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Q1

RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR

N°4 - PREMIER QUADRIMESTRE 2019

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CHU UCL NAMUR

SUPPLÉMENT
2018

Controversies in the Treatment of Classical Hodgkin Lymphoma

Eichenauer DA, **André M**, Johnson P, Fossa A, Casasnovas O, Engert A.

Références	*Doi*	*IF*
Hemasphere. 2018;2(5):e149	*10.1097/HS9.0000000000000149*	*4.427*

Abstract

Hodgkin lymphoma (HL) is a B-cell-derived malignancy that mostly affects young adults. Pathologically, HL is divided into classical HL (cHL) and the rare entity of nodular lymphocyte-predominant HL. Classical HL is characterized by few malignant cells termed Hodgkin and Reed-Sternberg cells embedded in an inflammatory background. The treatment of cHL has consistently improved over the last decades so that current standard approaches result in long-term remission rates in excess of 80%. However, potentially lethal therapy-related late complications affect an increasing number of survivors. For this reason, issues regarding the optimal treatment of cHL patients are still fiercely debated. Questions under discussion include how treatment can be guided by interim positron emission tomography, the best initial treatment for advanced-stage disease and the use of targeted drugs such as the antibody-drug conjugate brentuximab vedotin and the anti-PD-1 antibodies nivolumab and pembrolizumab. The identification of patients who should undergo allogeneic stem cell transplantation is another unsolved issue. The present article highlights the most relevant clinical trials and addresses controversial open questions in the treatment of cHL

Mots-clefs

Traumatic bipolar dislocation of the clavicle

Colette A, Toussaint A, Vandemeulebroecke G.

Références	*Doi*	*IF*
Louv Med, 2019;137(11):732-736		

Abstract

While acromio-clavicular dislocations are common lesions, the association with sterno-clavicular joint dislocation proves to be very rare, with less than fifty cases reported worldwide. We have herein presented the case of a 56-year-old man with a traumatic postero-superior acromio-clavicular and anterior sternoclavicular dislocation following a car accident. Due to late presentation, he received a conservative treatment with excellent results regarding pain, mobility, and strength, yet with poor cosmetic outcome. In spite of the current trend towards surgical reduction and lesion stabilization, conservative treatment of bipolar clavicle dislocation proves to be a safe and easy means to obtain functional recovery. Of note is that this measure does not correct esthetic deformity, with uncertain long-term consequences.

Mots-clefs

Promouvoir le dialogue entre les médecins et leur management, un enjeu éthique pour la pratique clinique

Guillaume G.

Références	*Doi*	*IF*
Ethica Clinica 2019;91(3):79-94		

Abstract

Mots-clefs

Nasal Obstruction Symptom Evaluation Score to Guide Mask Selection in CPAP-Treated Obstructive Sleep Apnea

Lebret M, Arnol N, **Martinot JB**, Tamisier R, Deschaux C, Pepin JL, Borel JC

Références	*Doi*	*IF*
Otolaryngology–Head and Neck Surgery. 2018;159(3): 590-592	*10.1177/0194599818773993*	*1.247*

Abstract

Nasal obstruction is frequently reported by patients with sleep apnea and complicates the choice of a nasal or oronasal mask for continuous positive airway pressure (CPAP) therapy. However, the type of interface used for the delivery of CPAP is crucial to ensure tolerance and compliance. The aim of this prospective pilot study was to identify whether the validated Nasal Obstruction Symptom Evaluation (NOSE) score rated at CPAP initiation was associated with the type of mask used after 4 months of treatment. Patients completed the NOSE questionnaire before initiation with automatic CPAP. The mask used (nasal/oronasal) after 4 months was documented. In total, 198 consecutive patients with sleep apnea were included. NOSE score (›50/100) was independently associated with the use of an oronasal mask at 4 months (sensitivity, 34.8%; specificity, 87.5%). The NOSE questionnaire could be a simple decision-making tool to guide the choice of mask during CPAP initiation.

Mots-clefs

CPAP; NOSE questionnaire; compliance; masks; nasal obstruction; sleep apnea

Interview : Welcoming the Belgian Society of Radiology to CIRSE

Deprez F, de Beule T.

Références	*Doi*	*IF*
Journal d'information du CIRSE (Cardiovascular and Interventional Radiological Society of Europe		*2.210*

Abstract

In 2017, the CIRSE family acquired several new group members, bringing the number of national and regional societies under the CIRSE umbrella to 38: 25 European Group Member Societies and 13 Group Members from South America, the Middle East and the Asia-Pacific region makes CIRSE membership truly international: over 7,000 academic members with a near complete, yet further expanding European base and one quarter of CIRSE members practising IR outside of Europe Amongst these new members, an important partner is the Belgian society of Radiology, who help close one of the few remaining gaps in the European network of IRs. The society has an active IR section, headed by two energetic young interventionalists : Dr. Fabrice Deprez, representing the French-speaking community of Belgian IRs, and Dr. Tom de Beule, representing the Flemish-speaking community. CIRSE spoke with both to find out how IR is currently faring in Belgium, and how they hope to advance the specialty further.

Mots-clefs

RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR

N°4 - PREMIER QUADRIMESTRE 2019

JANVIER

1

Communication between the distal interphalangeal joint and the navicular bursa in the horse at Computed Tomography Arthrography

Hontoir F, Rejas E, **Falticeanu A, Nisolle JF**, Simon V, Nicaise C, Clegg PD, Vandeweerd JE.

Références	*Doi*	*IF*
Anat Histol Embryol. 2019 Mar;48(2):133-141	*10.1111/ahe.12421*	*0.731*

Abstract

Diffusion of drugs injected into the distal interphalangeal joint or the navicular (podotrochlear) bursa can influence diagnosis and treatment of foot pain. Previous anatomical and radiographic studies of the communication between these synovial structures have produced conflicting results and did not identify the location of any communication if present. This anatomic study aimed to assess the presence and site of communication between the distal interphalangeal joint and the navicular bursa in the horse by computed tomography arthrography. Sixty-six pairs of cadaver forelimbs were injected with contrast medium into the distal interphalangeal joint and imaged by computed tomography arthrography. The presence of a communication, location of the communication and additional structural changes were assessed. Navicular bursa opacification occurred in 7 distal limbs (5.3%) following distal interphalangeal joint injection. One limb showed a communication through the T-ligament and 6 limbs showed a communication through the distal sesamoidean impar ligament. In 3 cases, the communication through the distal sesamoidean impar ligament was associated with a distal border fragment. Our study showed that communication between the distal interphalangeal joint and navicular bursa is uncommon and inconsistent. Clinically, the presence of a communication could (1) influence the interpretation of diagnostic analgesia of the distal interphalangeal joint or the navicular bursa by facilitating the diffusion of local anaesthetic between these structures; (2) allow the drug and its potential adverse effects to spread from the treated synovial cavity to the non-targeted synovial cavity; (3) be responsible for the failure of joint drainage in the case of sepsis.

Mots-clefs

arthrography; foot; horses; joints; synovial bursa

2

Biomarkers in Adult Dermatomyositis: Tools to Help the Diagnosis and Predict the Clinical Outcome

Cassius C, Le Buanec H, Bouaziz JD, Amode R.

Références	*Doi*	*IF*
J Immunol Res. 2019 Jan 14;2019:9141420	*10.1155/2019/9141420*	*2.487*

Abstract

Dermatomyositis pathophysiology is complex. In recent years, medical research has identified molecules associated with disease activity. Besides providing insights into the driving mechanisms of dermatomyositis, these findings could provide potential biomarkers. Activity markers can be used to monitor disease activity in clinical trials and may also be useful in daily practice. This article reviews molecules that could be used as biomarkers for diagnosis and monitoring dermatomyositis disease activity.

Mots-clefs

3

Development of new methodologies for the chromogenic estimation of betrixaban concentrations in plasma

Siriez R, Evrard J, Dogné JM, Pochet L, Bouvy C, **Lessire S, Mullier F,** Douxfils J.

Références	*Doi*	*IF*
Int J Lab Hematol. 2019 Apr;41(2):250-261.	*10.1111/ijlh.12963*	*1.919*

Abstract

INTRODUCTION:
Chromogenic anti-Xa assays are the most appropriate tests to estimate the amount of betrixaban in plasma but the sensitivity of available tests is limited and improvements are needed to encompass the on-therapy range.
METHODS:
Betrixaban was spiked at concentrations ranging from 0 to 500 ng/mL in plasma from healthy donors. Three commercial tests were used (Biophen® DiXaI® , STA® Liquid Anti-Xa, and HemosIL® Liquid Anti-Xa), and adaptation of their sample dilution scheme was performed. These new methodologies were also tested on plasma spiked with amounts of unfractionated heparin (UFH), low molecular weight heparins (LMWH), or fondaparinux covering the on-therapy ranges to evaluate their sensitivity to indirect factor Xa inhibitors.
RESULTS:
Results showed concentration-dependent decreases in OD/min inversely proportional to the dilutions. While modifications improve the sensitivity of these tests to betrixaban (eg, ½*OD/min of 502 ng/mL [95% CI: 495-508 ng/mL] for Biophen® DiXaI® [1:50] is reduced to 51 ng/mL [95% CI: 50-52 ng/mL] for improved Biophen® DiXaI® [1:5]), results also showed an increased sensitivity to indirect factor Xa inhibitors, except for Biophen® DiXaI® which remains insensitive to UFH and LMWH.
CONCLUSIONS:
Results showed that the improvement of current chromogenic anti-Xa methodologies enhances the sensitivity of these assays to betrixaban but also to indirect factor Xa inhibitors. This lack of specificity may lead to overestimation of betrixaban concentrations in patients bridged with heparins. To avoid this cross-interference, the use of the Biophen® DiXaI® may be a solution except for fondaparinux which remains active even in the presence of the Biophen® DiXaI® ‘s specific buffer. For the other chromogenic assays, the conception and validation of specific buffer is required.

Mots-clefs
betrixaban; chromogenic anti-Xa assays; factor Xa inhibitors; fondaparinux; guidance; heparins

Azacitidine maintenance after intensive chemotherapy improves DFS in older AML patients

Huls G, Chitu DA, Havelange V, Jongen-Lavrencic M, van de Loosdrecht AA, Biemond BJ, Sinnige H, Hodossy B, **Graux C**, Kooy RVM, de Weerdt O, Breems D, Klein S, Kuball J, Deeren D, Terpstra W, Vekemans MC, Ossenkoppele GJ, Vellenga E, Löwenberg B; Dutch-Belgian Hemato-Oncology Cooperative Group (HOVON).

Références	*Doi*	*IF*
Blood. 2019 Mar 28;133(13):1457-1464	*10.1182/blood-2018-10-879866*	*15.132*

Abstract

The prevention of relapse is the major therapeutic challenge in older patients with acute myeloid leukemia (AML) who have obtained a complete remission (CR) on intensive chemotherapy. In this randomized phase 3 study (HOVON97) in older patients (≥60 years) with AML or myelodysplastic syndrome with refractory anemia with excess of blasts, in CR/CR with incomplete hematologic recovery (CRi) after at least 2 cycles of intensive chemotherapy, we assessed the value of azacitidine as postremission therapy with respect to disease-free survival (DFS; primary end point) and overall survival (OS; secondary end point). In total, 116 eligible patients were randomly (1:1) assigned to either observation (N = 60) or azacitidine maintenance (N = 56; 50 mg/m2, subcutaneously, days 1-5, every 4 weeks) until relapse, for a maximum of 12 cycles. Fifty-five patients received at least 1 cycle of azacitidine, 46 at least 4 cycles, and 35 at least 12 cycles. The maintenance treatment with azacitidine was feasible. DFS was significantly better for the azacitidine treatment group (logrank; P = .04), as well as after adjustment for poor-risk cytogenetic abnormalities at diagnosis and platelet count at randomization (as surrogate for CR vs CRi; Cox regression; hazard ratio, 0.62; 95% confidence interval, 0.41-0.95; P = .026). The 12-month DFS was estimated at 64% for the azacitidine group and 42% for the control group. OS did not differ between treatment groups, with and without censoring for allogeneic hematopoietic cell transplantation. Rescue treatment was used more often in the observation group (n = 32) than in the azacitidine maintenance group (n = 9). We conclude that azacitidine maintenance after CR/CRi after intensive chemotherapy is feasible and significantly improves DFS. The study is registered with The Netherlands Trial Registry (NTR1810) and EudraCT (2008-001290-15).

