2020

Q1

# RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR

N°7 - PREMIER QUADRIMESTRE 2020

**Dinant • Godinne • Sainte-Elisabeth**

CHU UCL NAMUR

# SUPPLÉMENT
2019

# Laboratory diagnostic of venous thromboembolism : Where are D-dimer in 2019 ?

**Mullier F.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *"The EFLM Newsletter" ;3:3-4* | | |


## Abstract

**Mots-clefs**

# Pulmonary embolism : about two pediatric observations

**Gueulette E, Somville V, Bodart E.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Bel Ped. 2019:178-180* | | |




## Abstract

Pulmonary embolism is a rare and underestimated pathology within the paediatric population. The diagnosis is often delayed in children and teenagers, potentially increasing paediatric morbidity and mortality. Specific paediatric risk factors may be detected. Diagnostic, treatment and follow-up guidelines only exist for adults but are currently applied to children. The purpose of this article is to discuss clinical signs, assessment and paediatric management. Further studies will be required in order to establish standard paediatric guidelines.


**Mots-clefs**

# Analysis of Malpractice Claims: The Franco-Belgian "Cœlio Club" Experience

Delaunay F, Delaunay T, Van Vyve E, Cardin JL, Club Celio, **Bertrand C.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Visc Surg. 2019 Sep;156 Suppl 1:S33-S39* | *10.1016/j.jviscsurg.2019.04.011* | *2,012* |




## Abstract

Malpractice claims are a regularly increasing concern in gastrointestinal surgery. The goal of this study was to compare the current status of claims in two different French-speaking communities by a retrospective descriptive study of surgeons' experiences, from the beginning of their practice up until December 31 2014. Data included the number, the reasons, and the results of medicolegal claims and their jurisdictions. Forty-three surgeons participated in this study. Two hundred medicolegal claims were analyzed. The mean number was 5.8 per surgeon. Bariatric surgery, colorectal surgery and parietal surgery were the most exposed. Forty-six (23%) faults were noted, while no fault was pronounced in 139 (69.5%) cases. The main reasons for lodging complaints were nosocomial infections, anastomotic leaks, poor postoperative care, hollow organ perforation, peripheral neurologic complication, and insufficient preoperative information. Forty-four percent of the complaints were analyzed by the conciliation and compensation commissions and 43.5% by the High Court. In the French-speaking group, there were 13 complaints, two of which gave rise to compensation. French surgeons are highly exposed to complaints: in French law, clumsiness or technical maladdress is considered as a fault. The patient should be informed preoperatively of all possible severe risks of a medical procedure. In Belgium, complications are exceptional and are considered random therapeutic events. Adhering to the recommendations emanating from the French High Authority of Health and Learned Societies as well as accreditation issued by the same High Authority should allow to decrease the number of undesirable events related to care and malpractice.



## Mots-clefs

Clumsiness; Fault; Lawsuit; Medical responsibility; Visceral surgery.

# Histoire des stomies ...

**Lemaire J.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Rev Francophone de stomathérapie & soins de plaie. 2019;28:26-27* | | |


## Abstract

## Mots-clefs

# Comparative Performances of Machine Learning Methods for Classifying Crohn Disease Patients Using Genome-Wide Genotyping Data

Romagnoni A, Jégou S, Van Steen K, Wainrib G, Hugot JP, International Inflammatory Bowel Disease Genetics Consortium (IIBDGC) **(Rahier JF.).**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Sci Rep. 2019 Jul 17;9(1):10351* | *10.1038/s41598-019-46649-z* | *4,011* |



