus splénique, bloc auriculo-ventriculaire

The DaXa-inhibition assay: A concept for a readily available, universal aXa assay that measures the direct inhibitory effect of all anti-Xa drugs.

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Van Pelt LJ, Lukens MV, Testa S, Chatelain B, Douxfils J, Mullier F.

Références	Doi	IF
Thromb Res. 2018 Apr 30;168:63-66	10.1016/j.thromres.2018.04.024	2.779

Abstract

Mots-clefs

Cytomegalovirus infection associated with portal vein thrombosis and thrombocytopenia: a case report.

Di Prinzio G, Nguyen Ung P, Valschaerts AS, Borgniet O.

Références	Doi	IF
Louv Med 2018 ;137(4)224-227		

Abstract

Le Cytomegalovirus (CMV) est responsable d'une infection virale commune et souvent banale chez le sujet immunocompétent, mais qui n'est pas dépourvue de complications potentiellement graves. La thrombose porte en est un exemple. Le cas que nous décrivons concerne une patiente atteinte d'une infection à CMV, s'étant révélée par une éruption cutanée et s'étant compliquée d'une thrombose porte, en l'absence de thrombophilie connue. Une thrombopénie auto-immune est la seconde complication survenue dans notre cas. Cet article a pour but de souligner l'enjeu d'un tel diagnostic et de stimuler la réflexion sur l'intérêt du dépistage échographique précoce d'une thrombose splanchnique associée à une infection par le CMV.

Mots-clefs

Thrombose veineuse, thrombose portale, purpura, infection virale, thrombocytopénie, immunoglobulines intra-veineuses

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