Mots-clefs

Basic bodily needs, context, fibromyalgia, hyperactivity, personality

DNMT3A mutation is associated with increased age and adverse outcome in adult T-acute lymphoblastic leukemia

Bond J, Touzart A, Leprêtre S, **Graux C**, Bargetzi M, Lhermitte L, Hypolite G, Leguay T, Hicheri Y, Guillerm G, Bilger K, Lhéritier V, Hunault M, Huguet F, Chalandon Y, Ifrah N, Macintyre E, Dombret H, Asnafi V, Boissel N.

Références	*Doi*	*IF*
Haematologica. 2019 Jan 17. pii: haematol.2018.197848 [Epub ahead of print]	*10.3324/haematol.2018.197848*	*9.090*

Abstract

The prognostic implications of DNMT3A genotype in T-ALL are incompletely understood. We performed comprehensive genetic and clinicobiological analyses of T-ALL patients with DNMT3A mutations treated during the GRAALL-2003 and -2005 studies. Eighteen of 198 cases (9.1%) had DNMT3A alterations. Two patients also had DNMT3A mutations in non-leukemic cell DNA, providing the first potential evidence of age-related clonal hematopoiesis in T-ALL. DNMT3A mutation was associated with older age (median 43.9 years v 29.4 years, p ‹ 0.001), immature T-receptor genotype (53.3% v 24.4%, p = 0.016) and lower remission rates (72.2% mutated v 94.4% non-mutated, p = 0.006). DNMT3A alterations were significantly associated with worse clinical outcome, with higher cumulative incidence of relapse (CIR, HR 2.33, 95% CI 1.05-5.16, p = 0.037) and markedly poorer event-free survival (EFS, HR 3.22, 95% CI 1.81-5.72, p ‹ 0.001) and overall survival (OS, HR 2.91, 95% CI 1.56-5.43, p = 0.001). Adjusting for age as a covariate, or restricting the analysis to patients over 40 years, who account for almost 90% of DNMT3A-mutated cases, did not modify these observations. In multivariate analysis using the risk factors that were used to stratify treatment during the GRAALL studies, DNMT3A mutation was significantly associated with shorter EFS (HR 2.33, 95% CI 1.06 - 4.04, p = 0.02). Altogether, these results identify DNMT3A genotype as a predictor of aggressive T-ALL biology. The GRAALL-2003 and -2005 studies were registered at http://www.clinicaltrials.gov as #NCT00222027 and #NCT00327678, respectively.

Mots-clefs

Adult Acute Lymphoblastic Leukemia; Cytogenetics and Molecular Genetics; DNMT3A; Prognosis

Asymptomatic bradycardia amongst endurance athletes

Doyen B, Matelot D, Carré F.

Références	*Doi*	*IF*
Phys Sportsmed. 2019 Jan 14:1-4 [Epub ahead of print]	*10.1080/00913847.2019.1568769*	*1.545*

Abstract

It is established that an intensive training results in a lower average resting heart rate. Management of bradycardia in an athlete can be difficult given the underlying mechanisms are not clearly understood. The authors reviewed the different mechanisms described in the literature, including recent advances in physiology regarding remodeling of ion channels, which may partially explain bradycardia in athletes. Sinus bradycardia amongst athletes, especially endurance focused athletes, is common but difficult to apprehend. The underlying mechanisms are observably of multifactorial origin and likely incompletely elucidated by the current body of knowledge.

Mots-clefs

Athlete's heart; autonomic balance; bradycardia; endurance athletes; ion channel; physiology

Successful double mechanical thrombectomy in bilateral M1 middle cerebral artery occlusion

London D, London F, Vandermeeren Y, Deprez FC.

Références	*Doi*	*IF*
Acta Neurol Belg. 2019 Jan 12 [Epub ahead of print]	*10.1007/s13760-019-01079-6*	*2.72*

Abstract

Mots-clefs
Bilateral M1 occlusion; Mecanical thrombectomy; Stroke

PET-adapted treatment for newly diagnosed advanced Hodgkin lymphoma (AHL2011): a randomised, multicentre, non-inferiority, phase 3 study

Casasnovas RO, Bouabdallah R, Brice P, Lazarovici J, Ghesquieres H, Stamatoullas A, Dupuis J, Gac AC, Gastinne T, Joly B, Bouabdallah K, Nicolas-Virelizier E, Feugier P, Morschhauser F, Delarue R, Farhat H, Quittet P, Berriolo-Riedinger A, Tempescul A, Edeline V, Maisonneuve H, Fornecker LM, Lamy T, Delmer A, Dartigues P, Martin L, **André M**, Mounier N, Traverse-Glehen A, Meignan M.

Références	*Doi*	*IF*
Lancet Oncol. 2019 Feb;20(2):202-215	*10.1016/S1470-2045(18)30784-8*	*36.418*

Abstract

BACKGROUND:
Increased-dose bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPPescalated) improves progression-free survival in patients with advanced Hodgkin lymphoma compared with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD), but is associated with increased risks of haematological toxicity, secondary myelodysplasia or leukaemia, and infertility. We investigated whether PET monitoring during treatment could allow dose de-escalation by switching regimen (BEACOPPescalated to ABVD) in early responders without loss of disease control compared with standard treatment without PET monitoring.

METHODS:
AHL2011 is a randomised, non-inferiority, phase 3 study done in 90 centres across Belgium and France. Eligible patients were aged 16-60 years and had newly diagnosed Hodgkin lymphoma, excluding nodular lymphocyte predominant subtype, an Eastern Cooperative Oncology Group performance status score less than 3, a life expectancy of at least 3 months, an Ann Arbor disease stage III, IV, or IIB with mediastinum-to-thorax ratio of 0•33 or greater than or extranodal localisation, and had received no previous treatment for Hodgkin lymphoma. Randomisation was unmasked and done centrally by the permuted block method. Patients were randomly assigned to standard treatment (BEACOPPescalated given every 21 days for six cycles) or PET-driven treatment. All patients received two cycles of upfront BEACOPPescalated, after which PET assessment was done (PET2). In the standard treatment group, PET2 patients completed two additional cycles of BEACOPPescalated induction therapy irrespective of PET2 findings. In the PET-driven treatment group, patients with positive PET2 scans received the further two cycles of BEACOPPescalated and those with a negative PET2 scan switched to two cycles of ABVD for the remaining induction therapy. In both treatment groups, PET at the end of induction therapy was used to decide whether to continue with consolidation therapy in those with negative scans or start salvage therapy in patients with positive scans (either two cycles of ABVD in PET2-negative patients in the PET-driven arm or two cycles of BEACOPPescalated). BEACOPPescalated consisted of bleomycin 10 mg/m2 and vincristine 1•4 mg/m2 intravenously on day 8, etoposide 200 mg/m2 intravenously on days 1-3, doxorubicin 35 mg/m2 and cyclophosphamide 1250 mg/m2 intravenously on day 1, 100 mg/m2 oral procarbazine on days 1-7, and 40 mg/m2 oral prednisone on days 1-14. ABVD was given every 28 days (doxorubicin 25 mg/m2, bleomycin 10 mg/m2, vinblastine 6 mg/m2, and dacarbazine 375 mg/m2 intravenously on days 1 and 15). The primary endpoint was investigator-assessed progression-free survival. Non-inferiority analyses were done by intention to treat and per protocol. The study had a non-inferiority margin of 10%, to show non-inferiority of PET-guided treatment versus standard care with 80% power and an alpha of 2•5% (one-sided). This study is registered with ClinicalTrials.gov, number NCT01358747.

FINDINGS:
From May 19, 2011, to April 29, 2014, 823 patients were enrolled-413 in the standard care group and 410 in the PET-driven group. 346 (84%) of 410 patients in the PET-driven treatment group were assigned to receive ABVD and 51 (12%) to continue receiving BEACOPPescalated after PET2. With a median follow-up of 50•4 months (IQR 42•9-59•3), 5-year progression-free survival by intention to treat was 86•2%, 95% CI 81•6-89•8 in the standard treatment group versus 85•7%, 81•4-89•1 in the PET-driven treatment group (hazard ratio [HR] 1•084, 95% CI 0•737-1•596; p=0•65) and per protocol the values were 86•7%, 95% CI 81•9-90•3 and 85•4%, 80•7-89•0, respectively (HR 1•144, 0•758-1•726; p=0•74). The most common grade 3-4 adverse events were leucopenia (381 [92%] in the standard treatment group and 387 [95%] in the PET-driven treatment group), neutropenia (359 [87%] and 366 [90%]), anaemia (286 [69%] vs 114 [28%]), thrombocytopenia (271 [66%] and 163 [40%]), febrile neutropenia (145 [35%] and 93 [23%]), infections (88 [22%] and 47 [11%]), and gastrointestinal disorders (49 [11%] and 48 [11%]). Serious adverse events related to treatment were reported in 192 (47%) patients in the standard treatment group and 114 (28%) in the PET-driven treatment group, including infections (84 [20%] of 412 vs 50 [12%] of 407) and febrile neutropenia (21 [5%] vs 23 [6%]). Six (1%) patients in the standard care group died from treatment-related causes (two from septic shock, two from pneumopathy, one from heart failure, and one from acute myeloblastic leukaemia), as did two (‹1%) in the PET-driven treatment group (one from septic shock and one from acute myeloblastic leukaemia).
INTERPRETATION:
PET after two cycles of induction BEACOPPescalated chemotherapy safely guided treatment in patients with advanced Hodgkin lymphoma and allowed the use of ABVD in early responders without impairing disease control and reduced toxicities. PET staging allowed accurate monitoring of treatment in this trial and could be considered as a strategy for the routine management of patients with advanced Hodgkin lymphoma.
FUNDING:
Programme Hospitalier de Recherche Clinique.

Mots-clefs

Primary cutaneous CD8+ and CD30+ T-cell lymphoproliferative disorders: case reports and clinical implications

Baldin P, Shwe MM, Marot L, Eeckout PVV, **Dachelet C, Sacré L, Berners A, Olivier S**, Camboni A.

Références	*Doi*	*IF*
Eur J Dermatol. 2019 Feb 1;29(1):39-44	*10.1684/ejd.2018.3493*	*1,944*

Abstract

BACKGROUND:
CD8+ CD30+ primary cutaneous T-cell lymphomas (PCTCL) are rare entities with overlapping pathological features and variable outcome.
OBJECTIVES:
We sought to highlight the importance of correlation between pathological findings and clinical presentation for correct classification of the disease.
MATERIALS & METHODS:
Two cases of CD8+ CD30+ PCTCL were investigated. The first patient presented with a multiple necro-erythematous lesion of the limb and the second with a papulo-necrotic lesion of the eyelid.
RESULTS:
Despite a different clinical presentation, pathological findings were similar in both cases. Clinico-pathological correlation led to a diagnosis of primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma in the first case and primary cutaneous anaplastic large-cell lymphoma in the second. The first patient died shortly after diagnosis and the second is alive without recurrence.
CONCLUSIONS:
Clinico-pathological correlation is essential for the correct identification of these rare diseases.

Mots-clefs

CD8+ CD30+ primary cutaneous T-cell lymphoma; CD8+ epidermotropic cytotoxic T-cell lymphoma; PCTCL; anaplastic large-cell lymphoma; clinico-pathological correlation

Epigenetic Silencing Affects l-Asparaginase Sensitivity and Predicts Outcome in T-ALL

Touzart A, Lengliné E, Latiri M, Belhocine M, Smith C, Thomas X, Spicuglia S, Puthier D, Pflumio F, Leguay T, **Graux C,** Chalandon Y, Huguet F, Leprêtre S, Ifrah N, Dombret H, Macintyre E, Hunault M, Boissel N, Asnafi V.