**Abstract**

Crohn Disease (CD) is a complex genetic disorder for which more than 140 genes have been identified using genome wide association studies (GWAS). However, the genetic architecture of the trait remains largely unknown. The recent development of machine learning (ML) approaches incited us to apply them to classify healthy and diseased people according to their genomic information. The Immunochip dataset containing 18,227 CD patients and 34,050 healthy controls enrolled and genotyped by the international Inflammatory Bowel Disease genetic consortium (IIBDGC) has been re-analyzed using a set of ML methods: penalized logistic regression (LR), gradient boosted trees (GBT) and artificial neural networks (NN). The main score used to compare the methods was the Area Under the ROC Curve (AUC) statistics. The impact of quality control (QC), imputing and coding methods on LR results showed that QC methods and imputation of missing genotypes may artificially increase the scores. At the opposite, neither the patient/control ratio nor marker preselection or coding strategies significantly affected the results. LR methods, including Lasso, Ridge and ElasticNet provided similar results with a maximum AUC of 0.80. GBT methods like XGBoost, LightGBM and CatBoost, together with dense NN with one or more hidden layers, provided similar AUC values, suggesting limited epistatic effects in the genetic architecture of the trait. ML methods detected near all the genetic variants previously identified by GWAS among the best predictors plus additional predictors with lower effects. The robustness and complementarity of the different methods are also studied. Compared to LR, non-linear models such as GBT or NN may provide robust complementary approaches to identify and classify genetic markers.

**Mots-clefs**

# IBD Risk Loci Are Enriched in Multigenic Regulatory Modules Encompassing Putative Causative Genes

Momozawa Y, Dmitrieva J, Théâtre E, Deffontaine V, Rahmouni S, Charloteaux B, Crins F, Docampo E, Elansary M, Gori AS, Lecut C, Mariman R, Mni M, Oury C, Altukhov I, Alexeev D, Aulchenko Y, Amininejad L, Bouma G, Hoentjen F, Löwenberg M, Bas Oldenburg B, Pierik MJ, Vander Meulen-de Jong AE, van der Woude CJ, Visschedijk MC, International IBD Genetics Consortium; Lathrop M, Hugot JP, Weersma RK, De Vos M, Franchimont D, Vermeire S, Kubo M, Louis E, Georges M. **(Rahier JF)**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Nat Commun. 2018 Jun 21;9(1):2427* | *10.1038/s41467-018-04365-8* | *11,880* |



**Abstract**

GWAS have identified ›200 risk loci for Inflammatory Bowel Disease (IBD). The majority of disease associations are known to be driven by regulatory variants. To identify the putative causative genes that are perturbed by these variants, we generate a large transcriptome data set (nine disease-relevant cell types) and identify 23,650 cis-eQTL. We show that these are determined by ~9720 regulatory modules, of which ~3000 operate in multiple tissues and ~970 on multiple genes. We identify regulatory modules that drive the disease association for 63 of the 200 risk loci, and show that these are enriched in multigenic modules. Based on these analyses, we resequence 45 of the corresponding 100 candidate genes in 6600 Crohn disease (CD) cases and 5500 controls, and show with burden tests that they include likely causative genes. Our analyses indicate that ≥10-fold larger sample sizes will be required to demonstrate the causality of individual genes using this approach.

**Mots-clefs**

# Genetic Variation in HSD17B13 Reduces the Risk of Developing Cirrhosis and Hepatocellular Carcinoma in Alcohol Misuser

Stickel F, Lutz P, Buch S, Dieter Nischalke H, Silva I, Rausch V, Fischer J, Heinz Weiss K, Gotthardt D, Rosendahl J, **Marot A,** Elamly M, Krawczyk M, Casper M, Lammert F, Buckley T, McQuillin A, Spengler U, Eyer F, Vogel A, Marhenke S, von Felden J, Wege H, Sharma R, Atkinson S, Franke A, Nehring S, Moser V, Schafmayer C, Spahr L, Lackner C, Stauber RE, Canbay A, Link A, Valenti L, Grove JI, Aithal GP, Marquardt JU, Fateen W, Zopf S, Dufour JF, Trebicka J, Datz C, Deltenre P, Mueller S, Berg T, Hampe J, Morgan MY.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Hepatology. 2019 Oct 19. Online ahead of print* | *10.1002/hep.30996* | *14,971* |



## Abstract

**BACKGROUND AND AIMS:** Carriage of rs738409:G in patatin-like phospholipase domain containing 3 (PNPLA3) is associated with an increased risk for developing alcohol-related cirrhosis and hepatocellular carcinoma (HCC). Recently, rs72613567:TA in hydroxysteroid 17-beta dehydrogenase 13 (HSD17B13) was shown to be associated with a reduced risk for developing alcohol-related liver disease and to attenuate the risk associated with carriage of PNPLA3 rs738409:G. This study explores the risk associations between these two genetic variants and the development of alcohol-related cirrhosis and HCC.

**APPROACH AND RESULTS:** Variants in HSD17B13 and PNPLA3 were genotyped in 6,171 participants, including 1,031 with alcohol-related cirrhosis and HCC, 1,653 with alcohol-related cirrhosis without HCC, 2,588 alcohol misusers with no liver disease, and 899 healthy controls. Genetic associations with the risks for developing alcohol-related cirrhosis and HCC were determined using logistic regression analysis. Carriage of HSD17B13 rs72613567:TA was associated with a lower risk for developing both cirrhosis (odds ratio [OR], 0.79; 95% confidence interval [CI], 0.72-0.88; P = 8.13 × 10-6 ) and HCC (OR, 0.77; 95% CI, 0.68-0.89; P = 2.27 × 10-4 ), whereas carriage of PNPLA3 rs738409:G was associated with an increased risk for developing cirrhosis (OR, 1.70; 95% CI, 1.54-1.88; P = 1.52 × 10-26 ) and HCC (OR, 1.77; 95% CI, 1.58-1.98; P = 2.31 × 10-23 ). These associations remained significant after adjusting for age, sex, body mass index, type 2 diabetes, and country. Carriage of HSD17B13 rs72613567:TA attenuated the risk for developing cirrhosis associated with PNPLA3 rs738409:G in both men and women, but the protective effect against the subsequent development of HCC was only observed in men (ORallelic , 0.75; 95% CI, 0.64-0.87; P = 1.72 × 10-4 ).

**CONCLUSIONS**: Carriage of variants in PNPLA3 and HSD17B13 differentially affect the risk for developing advanced alcohol-related liver disease. A genotypic/phenotypic risk score might facilitate earlier diagnosis of HCC in this population.

**Mots-clefs**

# Publisher Correction: Microbial Network Disturbances in Relapsing Refractory Crohn's Disease

Yilmaz B, Juillerat P, Øyås O, Ramon C, Bravo FD, Franc Y, Fournier N, Michetti P, Mueller C, Geuking M, Pittet V, Maillard M, Rogler G, Swiss IBD Cohort Investigators; Wiest R, Stelling J, Macpherson A. **(Marot A.)**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Nat Med. 2019 Apr;25(4):701* | *10.1038/s41591-019-0411-9* | *30,641* |



**Abstract**

Owing to an error during typesetting, a number of references were deleted from the Methods reference list. This altered all of the references in the Methods section and some of the references in Extended Data Fig. 5, making them inaccurate. References 121-134 were added back into the Methods reference list, and the references in the Methods section and in Extended Data Fig. 5 were renumbered accordingly. The error has been corrected in the PDF and HTML versions of this article.