Références	*Doi*	*IF*
Clin Cancer Res. 2019 Apr 15;25(8):2483-2493	*10.1158/1078-0432.CCR-18-1844*	*4,47*

Abstract

PURPOSE:
Biological explanation for discrepancies in patient-related response to chemotherapy depending on the underlying oncogenic events is a promising research area. TLX1- or TLX3-deregulated T-cell acute lymphoblastic leukemias (T-ALL; TLX1/3+) share an immature cortical phenotype and similar transcriptional signatures. However, their prognostic impacts differ, and inconsistent clinical outcome has been reported for TLX3. We therefore hypothesized that the overlapping transcriptional profiles of TLX1+ and TLX3+ T-ALLs would allow identification of candidate genes, which might determine their distinct clinical outcomes.
EXPERIMENTAL DESIGN:
We compared TLX1+ and TLX3+ adult T-ALL outcome in the successive French national LALA-94 and GRAALL-2003/2005 multicentric trials and analyzed transcriptomic data to identify differentially expressed genes. Epigenetic regulation of asparagine synthetase (ASNS) and in vitro l-asparaginase sensitivity were evaluated for T-ALL cell lines and primary samples.
RESULTS:
We show that TLX1+ patients expressed low levels of ASNS when compared with TLX3+ and TLX-negative patients, due to epigenetic silencing of ASNS by both DNA methylation and a decrease of active histone marks. Promoter methylation of the ASNS gene correlated with l-asparaginase sensitivity in both T-ALL cell lines and patient-derived xenografts. Finally, ASNS promoter methylation was an independent prognostic factor for both event-free survival [HR, 0.42; 95% confidence interval (CI), 0.24-0.71; P = 0.001] and overall survival (HR, 0.40; 95% CI, 0.23-0.70; P = 0.02) in 160 GRAALL-2003/2005 T-ALL patients and also in an independent series of 47 LL03-treated T lymphoblastic lymphomas (P = 0.012).
CONCLUSIONS:
We conclude that ASNS methylation status at diagnosis may allow individual adaptation of l-asparaginase dose

Mots-clefs

GRIN2A-related disorders: genotype and functional consequence predict phenotype

Strehlow V, Heyne HO, Vlaskamp DRM, Marwick KFM, Rudolf G, de Bellescize J, Biskup S, Brilstra EH, Brouwer OF, Callenbach PMC, Hentschel J, Hirsch E, Kind PC, Mignot C, Platzer K, Rump P, Skehel PA, Wyllie DJA, Hardingham GE, van Ravenswaaij-Arts CMA, Lesca G, Lemke JR; GRIN2A study group. Arzimanoglou A, Augustijn PB, Van Bogaert P, Bourry H, Burfeind P, Chu Y, Chung B, Doummar D, Edery P, Fattal-Valevski A, Fradin M, Gerard M, de Geus C, Gunning B, Hasaerts D, Helbig I, Helbig KL, Jamra R, Lyver MJ, Wassink-Ruiter JSK, Koolen DA, Lederer D, Lunsing RJ, **Mathot M**, Maurey H, Menascu S, Michel A, Mirzaa G, Mitter D, Muhle H, Møller RS, Nava C, O'Brien M, van Pinxteren-Nagler E, van Riesen A, Rougeot C, Sanlaville D, Schieving JH, Syrbe S, Veenstra-Knol HE, Verbeek N, Ville D, Vos YJ, Vrielynck P, Wagner S, Weckhuysen S, Willemsen MH.

Références	*Doi*	*IF*
Brain. 2019 Jan 1;142(1):80-92	*10.1093/brain/awy304*	*10,840*

Abstract

Alterations of the N-methyl-d-aspartate receptor (NMDAR) subunit GluN2A, encoded by GRIN2A, have been associated with a spectrum of neurodevelopmental disorders with prominent speech-related features, and epilepsy. We performed a comprehensive assessment of phenotypes with a standardized questionnaire in 92 previously unreported individuals with GRIN2A-related disorders. Applying the criteria of the American College of Medical Genetics and Genomics to all published variants yielded 156 additional cases with pathogenic or likely pathogenic variants in GRIN2A, resulting in a total of 248 individuals. The phenotypic spectrum ranged from normal or near-normal development with mild epilepsy and speech delay/apraxia to severe developmental and epileptic encephalopathy, often within the epilepsy-aphasia spectrum. We found that pathogenic missense variants in transmembrane and linker domains (misTMD+Linker) were associated with severe developmental phenotypes, whereas missense variants within amino terminal or ligand-binding domains (misATD+LBD) and null variants led to less severe developmental phenotypes, which we confirmed in a discovery (P = 10-6) as well as validation cohort (P = 0.0003). Other phenotypes such as MRI abnormalities and epilepsy types were also significantly different between the two groups. Notably, this was paralleled by electrophysiology data, where misTMD+Linker predominantly led to NMDAR gain-of-function, while misATD+LBD exclusively caused NMDAR loss-of-function. With respect to null variants, we show that Grin2a+/- cortical rat neurons also had reduced NMDAR function and there was no evidence of previously postulated compensatory overexpression of GluN2B. We demonstrate that null variants and misATD+LBD of GRIN2A do not only share the same clinical spectrum (i.e. milder phenotypes), but also result in similar electrophysiological consequences (loss-of-function) opposing those of misTMD+Linker (severe phenotypes; predominantly gain-of-function). This new pathomechanistic model may ultimately help in predicting phenotype severity as well as eligibility for potential precision medicine approaches in GRIN2A-related disorders.

Mots-clefs

D-dimer: Preanalytical, analytical, postanalytical variables, and clinical applications

Favresse J, Lippi G, Roy PM, **Chatelain B, Jacqmin H,** Ten Cate H, **Mullier F**.

Références	*Doi*	*IF*
Crit Rev Clin Lab Sci. 2018 Dec;55(8):548-577	*10.1080/10408363.2018.1529734*	*6,481*

Abstract

D-dimer is a soluble fibrin degradation product deriving from the plasmin-mediated degradation of cross-linked fibrin. D-dimer can hence be considered a biomarker of activation of coagulation and fibrinolysis, and it is routinely used for ruling out venous thromboembolism (VTE). D-dimer is increasingly used to assess the risk of VTE recurrence and to help define the optimal duration of anticoagulation treatment in patients with VTE, for diagnosing disseminated intravascular coagulation, and for screening medical patients at increased risk of VTE. This review is aimed at (1) revising the definition of D-dimer; (2) discussing preanalytical variables affecting the measurement of D-dimer; (3) reviewing and comparing assay performance and some postanalytical variables (e.g. different units and age-adjusted cutoffs); and (4) discussing the use of D-dimer measurement across different clinical settings.

Mots-clefs

D-dimer; analytical; postanalytical; preanalytical; venous thromboembolism

Providing both autologous and allogeneic hematopoietic stem cell transplants (HSCT) may have a stronger impact on the outcome of autologous HSCT in adult patients than activity levels or implementation of JACIE at Belgian transplant centres

Poirel HA, Vanspauwen M, Macq G, De Geyndt A, Maertens J, Willems E, Selleslag D, Poiré X, Theunissen K, **Graux C,** Kerre T, Zachée P, Meuleman N, De Becker A, Verlinden A, Van Obbergh F, Schuermans C, De Wilde V, Jaspers A, Pranger D, Deeren D, Van Riet I, Vaes E, Beguin Y; Belgian Transplant Registry and the Belgian Haematological Society's Transplant committee.

Références	*Doi*	*IF*
Bone Marrow Transplant. 2019 Jan 29 [Epub ahead of print]	*10.1038/s41409-019-0458-8*	*4,497*

Abstract

While performance since the introduction of the JACIE quality management system has been shown to be improved for allogeneic hematopoietic stem cell transplants (HSCT), impact on autologous-HSCT remains unclear in Europe. Our study on 2697 autologous-HSCT performed in adults in 17 Belgian centres (2007-2013) aims at comparing the adjusted 1 and 3-yr survival between the different centres & investigating the impact of 3 centre-related factors on performance (time between JACIE accreditation achievement by the centre and the considered transplant, centre activity volume and type of HSCT performed by centres: exclusively autologous vs both autologous & allogeneic). We showed a relatively homogeneous performance between Belgian centres before national completeness of JACIE implementation. The 3 centre-related factors had a significant impact on the 1-yr survival, while activity volume and type of HSCT impacted the 3-yr survival of autologous-HSCT patients in univariable analyses. Only activity volume (impact on 1-yr survival only) and type of HSCT (impact on 1 and 3-yr survivals) remained significant in multivariable analysis. This is explained by the strong relationship between these 3 variables. An extended transplantation experience, i.e., performing both auto & allo-HSCT, appears to be a newly informative quality indicator potentially conveying a multitude of underlying complex factors.

Mots-clefs

Cytotoxic Lesion of the Corpus Callosum Caused by Puumala Hantavirus Infection

Lebecque O, Mulquin N, Dupont M

Références	*Doi*	*IF*
J Belg Soc Radiol. 2019 Jan 21;103(1):11	*10.5334/jbsr.1616*	*0,27*

Abstract

We report the case of a 45-year-old male referred to our hospital with fever, asthenia, visual disturbances and increasing headaches. Diffusion-weighted imaging of the brain showed high signal intensity in the splenium of corpus callosum with low apparent diffusion coefficient values. Diagnosis of cytotoxic lesion of corpus callosum was made with Puumala Hantavirus infection serologically confirmed and should not be mistaken for ischemia. Patient was discharged 8 days after admission and imaging findings had resolved 3 weeks later.

Mots-clefs

callosum; clocc; corpus; cytotoxic; edema; hantavirus; puumala; reversible; splenial

Evaluation of the OXA-23 K-SeT® immunochromatographic assay for the rapid detection of OXA-23-like carbapenemase-producing Acinetobacter spp

Riccobono E, **Bogaerts P**, Antonelli A, **Evrard S**, Giani T, Rossolini GM, **Glupczynski Y**.

Références	*Doi*	*IF*
J Antimicrob Chemother. 2019 Jan 25 [Epub ahead of print]	*10.1093/jac/dkz001*	*5,217*

Abstract

Mots-clefs

Comparing the Host Reaction to CorMatrix and Different Cardiac Patch Materials Implanted Subcutaneously in Growing Pigs

Mosala Nezhad Z, Poncelet A, **Fervaille C**, Gianello P.

Références	*Doi*	*IF*
Thorac Cardiovasc Surg. 2019 Jan;67(1):44-49	*10.1055/s-0037-1607332*	*4,880*

Abstract

BACKGROUND:
Comparing the structural changes, and local host reactions to CorMatrix (CorMatrix Cardiovascular Inc., Roswell, Georgia, United States) and different biomaterials implanted subcutaneously in growing pig model.
METHODS:
Four pigs harboring implanted patches of CorMatrix, Vascutek porcine pericardium (Vascutek; Scotland, United Kingdom), SJM bovine pericardium (St. Jude Medical, Inc., Minnesota, United States), and Gore-Tex (W. L. Gore & Associates GmbH, Flagstaff, Arizona, United States) were studied for 1, 3, 6, and 12 months. The explants were examined histologically.
RESULTS:
CorMatrix showed gradual and consistent patch resorption and subsiding inflammatory and fibrosis process. Full scaffold degradation and replacement by mild fibrosis and subcutaneous tissue were seen by 1 year. Xenopericardial patches remained intact, and the initially severe inflammatory and fibrotic reactions reduced gradually to moderate fibrosis and chronic inflammation. Gore-Tex showed foreign body reaction.
CONCLUSIONS:
Patches were biotolerated by pigs. Xenopericardial patches elicited encapsulating fibrosis and no remodeling. CorMatrix resorbs completely and degrades consistently without leaving residues. Lack of encapsulating fibrosis toward CorMatrix allows tissue ingrowth and matrix remodeling.

Mots-clefs

Durvalumab for recurrent or metastatic head and neck squamous cell carcinoma: Results from a single-arm, phase II study in patients with ≥25% tumour cell PD-L1 expression who have progressed on platinum-based chemotherapy

Zandberg DP, Algazi AP, Jimeno A, Good JS, Fayette J, Bouganim N, Ready NE, Clement PM, Even C, Jang RW, Wong S, Keilholz U, Gilbert J, Fenton M, Braña I, **Henry S**, Remenar E, Papai Z, Siu LL, Jarkowski A, Armstrong JM, Asubonteng K, Fan J, Melillo G, Mesía R.