**Erratum for**

Microbial network disturbances in relapsing refractory Crohn's disease.
Yilmaz B, Juillerat P, Øyås O, Ramon C, Bravo FD, Franc Y, Fournier N, Michetti P, Mueller C, Geuking M, Pittet VEH, Maillard MH, Rogler G; Swiss IBD Cohort Investigators, Wiest R, Stelling J, Macpherson AJ.Nat Med. 2019 Feb;25(2):323-336. doi: 10.1038/s41591-018-0308-z. Epub 2019 Jan 21.PMID: 30664783

**Mots-clefs**

# Microbial Network Disturbances in Relapsing Refractory Crohn's Disease

Yilmaz B, Juillerat P, Øyås O, Ramon C, Bravo FD, Franc Y, Fournier N, Michetti P, Mueller C, Geuking M, Pittet V, Maillard M, Rogler G, Swiss IBD Cohort Investigators; Wiest R, Stelling J, Macpherson A. **(Marot A.)**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Nat Med. 2019 Feb;25(2):323-336* | *10.1038/s41591-018-0308-z* | *30,641* |



**Abstract**

Inflammatory bowel diseases (IBD) can be broadly divided into Crohn's disease (CD) and ulcerative colitis (UC) from their clinical phenotypes. Over 150 host susceptibility genes have been described, although most overlap between CD, UC and their subtypes, and they do not adequately account for the overall incidence or the highly variable severity of disease. Replicating key findings between two long-term IBD cohorts, we have defined distinct networks of taxa associations within intestinal biopsies of CD and UC patients. Disturbances in an association network containing taxa of the Lachnospiraceae and Ruminococcaceae families, typically producing short chain fatty acids, characterize frequently relapsing disease and poor responses to treatment with anti-TNF-α therapeutic antibodies. Alterations of taxa within this network also characterize risk of later disease recurrence of patients in remission after the active inflamed segment of CD has been surgically removed.

**Erratum for**

Publisher Correction: Microbial network disturbances in relapsing refractory Crohn's disease.
Yilmaz B, Juillerat P, Øyås O, Ramon C, Bravo FD, Franc Y, Fournier N, Michetti P, Mueller C, Geuking M, Pittet VEH, Maillard MH, Rogler G; Swiss IBD Cohort Investigators, Wiest R, Stelling J, Macpherson AJ.Nat Med. 2019 Apr;25(4):701. doi: 10.1038/s41591-019-0411-9. PMID: 30846883

**Mots-clefs**

# The Impact of the rs8005161 Polymorphism on G Protein-Coupled Receptor GPR65 (TDAG8) pH-associated Activation in Intestinal Inflammation

Tcymbarevich I, Eloranta JJ, Rossel JB, Obialo N, Spalinger M, Cosin-Roger J, Lang S, Kullak-Ublick G, Wagner C, Scharl M, Seuwen K, Ruiz P, Rogler G, de Vallière C, Misselwitz B, Swiss IBD Cohort Study Group **(Marot A.)**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *BMC Gastroenterol. 2019 Jan 7;19(1):2* | *10.1186/s12876-018-0922-8* | *2,346* |



## Abstract

**BACKGROUND:** Tissue inflammation in inflammatory bowel diseases (IBD) is associated with a decrease in local pH. The gene encoding G-protein-coupled receptor 65 (GPR65) has recently been reported to be a genetic risk factor for IBD. In response to extracellular acidification, proton activation of GPR65 stimulates cAMP and Rho signalling pathways. We aimed to analyse the clinical and functional relevance of the GPR65 associated single nucleotide polymorphism (SNP) rs8005161.

**METHODS:** 1138 individuals from a mixed cohort of IBD patients and healthy volunteers were genotyped for SNPs associated with GPR65 (rs8005161, rs3742704) and galactosylceramidase (rs1805078) by Taqman SNP assays. 2300 patients from the Swiss IBD Cohort Study (SIBDC) were genotyped for rs8005161 by mass spectrometry based SNP genotyping. IBD patients from the SIBDC carrying rs8005161 TT, CT, CC and non-IBD controls (CC) were recruited for functional studies. Human CD14+ cells were isolated from blood samples and subjected to an extracellular acidic pH shift, cAMP accumulation and RhoA activation were measured.

**RESULTS:** In our mixed cohort, but not in SIBDC patients, the minor variant rs8005161 was significantly associated with UC. In SIBDC patients, we observed a consistent trend in increased disease severity in patients carrying the rs8005161-TT and rs8005161-CT alleles. No significant differences were observed in the pH associated activation of cAMP production between IBD (TT, CT, WT/CC) and non-IBD (WT/CC) genotype carriers upon an acidic extracellular pH shift. However, we observed significantly impaired RhoA activation after an extracellular acidic pH shift in IBD patients, irrespective of the rs8005161 allele.

**CONCLUSIONS:** The T allele of rs8005161 might confer a more severe disease course in IBD patients. Human monocytes from IBD patients showed impaired pH associated RhoA activation upon an acidic pH shift.

## Mots-clefs

Acidic pH; CD; IBD; Inflammatory bowel diseases; RhoA; UC; cAMP; pH-sensing.

# RECUEIL DES PUBLICATIONS DU CHU UCL NAMUR

N°7 - PREMIER QUADRIMESTRE 2020

# JANVIER

# A Validated UHPLC-MS/MS Method for Simultaneous Quantification of 9 Exocyclic DNA Adducts Induced by 8 Aldehydes

Alamil H, Lechevrel M, Lagadu S, **Galanti L**, Dagher Z, Delépée R.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Pharm Biomed Anal. 2020 Feb 5;179:113007* | *10.1016/j.jpba.2019.113007* | *2,983* |



**Abstract**

Human exposure to aldehydes is implicated in several diseases including cancer. These strong electrophilic compounds can react with nucleophilic sites in DNA to form reversible and irreversible modifications. These modifications, if not repaired, can contribute to pathogenesis. The aim of our study was to provide a mass spectrometry (MS)-based profiling method for identifying potential biomarkers of aldehydes exposure. We have developed and validated a highly sensitive method using ultra high performance liquid chromatography-electrospray ionization-tandem mass spectrometry (UHPLC-ESI-MS/MS) for the simultaneous quantitation of 9 exocyclic DNA adducts derived from 8 main exogenous and endogenous aldehydes, namely formaldehyde, acetaldehyde, acrolein, crotonaldehyde, malondialdehyde, 4-hydroxy-2-nonenal, glyoxal and methylglyoxal. Finally, we applied the established method to quantify adducts in genomic DNA isolated from the blood of a smoker and a non-smoker blood samples in order to demonstrate its applicability.

**Mots-clefs**

Adductomic; Aldehydes; Analytical method validation; Cancer; Exposure biomarkers; Oxidative stress; Ultrahigh performance liquid chromatography -electrospray ionization- tandem mass spectrometry

# Pregnancy Outcomes in Inflammatory Bowel Disease Patients Treated With Vedolizumab, anti-TNF or Conventional Therapy: Results of the European CONCEIVE Study

Moens A, van der Woude CJ, Julsgaard M, Humblet E, Sheridan J, Baumgart DC, De Saint-Joseph CG, Nancey S, **Rahier JF,** Bossuyt P, Cremer A, Dewit S, Eriksson C, Hoentjen F, Krause T, Louis E, Macken E, Milenkovic Z, Nijs J, Posen A, Van Hootegem A, Van Moerkercke W, Vermeire S, Bar-Gil Shitrit A, Ferrante M.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Aliment Pharmacol Ther. 2020 Jan;51(1):129-138* | *10.1111/apt.15539* | |