Références	*Doi*	*IF*
Eur J Cancer. 2019 Jan;107:142-152	*10.1016/j.ejca.2018.11.015*	*7,191*

Abstract

BACKGROUND:
Patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) progressing on platinum-based chemotherapy have poor prognoses and limited therapeutic options. Programmed cell death-1 (PD-1) and its ligand 1 (PD-L1) are frequently upregulated in HNSCC. The international, multi-institutional, single-arm, phase II HAWK study (NCT02207530) evaluated durvalumab monotherapy, an anti-PD-L1 monoclonal antibody, in PD-L1-high patients with platinum-refractory R/M HNSCC.
PATIENTS AND METHODS:
Immunotherapy-naïve patients with confirmed PD-L1-high tumour cell expression (defined as patients with ≥25% of tumour cells expressing PD-L1 [TC ≥ 25%] using the VENTANA PD-L1 [SP263] Assay) received durvalumab 10 mg/kg intravenously every 2 weeks for up to 12 months. The primary end-point was objective response rate; secondary end-points included progression-free survival (PFS) and overall survival (OS).
RESULTS:
Among evaluable patients (n = 111), objective response rate was 16.2% (95% confidence interval [CI], 9.9-24.4); 29.4% (95% CI, 15.1-47.5) for human papillomavirus (HPV)-positive patients and 10.9% (95% CI, 4.5-21.3) for HPV-negative patients. Median PFS and OS for treated patients (n = 112) was 2.1 months (95% CI, 1.9-3.7) and 7.1 months (95% CI, 4.9-9.9); PFS and OS at 12 months were 14.6% (95% CI, 8.5-22.1) and 33.6% (95% CI, 24.8-42.7). Treatment-related adverse events were 57.1% (any grade) and 8.0% (grade ≥3); none led to death. At data cut-off, 24.1% of patients remained on treatment or in follow-up.
CONCLUSION:
Durvalumab demonstrated antitumour activity with acceptable safety in PD-L1-high patients with R/M HNSCC, supporting its ongoing evaluation in phase III trials in first- and second-line settings. In an ad hoc analysis, HPV-positive patients had a numerically higher response rate and survival than HPV-negative patients.

Mots-clefs

Antibodies; HPV; Head and neck cancer; Immunotherapy; Monoclonal; Recurrent or metastatic; Survival rate

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS): establishment of an innovating animal model with insufficient liver remnant

Dili A, Lebrun V, **Bertrand C**, Leclercq I.

Références	*Doi*	*IF*
Lab Invest. 2019 May;99(5):698-707	*10.1038/s41374-018-0155-z*	*4,254*

Abstract

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) allows extended hepatectomy in patients with an extremely small future liver remnant (FLR). Current rodent models of ALPPS do not include resection resulting in insufficient-for-survival FLR, or they do incorporate liver mass reduction prior to ALPPS. Differences in FLR volume and surgical procedures could bias our understanding of physiological and hemodynamic mechanisms. We aimed to establish a rat ALPPS model with minimal FLR without prior parenchymal resection. In rodents, the left median lobe (LML) represents 10% of total liver. Partial hepatectomy (PHx) sparing LML and pericaval parenchyma represents our reference 87% resection. The first step in the procedure is either portal vein ligation (PVL) corresponding to ligation of all but the LML portal branches, or PVL with transection between the left and right median lobe segments (PVLT), and is defined as ALPPS stage-1. Second, ligated lobes were removed: PVL-PHx represents a conventional 2-stage hepatectomy, while PVLT followed by PHx is a strict reproduction of human ALPPS. In Group A, liver hypertrophy was analyzed after PVL (n = 38), PVLT (n = 47), T (n = 10), and sham (n = 10); In group B, mortality and FLR hypertrophy was assessed after PHx (n = 42), Sham-PHx (n = 6), PVL-PHx (n = 37), and PVLT-PHx (n = 45). In group A, PVLT induced rapid FLR hypertrophy compared to PVL ($p < 0,05$). Hepatocyte proliferation was higher in PVLT remnants ($p < 0,05$). In group B, PHx had a 5-day mortality rate of 84%. Sham operation prior to PHx did not improve survival ($p = 0.23$). In both groups, major fatalities occurred within 48 h after resection. PVL or PVLT prior to PHx reduced mortality to 33.3% ($p = 0,007$) or 25% ($p = 0.0002$) respectively, with no difference between the 2 two-stage procedures ($p = 0.6$). 7-day FLR hypertrophy was higher after the PVLT-PHx compared to PVL-PHx and PHx ($p = 0.024$). Our model reproduces human ALPPS with FLR that is insufficient for survival without liver resection prior to the stage-1 procedure. It offers an appropriate model for analyzing the mechanisms driving survival rescue and increased hypertrophy.

Mots-clefs

Pr Bertrand Coiffier

Salles G, **Bosly A**, Gaulard Ph, Gisselbrecht Ch, Haioun C, Tilly H.

Références	*Doi*	*IF*
Bulletin du Cancer 2019;106(1):88-89	*10.1016/j.bulcan.2019.01.005*	*0,840*

Abstract

Mots-clefs
Cancer Research ; Oncology ; Radiology Nuclear Medicine and imaging ; Hematology ; General Medicine

Creation of an out of hours child and Adolescent Mental Health emergency service

Naviaux AF, **Zdanowicz N.**

Références	*Doi*	*IF*
Int J Psy and Ment Health 2019;1(1):13-19		*0,875*

Abstract

Both Wexford and Waterford Counties are badly suffering from the lack of Child and Adolescent Mental Health Services (CAMHS). This is directly connected to the lack of CAMHS consultants to lead these services. Accessing the existing CAMHS services, especially in emergency, is particularly difficult as the waiting lists are ever growing, and therefore delaying the possibility of an early first appointment. An emergency “out of hours” child psychiatric service has been developed, in order to provide help when the CAMHS services are not accessible. Providing a service for under 18 years old patients with mental health issues presenting in Accident and Emergency (A&E) or hospitalised on a Ward (Paediatric, psychiatric or other) and also sometimes “off-site”, it functions with extremely limited resources (a consultant psychiatrist and a doctor in psychiatric training), and therefore needs an efficient triage procedure. The triage tool that was chosen is the Irish Child Triage System (ICTS) that was launched in Ireland by the RCSI in 2016. It operates in Wexford General Hospital (WGH) and in University Hospital Waterford (UHW). Between February and August 2018, every intervention provided by the Consultant Psychiatrist responsible for this “emergency out of hours” service was recorded; this includes interventions on both sites (WGH and UHW), In A&E but also on the Wards (Pediatric, Psychiatric, Medical and Surgical), both face to face consultations with the Consultant but also phone supervisions provided by the Consultant to the Doctor in psychiatric training on call for Psychiatry (UHW). The purpose of this article is to review the first figures of attendance of this new service provided and to discuss its profitability. Within 7 months, a total of 675 interventions was provided by the Consultant Psychiatrist on call for this new out of hours CAMHS service.

Mots-clefs

FEVRIER

Complete tumor response of a locally advanced lung large-cell neuroendocrine carcinoma after palliative thoracic radiotherapy and immunotherapy with nivolumab

Mauclet C, Duplaquet F, Pirard L, Rondelet B, Dupont M, Pop-Stanciu C, Vander Borght T, Remmelink M, D'Haene N, Lambin S, **Wanet M, Remouchamps V, Ocak S**.

Références	*Doi*	*IF*
Lung Cancer. 2019 Feb;128:53-56	*10.1016/j.lungcan.2018.12.006*	*4,486*

Abstract

Lung large-cell neuroendocrine carcinoma (L-LCNEC) is a rare subset of lung carcinoma associated with poor overall survival. Due to its rarity, little has been established about its optimal treatment in the advanced stage. We report the case of a 41-year-old woman diagnosed with an unresectable locally advanced L-LCNEC who presented an impressive tumor response to immunotherapy with nivolumab after non-curative thoracic radiotherapy. Salvage surgery was then performed, and pathologic analysis of the resected piece revealed the absence of residual viable tumor cells. Based on this case report, we discuss the literature regarding the efficacy of inhibitors of programmed death-1 protein (PD-1) in L-LCNEC and their use in association with radiotherapy and in the neoadjuvant setting.

Mots-clefs

Locally advanced stage; Lung large-cell neuroendocrine carcinoma; PD-1 inhibitor; Radiation therapy; Salvage surgery; Synergistic effect

Mucoviscidose : le tournant des modulateurs

Lebecq O, Leal T, Lebecque P.

Références	*Doi*	*IF*
Louv Med 2019;138(2):126-136		*0,02*

Abstract

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are small molecules aimed at improving CFTR function by specifically targeting the different classes of CFTR mutations. Recent Phase II studies of triple therapy, including new generation correctors, have demonstrated spectacular improvements in forced expiratory volume in 1s (FEV1), likely to translate into improved quality of life and increased life expectancy. Within the next 5 years, a highly effective CFTR modulator therapy will probably be approved for most cystic fibrosis patients, including those carrying at least one copy of the F508del mutation (88% of Belgian patients). Patients with well-preserved lungs will benefit most from these treatments.

Mots-clefs

Cystic fibrosis ; cystic fibrosis transmembrane conductance regulator (CFTR) ;modulators ; VX-445 ; VX-659

Prospective observational cohort study of the association between antiplatelet therapy, bleeding and thrombosis in patients with coronary stents undergoing noncardiac surgery

Howell SJ, Hoeks SE, West RM, Wheatcroft SB, Hoeft A; OBTAIN Investigators of European Society of Anaesthesiology (ESA) Clinical Trial Network. **Dincq AS.**

Références	*Doi*	*IF*
Br J Anaesth. 2019 Feb;122(2):170-179	*10.1016/j.bja.2018.09.029*	*6,499*

Abstract

BACKGROUND:
The perioperative management of antiplatelet therapy in noncardiac surgery patients who have undergone previous percutaneous coronary intervention (PCI) remains a dilemma. Continuing dual antiplatelet therapy (DAPT) may carry a risk of bleeding, while stopping antiplatelet therapy may increase the risk of perioperative major adverse cardiovascular events (MACE).
METHODS:
Occurrence of Bleeding and Thrombosis during Antiplatelet Therapy In Non-Cardiac Surgery (OBTAIN) was an international prospective multicentre cohort study of perioperative antiplatelet treatment, MACE, and serious bleeding in noncardiac surgery. The incidences of MACE and bleeding were compared in patients receiving DAPT, monotherapy, and no antiplatelet therapy before surgery. Unadjusted risk ratios were calculated taking monotherapy as the baseline. The adjusted risks of bleeding and MACE were compared in patients receiving monotherapy and DAPT using propensity score matching.
RESULTS:
A total of 917 patients were recruited and 847 were eligible for inclusion. Ninety-six patients received no antiplatelet therapy, 526 received monotherapy with aspirin, and 225 received DAPT. Thirty-two patients suffered MACE and 22 had bleeding. The unadjusted risk ratio for MACE in patients receiving DAPT compared with monotherapy was 1.9 (0.93-3.88), P=0.08. There was no difference in MACE between no antiplatelet treatment and monotherapy 1.03 (0.31-3.46), P=0.96. Bleeding was more frequent with DAPT 6.55 (2.3-17.96) P=0.0002. In a propensity matched analysis of 177 patients who received DAPT and 177 monotherapy patients, the risk ratio for MACE with DAPT was 1.83 (0.69-4.85), P=0.32. The risk of bleeding was significantly greater in the DAPT group 4.00 (1.15-13.93), P=0.031.
CONCLUSIONS:
OBTAIN showed an increased risk of bleeding with DAPT and found no evidence for protective effects of DAPT from perioperative MACE in patients who have undergone previous PCI.

Mots-clefs

acetylsalicylic acid; antiplatelet therapy; bleeding; major adverse cardiovascular events; outcome; percutaneous coronary intervention; surgery

Spontaneous Breathing in Early Acute Respiratory Distress Syndrome: Insights From the Large Observational Study to UNderstand the Global Impact of Severe Acute Respiratory FailurE Study

van Haren F, Pham T, Brochard L, Bellani G, Laffey J, Dres M, Fan E, Goligher EC, Heunks L, Lynch J, Wrigge H, McAuley D; Large observational study to UNderstand the Global impact of Severe Acute respiratory FailurE (LUNG SAFE) Investigators. **Bulpa PA, Dive AM**.