## Abstract

**BACKGROUND:** Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission. Data on outcome of vedolizumab-exposed pregnancies (VDZE) are sparse.
**AIMS:** To assess pregnancy and child outcomes of VDZE pregnancies and to compare these results to anti-TNF exposed (TNFE) or both immunomodulatory and biologic unexposed (CON IBD) pregnancies.
**METHODS:** A retrospective multicentre case-control observational study was performed.
**RESULTS:** VDZE group included 79 pregnancies in 73 IBD women. The TNFE and CON IBD group included 186 pregnancies (162 live births) in 164 IBD women and 184 pregnancies (163 live births) in 155 IBD women, respectively. At conception, cases more often had active disease ([VDZE: 36% vs TNFE: 17%, P = .002] and [VDZE: 36% vs CON IBD: 24%, P = .063]). No significant difference in miscarriage rates were found between groups (VDZE and TNFE: 16% vs 13%, P = .567; VDZE and CON IBD: 16% vs 10%, P = .216). In live-born infants, median gestational age and birthweight were similar between groups. Median Apgar score at birth was numerically equal. Prematurity was similar in the VDZE group compared to the control groups, even when correcting for disease activity during pregnancy. The frequency of congenital anomalies was comparable between groups as were the percentages of breastfed babies. During the first year of life, no malignancies were reported and infants' infection risk did not significantly differ between groups.
**CONCLUSION:** No new safety signal was detected in VDZE pregnancies although larger, prospective studies are required for confirmation.

## Mots-clefs

3

# Diagnosis and Management of Congenital Thrombophilia in the Era of Direct Oral Anticoagulants

Alameddine R, Nassabein R, Le Gal G, Sié P, **Mullier F**, Blais N.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Thromb Res 2020;185:72-77* | *10.1016/j.thromres.2019.11.008* | *3,266* |



**Abstract**

Direct oral anticoagulants (DOAC)s are often preferred to other anticoagulants as they are more practical and do not require routine laboratory monitoring. Less is known about their use in congenital thrombophilia. Efficacy of DOACs in congenital thrombophilia, effect of DOACs and other anticoagulants on diagnostic tests as well as efficacy and safety of anticoagulant use in this population is still a matter of debate. In this review we intended to analyze the potential pitfalls of testing for thrombophilia in patients using DOACs and vitamin K antagonists (VKA)s as well as to suggest strategies to improve diagnostic accuracy in this setting. We also reviewed the literature for evidence regarding the safety and efficacy of DOACs in patients with congenital thrombophilia. Some evidence was found supporting the use of DOACs in low risk thrombophilia, although evidence for their use in high risk thrombophilia is limited to small series and case reports. Our findings support the generation of better evidence to support DOAC use for congenital thrombophilia, especially in the high risk subgroups.

**Mots-clefs**

Congenital thrombophilia; DOAC; Thrombophilia testing; Thrombosis; Vitamin K antagonists.

# Therapeutic vascularization in regenerative medicine: Concise Review

Gianni-Barrera R, Di Maggio N, Melly L, Burger MG, Mujagic E, Gürke L, Schaefer DJ, Banfi A.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Stem Cells Transl Med. 2020 Jan 10 [Epub ahead of print]* | *10.1002/sctm.19-0319* | *5,980* |



**Abstract**

Therapeutic angiogenesis, that is, the generation of new vessels by delivery of specific factors, is required both for rapid vascularization of tissue-engineered constructs and to treat ischemic conditions. Vascular endothelial growth factor (VEGF) is the master regulator of angiogenesis. However, uncontrolled expression can lead to aberrant vascular growth and vascular tumors (angiomas). Major challenges to fully exploit VEGF potency for therapy include the need to precisely control in vivo distribution of growth factor dose and duration of expression. In fact, the therapeutic window of VEGF delivery depends on its amount in the microenvironment around each producing cell rather than on the total dose, since VEGF remains tightly bound to extracellular matrix (ECM). On the other hand, short-term expression of less than about 4 weeks leads to unstable vessels, which promptly regress following cessation of the angiogenic stimulus. Here, we will briefly overview some key aspects of the biology of VEGF and angiogenesis and discuss their therapeutic implications with a particular focus on approaches using gene therapy, genetically modified progenitors, and ECM engineering with recombinant factors. Lastly, we will present recent insights into the mechanisms that regulate vessel stabilization and the switch between normal and aberrant vascular growth after VEGF delivery, to identify novel molecular targets that may improve both safety and efficacy of therapeutic angiogenesis.