Références	*Doi*	*IF*
Crit Care Med. 2019 Feb;47(2):229-238	*10.1097/CCM.0000000000000*	*6,630*

Abstract

OBJECTIVES:
To describe the characteristics and outcomes of patients with acute respiratory distress syndrome with or without spontaneous breathing and to investigate whether the effects of spontaneous breathing on outcome depend on acute respiratory distress syndrome severity.
DESIGN: Planned secondary analysis of a prospective, observational, multicentre cohort study.
SETTING: International sample of 459 ICUs from 50 countries.
PATIENTS: Patients with acute respiratory distress syndrome and at least 2 days of invasive mechanical ventilation and available data for the mode of mechanical ventilation and respiratory rate for the 2 first days.
INTERVENTIONS: Analysis of patients with and without spontaneous breathing, defined by the mode of mechanical ventilation and by actual respiratory rate compared with set respiratory rate during the first 48 hours of mechanical ventilation.
MEASUREMENTS AND MAIN RESULTS: Spontaneous breathing was present in 67% of patients with mild acute respiratory distress syndrome, 58% of patients with moderate acute respiratory distress syndrome, and 46% of patients with severe acute respiratory distress syndrome. Patients with spontaneous breathing were older and had lower acute respiratory distress syndrome severity, Sequential Organ Failure Assessment scores, ICU and hospital mortality, and were less likely to be diagnosed with acute respiratory distress syndrome by clinicians. In adjusted analysis, spontaneous breathing during the first 2 days was not associated with an effect on ICU or hospital mortality (33% vs 37%; odds ratio, 1.18 [0.92-1.51]; p = 0.19 and 37% vs 41%; odds ratio, 1.18 [0.93-1.50]; p = 0.196, respectively). Spontaneous breathing was associated with increased ventilator-free days (13 [0-22] vs 8 [0-20]; p = 0.014) and shorter duration of ICU stay (11 [6-20] vs 12 [7-22]; p = 0.04).
CONCLUSIONS: Spontaneous breathing is common in patients with acute respiratory distress syndrome during the first 48 hours of mechanical ventilation. Spontaneous breathing is not associated with worse outcomes and may hasten liberation from the ventilator and from ICU. Although these results support the use of spontaneous breathing in patients with acute respiratory distress syndrome independent of acute respiratory distress syndrome severity, the use of controlled ventilation indicates a bias toward use in patients with higher disease severity. In addition, because the lack of reliable data on inspiratory effort in our study, prospective studies incorporating the magnitude of inspiratory effort and adjusting for all potential severity confounders are required.

Mots-clefs

The combined impact of dependency on caregivers, disability, and coping strategy on quality of life after ischemic stroke

Dewilde S, Annemans L, Lloyd A, Peeters A, Hemelsoet D, **Vandermeeren Y,** Desfontaines P, Brouns R, Vanhooren G, Cras P, Michielsens B, Redondo P, Thijs V.

Références	*Doi*	*IF*
Health Qual Life Outcomes. 2019 Feb 7;17(1):31	*10.1186/s12955-018-1069-6*	*2,278*

Abstract

BACKGROUND:
To estimate the additional impact of coping and of being dependent on caregivers, over and above the large effects of disability on utility after ischemic stroke.
METHODS:
A total of 539 patients were recruited into an observational, retrospective study when returning for a check-up between 3 and 36 months after an ischemic stroke. Patients' modified Rankin Scale (mRS), dependency on caregivers, the Brandtstädter and Renner Coping questionnaire (with summary scores: Tenacity of Goal Pursuit (TGP) and Flexible Goal Adjustment (FGA) coping styles), EQ-5D-3 L and co-morbidities were evaluated.
RESULTS:
In multivariable regression, greater disability (mRS) resulted in large utility losses, between 0.06 for mRS 1 to 0.65 for mRS 5 ($p < 0.0001$). Dependency on caregivers caused an additional dis-utility of 0.104 ($p = 0.0006$) which varied by mRS (0.044, 0.060, 0.083, 0.115, 0.150 and 0.173 for mRS 0-5). The effect of coping on utility varied by coping style, by the disability level of the patient and by his or her dependency on caregivers. FGA coping was associated with additional increases in utility ($p < 0.0001$) over and above the effect of disability and dependency, whereas TGA had no significant impact. FGA coping was associated with larger utility changes among more disabled patients (0.018 to 0.105 additional utility, for mRS 0 to mRS 5 respectively). Dependent patients had more to gain from FGA coping than patients who function independently of caregivers: utility gains were between 0.049 and 0.072 for moderate to high levels of FGA coping. In contrast, the same positive evolution in FGA coping resulted in 0.039 and 0.057 utility gain among independent patients. Finally, we found that important stroke risk factors and co-morbidities, such as diabetes and atrial fibrillation, were not predictors of EQ-5D utility in a multivariable setting.
CONCLUSIONS:
This study suggests that treatment strategies targeting flexible coping styles and decreasing dependency on caregivers may lead to significant gains in quality of life above and beyond treatment strategies that solely target disability.

Mots-clefs

Coping; Dependency on caregivers; Disability; EQ-5D; PRO; Stroke; Utilities

Optimal wavelength for the clot waveform analysis: Determination of the best resolution with minimal interference of the reagents

Evrard J, Siriez R, Morimont L, Thémans P, Laloy J, Bouvy C, Gheldof D, **Mullier F,** Dogné JM, Douxfils J.

Références	*Doi*	*IF*
Int J Lab Hematol. 2019 Feb 7. [Epub ahead of print]	*10.1111/ijlh.12975*	*1,919*

Abstract

INTRODUCTION:
Clot waveform analysis (CWA), a new methodology to assess coagulation process, can be usefully applied in various clinical settings. However, its clinical use is limited mainly because of the absence of standardization. No consensus exists regarding the wavelengths at which CWA has to be performed what is crucial for the sensitivity of the CWA.
OBJECTIVES:
The primary aim of this study is to determine which wavelength is the most sensitive and specific for CWA. Interindividual baseline absorbance will also be assessed as the impact of reagents from the intrinsic, extrinsic, and common coagulation pathway will be determined.
METHODS:
Plasma samples were screened at wavelengths from 280 to 700 nm to provide absorbance spectra in clotted and nonclotted plasma. The interindividual variability of baseline absorbance was obtained by screening plasma from 50 healthy individuals at 340, 635, and 671 nm. The inner-filter effect of reagents was assessed in plasma or serum when appropriate at the same wavelengths. The reagents were those commonly used for activated partial thromboplastin time, prothrombin time, thrombin time, and dilute Russell's viper venom time.
RESULTS:
Clotted plasma has higher absorbance value than nonclotted plasma ($P < 0.01$). The absorbance of all type of samples is higher at 340 nm than at >600 nm ($P < 0.01$). The interindividual variability at the different wavelengths was around 25%. However, except with the STA®-CKPrest® and STA®-NeoPTimal®, the reagents do not have a significant effect on the baseline absorbance.
CONCLUSIONS:
Wavelengths above 650 nm are recommended to perform CWA. Most of the commercialized reagents can be used for CWA.

Mots-clefs

Evaluation of the RESIST-4 K-SeT assay, a multiplex immunochromatographic assay for the rapid detection of OXA-48-like, KPC, VIM and NDM carbapenemases

Glupczynski Y, Evrard S, Huang TD, Bogaerts P

Références	*Doi*	*IF*
J Antimicrob Chemother. 2019 Feb 6. [Epub ahead of print]	*10.1093/jac/dkz031*	*5,217*

Abstract

Objectives:
Accurate and fast identification of carbapenemase producers is essential for optimal patient management. Here, a new lateral flow immunochromatographic RESIST-4 K-SeT assay was assessed for the detection of carbapenemases in Enterobacteriaceae and non-fermenters.
Methods:
The RESIST-4 K-SeT assay targets OXA-48-like, KPC, VIM and NDM, but not IMP carbapenemases. The assay was first evaluated using a collection of isolates with well-characterized resistance mechanisms to β-lactams (n = 134) and against an international external quality assessment carbapenemase panel (n = 8). The assay was then challenged prospectively using 345 consecutive, non-duplicate isolates including 279 Enterobacteriaceae and 66 non-fermenters (mostly Pseudomonas spp.) that were sent to the Belgian National Reference Centre for identification of the mechanisms related to carbapenem resistance.
Results:
Globally, for the collection of retrospective and prospective clinical isolates (n = 479), the assay showed a sensitivity ranging from 99% for the detection of VIM to 100% for the detection of OXA-48-like, KPC and NDM carbapenemase-producing strains. The specificity was 100% for each carbapenemase and a perfect match in results was observed for the external quality assessment for the carbapenemases targeted by the assay.
Conclusions:
The RESIST-4 K-SeT assay is a valuable alternative for detection and identification of carbapenemases from culture isolates compared with the more costly molecular assays, which may also further require skilled staff and dedicated facilities.

Mots-clefs

Cardiac computed tomography in asymptomatic siblings of patients with premature coronary disease: illustrations and current knowledge

Higny J, Dupont M, Guédès A

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

Abstract

A strong family history of early-onset coronary artery disease (CAD) may represent a substantial predictor of enhanced development of subclinical atherosclerosis in a sibling population. In this population, standard cardiovascular (CV) risk assessment could be underrated with the predictive capacity of the Framingham Risk Score. At present, cardiac computed tomography (CT) provides a high diagnostic performance for the detection of coronary atherosclerosis. Nevertheless, there is a paucity of data concerning the prognostic value of this technology in apparently healthy relatives of patients with premature coronary events. In addition, little is known about the prevalence of CAD in the siblings of patients with premature cardiac events. However, we are convinced that the reclassification of cardiac risk in middle-aged adults at familial risk is a fundamental issue in preventive cardiology. In this manuscript, we report cardiac CT findings in three subjects apparently free of CV disease from families with early-onset CAD. Afterwards, we provide a summary of the current knowledge and discuss the potential usefulness of this non-invasive imaging technique in susceptible individuals. Finally, we hope that this article will help to increase awareness for the management of middle-aged adults from high-risk families.

Mots-clefs

Cardiac computed tomography; cardiovascular risk assessment ; coronary artery disease; early-onset

Evolution of self-perceived swallowing function, tongue strength and swallow-related quality of life during radiotherapy in head and neck cancer patients

Van den Steen L, Van Gestel D, Vanderveken O, Vanderwegen J, Lazarus C, **Daisne JF**, Van Laer C, Specenier P, Van Rompaey D, Mariën S, **Lawson G**, Chantrain G, Desuter G, Van den Weyngaert D, Cvilic S, Beauvois S, Allouche J, **Delacroix L**, Vermorken JB, Peeters M, Dragan T, Van de Heyning P, De Bodt M, Van Nuffelen G.

Références	*Doi*	*IF*
Head Neck. 2019 Feb 14. [Epub ahead of print]	*10.1002/hed.25684*	*0,28*

Abstract

BACKGROUND:
Radiation-associated-dysphagia is a serious side effect of radiotherapy (RT) for head and neck cancer (HNC).
METHODS:
Seventy-six patients had a weekly prospective follow-up from baseline until one week post-RT. Combined mixed model analysis (n = 43) determined the evolution of self-perceived swallowing function, isometric tongue strength (MIP), tongue strength (TS) during swallowing (Pswal), and quality of life (QoL) in these patients during RT.
RESULTS:
Swallowing deteriorated from the third week on, resulting in an increase of tube dependency from 10% at baseline toward 31% post-RT. Both MIP and Pswal are reduced, with anterior MIP decreasing in 29% of patients and posterior MIP in 17%. Pswal decreases for saliva and a bolus swallow. All QoL subscales except «sleep» were affected during RT.
CONCLUSIONS:
Self-perceived swallowing function, TS and QoL decrease during RT for HNC. Current findings highlight the need for early monitoring of these parameters.

Mots-clefs

head and neck cancer; quality of life; radiotherapy; swallowing; tongue strength

An infant formula with large, milk phospholipid-coated lipid droplets containing a mixture of dairy and vegetable lipids supports adequate growth and is well tolerated in healthy, term infants

Breij LM, Abrahamse-Berkeveld M, Vandenplas Y, **Jespers SNJ,** de Mol AC, Khoo PC, Kalenga M, Peeters S, van Beek RHT, Norbruis OF, Schoen S, Acton D, Hokken-Koelega ACS; Mercurius Study Group.

Références	*Doi*	*IF*
Am J Clin Nutr. 2019 Mar 1;109(3):586-596	*10.1093/ajcn/nqy322*	*6,549*

Abstract

BACKGROUND:
Lipid droplets in human milk have a mode diameter of ~4 μm and are surrounded by a native phospholipid-rich membrane. Current infant milk formulas (IMFs) contain small lipid droplets (mode diameter ~0.5 μm) primarily coated by proteins. A concept IMF was developed mimicking more closely the structure and composition of human milk lipid droplets.
OBJECTIVES:
This randomized, controlled, double-blind equivalence trial evaluates the safety and tolerance of a concept IMF with large, milk phospholipid-coated lipid droplets (mode diameter 3-5 μm) containing vegetable and dairy lipids in healthy, term infants.
METHODS:
Fully formula-fed infants were enrolled up to 35 d of age and randomly assigned to 1 of 2 formulas until 17 wk of age: 1) Control IMF with small lipid droplets containing vegetable oils (n = 108); or 2) Concept IMF with large, milk phospholipid-coated lipid droplets comprised of 48% dairy lipids (n = 115). A group of 88 breastfed infants served as reference. Primary outcome was daily weight gain during intervention. Additionally, number and type of adverse events, growth, and tolerance parameters were monitored.
RESULTS:
Equivalence of daily weight gain was demonstrated (Concept compared with Control IMF: -1.37 g/d; 90% CI: -2.71, -0.02; equivalence margin ± 3 g/d). No relevant group differences were observed in growth, tolerance and number, severity, or relatedness of adverse events. We did observe a higher prevalence of watery stools in the Concept than in the Control IMF group between 5 and 12 wk of age (P < 0.001), closer to the stool characteristics observed in the breastfed group.
CONCLUSIONS:
An infant formula with large, milk phospholipid-coated lipid droplets containing dairy lipids is safe, well tolerated, and supports an adequate growth in healthy infants. This trial was registered in the Dutch Trial Register (www.trialregister.nl) as NTR3683.

Mots-clefs
Infant growth; Lipid droplet structure; Safety; dairy lipids; stool characteristics

Successful staged percutaneous transvalvular implantation in multivalvular heart disease

Jamart L, Hanet C, Dupont M, Guédès A.

Références	*Doi*	*IF*
Acta Cardiol. 2019 Feb 20:1-2. [Epub ahead of print]	*10.1080/00015385.2019.1569312*	*0,876*

Abstract

Mots-clefs
Multivalvular heart disease; TAVI; Transcatheter valve therapy; Tricuspid valve-in-valve

Philips Intellivue NMT module: precision and performance improvements to meet the clinical requirements of neuromuscular block management

Dubois V, Fostier G, Dutrieux M, Jamart J, Collet S, de Dorlodot C, Eloy P, Dubois PE.

Références	*Doi*	*IF*
J Clin Monit Comput. 2019 Feb 26. [Epub ahead of print]	*10.1007/s10877-019-00287-y*	*2,450*

Abstract

The variability or inaccuracy of acceleromyographic measurements could interfere with the interpretation of the train-of-four (TOF) ratio during neuromuscular block (NMB) recovery. This study evaluated the precision and performance of the Philips Intellivue NMT module (NMT) before (part 1) and after (part 2) several technical upgrades (i.e., firmware upgrade, new cable, and hand adapter) that were recently available. Two cohorts of 30 patients who were scheduled to undergo rhino/septoplasty under general anesthesia were included in the study. TOF ratios were recorded simultaneously every 15 s on both hands with the NMT and a TOF-Watch SX installed inside a SL TOF-Tube (TWX). Before rocuronium was administered and once final responses were stabilized, the average of the four successive measurements that determined the baselines and repeatability coefficients were compared using a z test. Simultaneous measurements were recorded at different NMB stages: onset, depth of NMB after intubation, when TWX recovered TOF count 2, TOF ratios 0.5 and 0.9, and when NMT recovered TOF ratio 0.9. The results were compared using a Student t test; $p < 0.05$ was considered significant. The NMT repeatability coefficients obtained in part 1 were significantly higher than with the TWX, they were significantly lower in part 2. Initially, the NMT significantly overestimated NMB recovery at every stage. Conversely, in the second part of the study, no difference reached statistical significance. With the recent upgrades and the new hand adapter, the NMT provided similar results compared with the TWX, Their implementation should be recommended in clinical practice.

Mots-clefs

Acceleromyography; Neuromuscular transmission monitoring; Residual paralysis; Train-of-four ratio

Graves' disease as a first autoimmune manifestation of a stiff person syndrome

Servais T, London F, Donckier JE.

Références	*Doi*	*IF*
Ann Endocrinol (Paris). 2019 Apr;80(2):134-136	*10.1016/j.ando.2019.01.002*	*1,444*

Abstract

Mots-clefs

GAPDH Expression Predicts the Response to R-CHOP, the Tumor Metabolic Status, and the Response of DLBCL Patients to Metabolic Inhibitors

Chiche J, Reverso-Meinietti J, Mouchotte A, Rubio-Patiño C, Mhaidly R, Villa E, Bossowski JP, Proics E, Grima-Reyes M, Paquet A, Fragaki K, Marchetti S, Briere J, Ambrosetti D, Michiels JF, Molina TJ, Copie-Bergman C, Lehmann-Che J, Peyrottes I, Peyrade F, de Kerviler E, Taillan B, Garnier G, Verhoeyen E, Paquis-Flucklinger V, Shintu L, Delwail V, Delpech-Debiais C, Delarue R, **Bosly A**, Petrella T, Brisou G, Nadel B, Barbry P, Mounier N, Thieblemont C, Ricci JE.

Références	*Doi*	*IF*
Cell Metab. 2019 Feb 26. [Epub ahead of print]	*10.1016/j.cmet.2019.02.002*	*20,565*

Abstract

Diffuse large B cell lymphoma (DLBCL) is a heterogeneous disease treated with anti-CD20-based immuno-chemotherapy (R-CHOP). We identified that low levels of GAPDH predict a poor response to R-CHOP treatment. Importantly, we demonstrated that GAPDHlow lymphomas use OxPhos metabolism and rely on mTORC1 signaling and glutaminolysis. Consistently, disruptors of OxPhos metabolism (phenformin) or glutaminolysis (L-asparaginase) induce cytotoxic responses in GAPDHlow B cells and improve GAPDHlow B cell-lymphoma-bearing mice survival, while they are low or not efficient on GAPDHhigh B cell lymphomas. Ultimately, we selected four GAPDHlow DLBCL patients, who were refractory to all anti-CD20-based therapies, and targeted DLBCL metabolism using L-asparaginase (K), mTOR inhibitor (T), and metformin (M) (called KTM therapy). Three out of the four patients presented a complete response upon one cycle of KTM. These findings establish that the GAPDH expression level predicts DLBCL patients' response to R-CHOP treatment and their sensitivity to specific metabolic inhibitors.

Mots-clefs

DLBCL; GAPDH; L-asparaginase; OxPhos; R-CHOP; glycolysis; mTOR; predictive marker

Extracellular Vesicles in Red Blood Cell Concentrates: An Overview

Wannez A, Devalet B, Chatelain B, Chatelain C, Dogné JM, **Mullier F.**

Références	*Doi*	*IF*
Transfus Med Rev. 2019 Feb 23. [Epub ahead of print]	*10.1016/j.tmrv.2019.02.002*	*4,111*

Abstract

Red blood cell (RBC) concentrates may be stored for up to 42 days before transfusion to a patient. During storage extracellular vesicles (EVs) develop and can be detected in significant amounts in RBC concentrates. The concentration of EVs is affected by component preparation methods, storage solutions, and inter-donor variation. Laboratory investigations have focused on the effect of EVs on in vitro assays of thrombin generation and immune responses. Assays for EVs in RBC concentrates are not standardized. The aims of this review are to describe the factors that determine the presence of erythrocyte-EVs in RBC concentrates, the current techniques used to characterize them, and the potential role of EV analysis as a quality control maker for RBC storage.

Mots-clefs

Blood transfusions; Extracellular vesicles; Microparticles; Red blood cell concentrate

A novel RAD21 mutation in a boy with mild Cornelia de Lange presentation: Further delineation of the phenotype

Dorval S, Masciadri M, **Mathot M**, Russo S, Revencu N, Larizza L.

Références	*Doi*	*IF*
Eur J Med Genet. 2019 Feb 2. [Epub ahead of print]	*10.1016/j.ejmg.2019.01.010*	*2,004*

Abstract

Cornelia de Lange syndrome is a rare autosomal dominant or X-linked developmental disorder characterized by characteristic facial dysmorphism, intellectual disability, growth retardation, upper limb and multiorgan anomalies. Causative mutations have been identified in five genes coding for the cohesion complex structure components or regulatory elements. Among them, RAD21 is associated with a milder phenotype. Very few RAD21 intragenic mutations have been identified so far. Thus, any new patient is a valuable tool to delineate the associated phenotype. We discuss a new patient with RAD21 confirmed molecular diagnosis and compare his clinical features to those of previously described patients carrying different RAD21 intragenic mutations

Mots-clefs

CdLS4; Microcephaly; RAD21; Speech delay

MARS

A Patient with GOLD Stage 3 COPD « cured » by One-Way Endobronchial Valves

Marchand E, d'Odemont JP, Dupont MV.

Références	*Doi*	*IF*
Medicina (Kaunas). 2019 Mar 11;55(3)	*10.3390/medicina55030065*	*0,33*

Abstract

Lung hyperinflation is a main determinant of dyspnoea in patients with chronic obstructive pulmonary disease (COPD). Surgical or bronchoscopic lung volume reduction are the most efficient therapeutic approaches for reducing hyperinflation in selected patients with emphysema. We here report the case of a 69-year old woman with COPD (GOLD stage 3-D) referred for lung volume reduction. She complained of persistent disabling dyspnoea despite appropriate therapy. Chest imaging showed marked emphysema heterogeneity as well as severe hyperinflation of the right lower lobe. She was deemed to be a good candidate for bronchoscopic treatment with one-way endobronchial valves. In the absence of interlobar collateral ventilation, 2 endobronchial valves were placed in the right lower lobe under general anaesthesia. The improvement observed 1 and 3 months after the procedure was such that the patient no longer met the pulmonary function criteria for COPD. The benefit persisted after 3 years.

Mots-clefs

COPD; endobronchial valves; lung hyperinflation; lung volume reduction; treatment

Microenvironment tailors nTreg structure and function

Schiavon V, Duchez S, Branchtein M, How-Kit A, **Cassius C**, Daunay A, Shen Y, Dubanchet S, Colisson R, Vanneaux V, Pruvost A, Roucairol C, Setterblad N, Bouaziz JD, Boissier MC, Semerano L, Graux C, Bensussan A, Burny A, Gallo R, Zagury D, Le Buanec H.

Références	*Doi*	*IF*
Proc Natl Acad Sci U S A. 2019 Mar 26;116(13):6298-6307	*10.1073/pnas.1812471116*	

Abstract

Natural regulatory T cells (nTregs) ensure the control of self-tolerance and are currently used in clinical trials to alleviate autoimmune diseases and graft-versus-host disease after hematopoietic stem cell transfer. Based on CD39/CD26 markers, blood nTreg analysis revealed the presence of five different cell subsets, each representing a distinct stage of maturation. Ex vivo added microenvironmental factors, including IL-2, TGFβ, and PGE2, direct the conversion from naive precursor to immature memory and finally from immature to mature memory cells, the latest being a no-return stage. Phenotypic and genetic characteristics of the subsets illustrate the structural parental maturation between subsets, which further correlates with the expression of regulatory factors. Regarding nTreg functional plasticity, both maturation stage and microenvironmental cytokines condition nTreg activities, which include blockade of autoreactive immune cells by cell-cell contact, Th17 and IL-10 Tr1-like activities, or activation of TCR-stimulating dendritic cell tolerization. Importantly, blood nTreg CD39/CD26 profile remained constant over a 2-y period in healthy persons but varied from person to person. Preliminary data on patients with autoimmune diseases or acute myelogenous leukemia illustrate the potential use of the nTreg CD39/CD26 profile as a blood biomarker to monitor chronic inflammatory diseases. Finally, we confirmed that naive conventional CD4 T cells, TCR-stimulated under a tolerogenic conditioned medium, could be ex vivo reprogrammed to FOXP3 lineage Tregs, and further found that these cells were exclusively committed to suppressive function under all microenvironmental contexts.

Mots-clefs

CD39 regulatory receptor; FOXP3 regulatory transcript; adenosine deaminase-binding CD26; microenvironmental cytokines; nTregs

Surgical consensus guidelines on sentinel node biopsy (SNB) in patients with oral cancer

Schilling C, Stoeckli SJ, Vigili MG, de Bree R, Lai SY, Alvarez J, Christensen A, Cognetti DM, D'Cruz AK, Frerich B, Garrel R, Kohno N, Klop WM, Kerawala C, **Lawson G**, McMahon J, Sassoon I, Shaw RJ, Tvedskov JF, von Buchwald C, McGurk M.

Références	*Doi*	*IF*
Head Neck. 2019 Mar 21. [Epub ahead of print]	*10.1002/hed.25739*	*0,28*

Abstract

BACKGROUND:
The eighth international symposium for sentinel node biopsy (SNB) in head and neck cancer was held in 2018. This consensus conference aimed to deliver current multidisciplinary guidelines. This document focuses on the surgical aspects of SNB for oral cancer.
METHOD:
Invited expert faculty selected topics requiring guidelines. Topics were reviewed and evidence evaluated where available. Data were presented at the consensus meeting, with live debate from panels comprising expert, nonexpert, and patient representatives followed by voting to assess the level of support for proposed recommendations. Evidence review, debate, and voting results were all considered in constructing these guidelines.
RESULTS/CONCLUSION:
A range of topics were considered, from patient selection to surgical technique and follow-up schedule. Consensus was not achieved in all areas, highlighting potential issues that would benefit from prospective studies. Nevertheless these guidelines represent an up-to-date pragmatic recommendation based on current evidence and expert opinion.