**Mots-clefs**

extracellular matrix; genetic therapy; ischemia; neovascularization; tissue engineering; vascular endothelial growth factor

# Overall survival with daratumumab, bortezomib, melphalan, and prednisone in newly diagnosed multiple myeloma (ALCYONE): a randomised, open-label, phase 3 trial

Mateos MV, Cavo M, Blade J, Dimopoulos MA, Suzuki K, Jakubowiak A, Knop S, **Doyen C**, Lucio P, Nagy Z, Pour L, Cook M, Grosicki S, Crepaldi A, Liberati AM, Campbell P, Shelekhova T, Yoon SS, Iosava G, Fujisaki T, Garg M, Krevvata M, Chen Y, Wang J, Kudva A, Ukropec J, Wroblewski S, Qi M, Kobos R, San-Miguel J.

| *Références* | *Doi* | *IF* |
|---|---|---|
| *Lancet. 2020 Jan 11;395(10218):132-141* | *10.1016/S0140-6736(19)32956-3* | *59,102* |

**Abstract**

**BACKGROUND:** Standard-of-care treatment for patients with newly diagnosed multiple myeloma includes combination therapies for patients who are not eligible for autologous stem-cell transplantation. At the primary analysis for progression-free survival of the phase 3 ALCYONE trial, progression-free survival was significantly longer with daratumumab in combination with bortezomib, melphalan, and prednisone (D-VMP) versus bortezomib, melphalan, and prednisone (VMP) alone in patients with transplant-ineligible, newly diagnosed multiple myeloma. Here we report updated efficacy and safety results from a prespecified, interim, overall survival analysis of ALCYONE with more than 36 months of follow-up.

**METHODS:** ALCYONE was a multicentre, randomised, open-label, active-controlled, phase 3 trial that enrolled patients between Feb 9, 2015, and July 14, 2016, at 162 sites in 25 countries across North America, South America, Europe, and the Asia-Pacific region. Patients were eligible for inclusion if they had newly diagnosed multiple myeloma and were ineligible for high-dose chemotherapy with autologous stem-cell transplantation, because of their age (≥65 years) or because of substantial comorbidities. Patients were randomly assigned in a 1:1 ratio and by permuted block randomisation to receive D-VMP or VMP. An interactive web-based randomisation system was used. Randomisation was stratified by International Staging System disease stage, geographical region, and age. There was no masking to treatment assignments. All patients received up to nine 6-week cycles of subcutaneous bortezomib (1·3 mg/m2 of body surface area on days 1, 4, 8, 11, 22, 25, 29, and 32 of cycle one and on days 1, 8, 22, and 29 of cycles two through nine), oral melphalan (9 mg/m2 once daily on days 1 through 4 of each cycle), and oral prednisone (60 mg/m2 once daily on days 1 through 4 of each cycle). Patients in the D-VMP group also received intravenous daratumumab (16 mg/kg of bodyweight, once weekly during cycle one, once every 3 weeks in cycles two through nine, and once every 4 weeks thereafter as maintenance therapy until disease progression or unacceptable toxicity). The primary endpoint was progression-free survival, which has been reported previously. Results presented are from a prespecified interim analysis for overall survival. The primary analysis population (including for overall survival) was the intention-to-treat population of all patients who were randomly assigned to treatment. The safety population included patients who received any dose of study treatment. This trial is registered with ClinicalTrials.gov, NCT02195479.