Mots-clefs

elective neck dissection; occult metastasis; operative technique; oral squamous cell cancer; sentinel node biopsy

Prevalence of multidrug-resistant organisms in nursing homes in Belgium in 2015

Latour K, **Huang TD**, Jans B, Berhin C, **Bogaerts P**, **Noel A,** Nonhoff C, Dodémont M, Denis O, Ieven M, Loens K, **Schoevaerdts D**, Catry B, **Glupczynski Y.**

Références	*Doi*	*IF*
PLoS One. 2019 Mar 28;14(3):e0214327	*10.1371/journal.pone.0214327*	*2,766*

Abstract

OBJECTIVES:
Following two studies conducted in 2005 and 2011, a third prevalence survey of multidrug-resistant microorganisms (MDRO) was organised in Belgian nursing homes (NHs) using a similar methodology. The aim was to measure the prevalence of carriage of methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum β-lactamase producing Enterobacteriaceae (ESBLE) and carbapenemase-producing Enterobacteriaceae (CPE) in NH residents. Risk factors for MDRO carriage were also explored.
METHODS:
Up to 51 randomly selected residents per NH were screened for MDRO carriage by trained local nurses between June and October 2015. Rectal swabs were cultured for ESBLE, CPE and VRE, while pooled samples of nose, throat and perineum and chronic wound swabs were obtained for culture of MRSA. Antimicrobial susceptibility testing, molecular detection of resistance genes and strain genotyping were performed. Significant risk factors for MDRO colonization MDRO was determined by univariate and multivariable analysis.
RESULTS:
Overall, 1447 residents from 29 NHs were enrolled. The mean weighted prevalence of ESBLE and MRSA colonization was 11.3% and 9.0%, respectively. Co-colonization occurred in 1.8% of the residents. VRE and CPE carriage were identified in only one resident each. Impaired mobility and recent treatment with fluoroquinolones or with combinations of sulphonamides and trimethoprim were identified as risk factors for ESBLE carriage, while for MRSA these were previous MRSA carriage/infection, a stay in several different hospital wards during the past year, and a recent treatment with nitrofuran derivatives. Current antacid use was a predictor for both ESBL and MRSA carriage.
CONCLUSIONS:
In line with the evolution of MRSA and ESBL colonization/infection in hospitals, a decline in MRSA carriage and an increase in ESBLE prevalence was seen in Belgian NHs between 2005 and 2015. These results show that a systemic approach, including surveillance and enhancement of infection control and antimicrobial stewardship programs is needed in both acute and chronic care facilities.

Mots-clefs

Overlooked guide wire: a multicomplicated Swiss Cheese Model example. Analysis of a case and review of the literature

Thonon H, Espeel F, Frederic F, **Thys F**.

Références	*Doi*	*IF*
Acta Clin Belg. 2019 Mar 30:1-7. [Epub ahead of print]	*10.1080/17843286.2019.1592738*	*0,916*

Abstract

OBJECTIVES:
Central venous catheter (CVC) implementation is now usual in emergency department. The most common complications are misplacement, bleeding, pleural perforation, thrombosis and sepsis. Forgetting a guide wire in the patient's body after catheterization is an underestimated complication of this procedure; only 76 cases are described. Even if the majority of patients remained asymptomatic, severe complications can happened even years later. This article's aim is to identify the sequence of elements that led to the event occurrence and to suggest recommendations of good practice to minimize complications related to central catheter placement.
METHOD:
After reviewing all the complications related to central venous catheterization and their frequencies, we analyse from a case report and a review of the literature the sequence of elements that led to the medical error. We use an Ishikawa diagram to show our results and the links between them.
RESULTS:
Our Ishikawa diagram shows that material, human resources, procedural and radiological involvement factors are the main elements on which we can act to reduce the complications rate after central venous catheterization. We advocate for the establishment of standardized procedures before, during and after the technical gesture.
CONCLUSIONS:
Because of human nature, errors will always be possible when taking care of a patient. However, we propose good practice recommendations to avoid the repetition of a forgetting guide wire after central venous catheterization

Mots-clefs

Central catheter; checklist; emergency department; human error; incident reporting; patient safety

Long-Term Stability of Lorazepam in Sodium Chloride 0.9% Stored at Different Temperatures in Different Containers

Colsoul ML, Breuer A, Goderniaux N, Hecq JD, Soumoy L, Bihin B, Jamart J, Galanti L.

Références	*Doi*	*IF*
Hospit Pharm 2019 p. 001857871983664	*10.1177/0018578719836649*	*0,31*

Abstract

Background and Objective: Infusion containing lorazepam is used by geriatric department to limit anxiety disorders in the elderly. Currently, these infusions are prepared according to demand by the nursing staff, but the preparation in advance in a centralized service could improve quality of preparation and time management. The aim of this study was to investigate the long-term stability of this infusion in polypropylene syringes stored at 5 ± 3°C. Then, results obtained were compared with stability data of lorazepam in syringes stored at room temperature, glass bottles at 5 ± 3°C, and glass bottles at room temperature. Method: Eight syringes and 6 bottles of infusion were prepared by diluting 1 mL lorazepam 4 mg in 23 mL of NaCl 0.9% under aseptic conditions. Five syringes and 3 bottles were stored at 5 ± 3°C and 3 syringes and 3 bottles were stored at room temperature for 30 days. During the storage period, particle appearance or color change were periodically checked by visual and microscope inspection. Turbidity was assessed by measurements of optical density (OD) at 3 wavelengths (350 nm, 410 nm, 550 nm). The stability of pH was also evaluated. The lorazepam concentrations were measured at each time point by high-performance liquid chromatography with ultraviolet detector at 220 nm. Results: Solutions were physically unstable in syringes at 5 ± 3°C after 4 days: crystals and a drop of OD at 350 nm were observed. However, pH was stable. After 2 days, solutions were considered as chemically unstable because a loss of lorazepam concentration higher than 10% was noticed: the lower 1-sided confidence limit at 95% was below 90% of the initial concentration. To assess temperature and polypropylene influence, results were compared with those obtained for syringes at room temperature and bottles at 5 ± 3°C and room temperature. Precipitation, drop of OD at 350 nm, and chemical instability were observed in all conditions. Conclusion: Solutions of lorazepam were unstable after 2 days in syringes at 5 ± 3°C. Preparation in advance appears, therefore, not possible for the clinical use. Storage conditions (temperature and form) do not improve the stability.

Mots-clefs

Evaluation of the Physicochemical Stability of Amiodarone Hydrochloride in Syringes for the Intensive Care Unit

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

Références	*Doi*	*IF*
Int J Pharm Comp 2019. 23(2):163-166		*0,07*

Abstract

In some emergency clinical situations, the injection of a more concentrated drug solution in the intensive care units is common. The purpose of this study was to evaluate the physicochemical stability of concentrated solutions of amiodarone hydrochloride in polypropylene syringes during 28 days of storage at 5°C ± 3°C, with protection from light. Five syringes of 50 mL, containing 25 mg/mL of amiodarone in dextrose 5%, were prepared and stored at 5°C ± 3°C with protection from light during 28 days. Immediately after preparation and periodically during the storage, amiodarone hydrochloride concentrations were measured by ultra-performance liquid chromatography. Spectrophotometric absorbance at different wavelengths, pH measurement, and microscopic observations were also performed. All solutions were physicochemically stable during the study period when stored at 5°C ± 3°C. No color change, turbidity, precipitation, opacity, significant pH variations, or optic densities were observed in the solutions. No crystals were seen by microscopic analysis. The concentration of amiodarone did not decrease during the 28 days of storage. Solutions of amiodarone 25 mg/mL in syringes of dextrose 5% are physically and chemically stable for at least 28 days when stored in syringes at 5°C ± 3°C with protection from light and may be prepared in advanced by a centralized intravenous additive service.

Mots-clefs

elective neck dissection; occult metastasis; operative technique; oral squamous cell cancer; sentinel node biopsy

Severe Occupational Asthma: Insights From a Multicenter European Cohort

Vandenplas O, Godet J, Hurdubaea L, Rifflart C, Suojalehto H, Walusiak-Skorupa J, Munoz X, Sastre J, Klusackova P, Moore V, Merget R, Talini D, Kirkeleit J, Mason P, Folletti I, 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*
J Allergy Clin Immunol Pract. 2019 Mar 23. [Epub ahead of print]	*10.1016/j.jaip.2019.03.017*	*13.258*

Abstract

BACKGROUND:
Although sensitizer-induced occupational asthma (OA) accounts for an appreciable fraction of adult asthma, the severity of OA has received little attention.
OBJECTIVE:
The aim of this study was to characterize the burden and determinants of severe OA in a large multicenter cohort of subjects with OA.
METHODS:
This retrospective study included 997 subjects with OA ascertained by a positive specific inhalation challenge completed in 20 tertiary centers in 11 European countries during the period 2006 to 2015. Severe asthma was defined by a high level of treatment and any 1 of the following criteria: (1) daily need for a reliever medication, (2) 2 or more severe exacerbations in the previous year, or (3) airflow obstruction.
RESULTS:
Overall, 162 (16.2%; 95% CI, 14.0%-18.7%) subjects were classified as having severe OA. Multivariable logistic regression analysis revealed that severe OA was associated with persistent (vs reduced) exposure to the causal agent at work (odds ratio [OR], 2.78; 95% CI, 1.50-5.60); a longer duration of the disease (OR, 1.04; 95% CI, 1.00-1.07); a low level of education (OR, 2.69; 95% CI, 1.73-4.18); childhood asthma (OR, 2.92; 95% CI, 1.13-7.36); and sputum production (OR, 2.86; 95% CI, 1.87-4.38). In subjects removed from exposure, severe OA was associated only with sputum production (OR, 3.68; 95% CI, 1.87-7.40); a low education level (OR, 3.41; 95% CI, 1.72-6.80); and obesity (OR, 1.98; 95% CI, 0.97-3.97).
CONCLUSIONS:
This study indicates that a substantial proportion of subjects with OA experience severe asthma and identifies potentially modifiable risk factors for severe OA that should be targeted to reduce the adverse impacts of the disease.

Mots-clefs
Airflow obstruction; Asthma control; Asthma exacerbations; Occupational asthma; Severe asthma

AVRIL

Response to correspondence: "Interferon alpha might be an alternative therapeutic choice for refractory neuro-Behçet's disease" - Authors reply

London F, Duprez T, van Pesch V.

Références	*Doi*	*IF*
Mult Scler Relat Disord. 2019 Apr;29:154	*10.1016/j.msard.2018.12.027*	

Abstract

Mots-clefs
Interferon-alpha; Neuro-Behçet's disease

Concentrations of direct oral anticoagulants according to guidelines for the periprocedural management of low bleeding risk procedures

Godier A, Martin AC, **Lessire S, Mullier F,** Leblanc I, Gouin-Thibault I.

Références	*Doi*	*IF*
Anaesth Crit Care Pain Med. 2019 Apr 13. [Epub ahead of print]	*10.1016/j.accpm.2019.04.004*	*2,2*

Abstract

Mots-clefs
Bleeding; Direct oral anticoagulant concentration; perioperative

Optical coherence tomography: a window to the optic nerve in clinically isolated syndrome

London F, Zéphir H, Drumez E, Labreuche J, Hadhoum N, Lannoy J, Hodel J, Vermersch P, Pruvo JP, Leclerc X, Outteryck O.

Références	*Doi*	*IF*
Brain. 2019 Apr 1;142(4):903-915.	*10.1093/brain/awz038*	*10,840*

Abstract

In this study, we aimed to evaluate the association of asymptomatic optic nerve demyelinating lesion in patients presenting a clinically isolated syndrome with the asymptomatic retinal neuro-axonal loss previously reported at clinically isolated syndrome. We prospectively recruited 66 patients presenting a clinically isolated syndrome and 66 healthy control subjects matched according to age and gender. All patients underwent brain magnetic resonance imaging including 3D-double inversion recovery (DIR) sequence, optical coherence tomography examination and visual function evaluation, at 2.5-4.5 months after CIS. Evaluation criteria were presence and length of optic nerve DIR hypersignal, retinal layers (including ganglion cell inner plexiform layer and inner nuclear layer) thickness/volume, and low contrast monocular vision acuity (number of letters correctly identified). All clinically isolated syndrome eyes with past history of optic neuritis (CIS-ON) presented an optic nerve DIR hypersignal. We observed asymptomatic optic nerve DIR hypersignal in 22.2% of clinically isolated syndrome eyes without optic neuritis (CIS-NON). In comparison with healthy control, GCIPL volume (in mm3) was significantly lower in CIS-ON eyes [β (95% confidence interval, CI) = -0.121 (-0.168 to -0.074); P ‹ 0.0001], and to a lesser extent in CIS-NON [β (95% CI) = -0.023 (-0.039 to -0.008); P = 0.004]. In comparison to healthy controls, eyes with asymptomatic optic nerve DIR hypersignal presented significantly lower macular ganglion cell inner plexiform layer volume [β (95% CI) = -0.043 (-0.068 to -0.019); P = 0.001], and eyes without did not [β (95% CI) = -0.016 (-0.034 to 0.003); P = 0.083]. Among CIS-NON, macular ganglion cell inner plexiform layer volume decrease was associated with asymptomatic optic nerve DIR hypersignal independently of optic radiations T2 lesions and primary visual cortex volumes (P = 0.012). Symptomatic optic nerve DIR hypersignal were significantly longer (13.8 ± 6.7 mm) than asymptomatic optic nerve hypersignal (10.0 ± 5.5 mm; P = 0.047). Length of optic nerve DIR hypersignal was significantly associated with thinner inner retinal layers (P ≤ 0.001), thicker inner nuclear layer (P = 0.017) and lower low contrast monocular vision acuity (P ‹ 0.05). Compared to healthy control, low contrast monocular vision acuity was significantly lower in CIS-ON eyes (P ‹ 0.0001) and CIS-NON eyes with (P = 0.03) or without asymptomatic optic nerve DIR hypersignal (P = 0.0005). Asymptomatic demyelinating optic nerve DIR hypersignal at the earliest clinical stage of multiple sclerosis is frequent and associated with asymptomatic retinal neuro-axonal loss reported at clinically isolated syndrome stage. Length of optic nerve DIR hypersignal is a biomarker of retinal neuro-axonal loss and visual disability at clinically isolated syndrome stage. Visual disability of clinically isolated syndrome eyes without clinical and subclinical optic nerve involvement might be due to missed optic nerve lesions on MRI. At the earliest clinical stage of multiple sclerosis, our results support considering optical coherence tomography as a window to the optic nerve rather than to the brain.

Mots-clefs

clinically isolated syndrome; double inversion recovery; multiple sclerosis; optic neuritis; optical coherence tomography

Exome sequencing identifies germline variants in DIS3 in familial multiple myeloma

Pertesi M, Vallée M, Wei X, Revuelta MV, Galia P, Demangel D, Oliver J, Foll M, Chen S, Perrial E, Garderet L, Corre J, Leleu X, Boyle EM, Decaux O, Rodon P, Kolb B, Slama B, Mineur P, Voog E, Le Bris C, Fontan J, Maigre M, Beaumont M, Azais I, Sobol H, Vignon M, Royer B, Perrot A, Fuzibet JG, Dorvaux V, Anglaret B, Cony-Makhoul P, Berthou C, **Desquesnes F**, Pegourie B, Leyvraz S, Mosser L, Frenkiel N, Augeul-Meunier K, Leduc I, Leyronnas C, Voillat L, Casassus P, Mathiot C, Cheron N, Paubelle E, Moreau P, Bignon YJ, Joly B, Bourquard P, Caillot D, Naman H, Rigaudeau S, Marit G, Macro M, Lambrecht I, Cliquennois M, Vincent L, Helias P, Avet-Loiseau H, Moreno V, Reis RM, Varkonyi J, Kruszewski M, Vangsted AJ, Jurczyszyn A, Zaucha JM, Sainz J, Krawczyk-Kulis M, Wątek M, Pelosini M, Iskierka-Jażdżewska E, Grząśko N, Martinez-Lopez J, Jerez A, Campa D, Buda G, Lesueur F, Dudziński M, García-Sanz R, Nagler A, Rymko M, Jamroziak K, Butrym A, Canzian F, Obazee O, Nilsson B, Klein RJ, Lipkin SM, McKay JD, Dumontet C.

Références	*Doi*	*IF*
Leukemia. 2019 Apr 9. [Epub ahead of print]	*10.1038/s41375-019-0452-6*	*10,023*

Abstract

Mots-clefs

PET-guided, BEACOPP escalated therapy in advanced Hodgkin lymphoma - Authors' reply

Casasnovas RO, Bouabdallah R, Brice P, Lazarovici J, Ghesquieres H, Stamatoullas A, Berriolo-Riedinger A, Fornecker LM, **André M**, Meignan M.

Références	*Doi*	*IF*
Lancet Oncol. 2019 Apr;20(4):e190	*10.1016/S1470-2045(19)30156-1.*	*36,418*

Abstract

Mots-clefs

Health related quality of life in older patients with solid tumors and prognostic factors for decline

Decoster L, Quinten C, Kenis C, Flamaing J, Debruyne PR, De Groof I, Focan C, Cornelis F, Verschaeve V, Bachmann C, Bron D, Luce S, Debugne G, den Bulck, **Goeminne JC**, Baitar A, 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*
J Geriatr Oncol. 2019 Apr 17. [Epub ahead of print]	*10.1016/j.jgo.2019.03.018*	*3,359*

Abstract

This study aims to investigate health-related quality of life (HRQOL) at baseline and at follow-up in older patients with cancer and to determine prognostic factors for HRQOL decline.

METHODS:

A prospective Belgian multicentre (n = 22) study was performed. Patients ≥70 years with a malignant tumor and abnormal G8 (≤14/17) screening tool were included. Patients underwent geriatric assessment (GA) and HRQOL evaluation with follow up at three months. Uni- and multivariate regression models were performed to determine factors associated ($p < .05$) with baseline HRQOL and HRQOL decline at follow-up.

RESULTS:

Results reflect data collected from 3673 patients. A multivariate analysis showed that younger patients, and those with poor Eastern Cooperative Oncology Group - Performance Status (ECOG-PS), specific tumor types (gastrointestinal, gynaecological and thorax) and higher stage had lower baseline HRQOL. In addition worse functional status and presence of pain, fatigue, depression and malnutrition were associated with lower baseline HRQOL. During treatment (n = 2972), improvement in HRQOL was observed in 1037 patients (35%) and a decline in 838 patients (28.2%). In multivariate analysis, stage and presence of baseline comorbidities, pain, fatigue or malnutrition were associated with HRQOL evolution.

CONCLUSION:

Baseline HRQOL in older patients with cancer and an abnormal G8 depends on tumor and age related parameters. During follow-up, HRQOL improved in one third of patients, indicating that they may benefit from cancer treatment while one quarter demonstrated a HRQOL decline for which prognostic factors were identified.

Mots-clefs

Cancer; Geriatric domains; Health-related quality of life; Older patients; Prognostic factors

Seborrheic keratosis evolution into squamous cell carcinoma: A truly modified sun-related tumor? A case report and review of the literature

Cimpean I, Theate I, **Vanhooteghem O**.

Références	*Doi*	*IF*
Dermatol Reports. 2019 Apr 17;11(1):7999	*10.4081/dr.2019.7999*	*0.50*

Abstract

The incidence of seborrheic keratosis (SK) generally increases with age and are mostly localized on the trunk, face and neck, especially on sun-exposed areas. The association between SK and skin malignancies appears to be accidental, but in situ transformation occurs more frequently in sun-exposed areas. Histopathological examination of all SK cases should be considered, especially when SK lesions exhibit atypical clinical manifestations, such as ulceration and cresting, as they may herald malignant transformation. In addition, other features associated with malignant transformation include excoriations or hemorrhages identified on the lesion, modification and evolution of the macroscopic characteristics, and the presence of local erythema or pruritus. Immunocompromised patients exhibit an increased risk of malignant transformation, even when radiation is involved.

Mots-clefs

Seborrheic keratosis; Squamous cell carcinoma; Sun

Long-term clinical effectiveness of ustekinumab in patients with Crohn's disease who failed biological therapies: a national cohort study

Liefferinckx C, Verstockt B, Gils A, Noman M, Van Kemseke C, Macken E, De Vos M, Van Moerkercke W, **Rahier JF**, Bossuyt P, Dutré J, Humblet E, Staessen D, Peeters H, Van Hootegem P, Louis E, Franchimont D, Baert F, Vermeire S; Belgian Inflammatory Bowel Disease Research and Development Group (BIRD group).

Références	*Doi*	*IF*
J Crohns Colitis. 2019 Apr 16. pii: jjz080 [Epub ahead of print]	*doi: 10.1093/ecco-jcc/jjz080*	*6.637*

Abstract

BACKGROUND:
Ustekinumab (UST) was recently approved in Europe for the treatment of moderate to severe Crohn's disease (CD). Long-term real-world data are currently scarce in CD patients previously exposed to several biologics.
METHODS:
This is an observational, national, retrospective multicenter study. Patients received intravenous UST ~ 6mg/kg at baseline, with 90mg subcutaneously thereafter every 8 weeks. Response and remission rates were assessed at week 8, 16 and 52.
RESULTS:
Data from 152 patients were analysed. All patients were exposed at least one anti-TNFβ agent, with 69.7 % even two anti-TNFβ and vedolizumab. After one year, 42.1 % and 25.7% experienced clinical response and clinical remission, respectively; 38.8% and 24.3% achieved steroid-free clinical response and remission, respectively at one year. Thirty-eight point eight per cent of patients discontinued therapy during the 12 months of follow-up. Colonic location was predictive of clinical response at one year, while low BMI at baseline was a negative predictor of clinical remission. Resolution of arthralgia was associated with clinical response over time. De novo arthralgia were reported by 17.9% of patients at week 8 and 13.5% at week 52. No impact of ustekinumab on arthralgia was observed in patients with concomitant ankylosing spondyloarthritis (n=17). Others adverse events were reported in 7.2% of patients.
CONCLUSIONS:
This real-world cohort study confirms the effectiveness of ustekinumab in CD patients previously exposed to several biologics. Ustekinumab was well tolerated with adverse events.

Mots-clefs
Clinical ; Crohn’s disease; effectiveness; real-life cohort; ustekinumab

Head and Body positions as risk-factors for sleep obstructive breathing

Martinot JB, Le-Dong N, Cuthbert V, Denison S, Tamisier R, Borel JC, Pepin JL.

Références	*Doi*	*IF*
ERJ Open Research 2019 5: P116	*10.1183/23120541*	*1.135*

Abstract

OBJECTIVE:

We explored the causal relationship between Head-Body positions (HBp) and Sleep obstructive apnea/hypopnea (OAH) to fill the evidence gap in this topic.

METHODS:

Rotations (pitch/yaw) and directions (prone, supine, up/left, supine, right) of HBp were captured by two miniaturized sensors under 45° segments during type1 PSG in 20 consecutive OSA patients. Sequential categorical data of Arousals (A, n=559) and OAH events (n=630) (accordingly to AASM2012) associated with HBp status (n=1633) were built. A timestamps-based algorithm was applied to extract every possible combinations between changes in HBp and events. The association between HBp and events risk was evaluated with Lasso-logistic and RandomForest models

RESULTS:

Head and body prone pitching (PP) and right yawing (RY) were found significantly associated to either A or OAH events. Head position played the most important role (OR=2.2 for PP and 3.9 for RY), compared to that of body postural changes (OR=1.2 for RY and OR=1.1 for PP). Chronological order analysis showed that HBp changes occurred after A (73.7%) or OAH (72.6%) episodes. A and OAH events were triggered by HBp in only 23% observations. Rarely, A and OAH events occurred during a long and stable HBp (2.5%).

CONCLUSION:

Prone pitching and right yawing were the most important positions contributing to the classification of A and OAH events. HBp seemed here more likely consequences than causes of A or OAH risk.

Mots-clefs

Seborrheic keratosis; Squamous cell carcinoma; Sun

Les mouvements de la mandibule informent sur l'effet thérapeutique de l'orthèse d'avancée mandibulaire

Martinot JB, Crespeigne E, Bolly A, Butenda D, Le-Dong NN

Références	*Doi*	*IF*
Vaisseaux, Coeur, Poumons Vol 24 N°2 2019		

Abstract

Mots-clefs

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