**FINDINGS:**706 patients were randomly assigned to treatment groups (350 to the D-VMP group, 356 to the VMP group). At a median follow-up of 40·1 months (IQR 37·4-43·1), a significant benefit in overall survival was observed for the D-VMP group. The hazard ratio (HR) for death in the D-VMP group compared with the VMP group was 0·60 (95% CI 0·46-0·80; p=0·0003). The Kaplan-Meier estimate of the 36-month rate of overall survival was 78·0% (95% CI 73·2-82·0) in the D-VMP group and 67·9% (62·6-72·6) in the VMP group. Progression-free survival, the primary endpoint, remained significantly improved for the D-VMP group (HR 0·42 [0·34-0·51]; p<0·0001). The most frequent adverse events during maintenance daratumumab monotherapy in patients in the D-VMP group were respiratory infections (54 [19%] of 278 patients had upper respiratory tract infections; 42 [15%] had bronchitis, 34 [12%] had viral upper respiratory tract infections), cough (34 [12%]), and diarrhoea (28 [10%]).

**INTERPRETATION:** D-VMP prolonged overall survival in patients with newly diagnosed multiple myeloma who were ineligible for stem-cell transplantation. With more than 3 years of follow-up, the D-VMP group continued to show significant improvement in progression-free survival, with no new safety concerns.

**FUNDING:** Janssen Research & Development.

**Mots-clefs**

# Cost-Effectiveness Analysis of Nintedanib Versus Pirfenidone in Idiopathic Pulmonary Fibrosis in Belgium

Rinciog C, Diamantopoulos A, Gentilini A, Bondue B, **Dahlqvist C,** Froidure A, Wuyts WA, Soulard S.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Pharmacoecon Open. 2020 Jan 14 [Epub ahead of print]* | *10.1007/s41669-019-00191-w* | *3,630* |




## Abstract

**BACKGROUND**: Nintedanib (Ofev®) and pirfenidone (Esbriet®) are recommended by international guidelines as treatment options for idiopathic pulmonary fibrosis (IPF).
**OBJECTIVES**: To compare the cost-effectiveness of nintedanib with that of pirfenidone for the treatment of IPF from a Belgian healthcare payer perspective.
**METHODS**: The economic analysis used a Markov model that calculated outcomes over patient lifetime. Overall survival was assumed to be the same for the two comparators. Data from a network meta-analysis were used for loss of lung function, acute exacerbation events, safety and treatment discontinuation (for any reason). The health-state utility estimates in the model were calculated from EQ-5D scores collected in nintedanib studies. The assumed resource use for background care was also based on patient-level data that were categorised to fit the health states in the model and synthesised with costs and tariffs from Belgian national databases.
**RESULTS**: Treatment with nintedanib resulted in an estimated total cost of €102,315, which was less than the total cost of treatment with pirfenidone (€113,313). Given the similarities in the survival and progression outcomes obtained with nintedanib and pirfenidone, the model predicted near equivalence in total QALYs (3.353 QALYs for the nintedanib arm and 3.318 for the pirfenidone arm). Results were largely driven by model assumptions underlying mortality, acute exacerbations and treatment discontinuation.
**CONCLUSIONS**: After performing a synthesis of the most recently published evidence for IPF patients and assuming a Belgian healthcare payer perspective, we found nintedanib to be more cost-saving than pirfenidone.



## Mots-clefs

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

# Do computerized clinical decision support systems improve the prescribing of oral anticoagulants? A systematic review

**Sennesael AL, Krug B, Sneyers B, Spinewine A.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Thromb Res. 2020 Mar;187:79-87* | *10.1016/j.thromres.2019.12.023* | *3,266* |



## Abstract

**BACKGROUND:** Serious adverse drug reactions have been associated with the underuse or the misuse of oral anticoagulant therapy. We systematically reviewed the impact of computerized clinical decision support systems (CDSS) on the prescribing of oral anticoagulants and we described CDSS features associated with success or failure.

**METHODS:** We searched Medline, Embase, CENTRAL, CINHAL, and PsycINFO for studies that compared CDSS for the initiation or monitoring of oral anticoagulants with routine care. Two reviewers performed study selection, data collection, and risk-of-bias assessment. Disagreements were resolved with a third reviewer. Potentially important CDSS features, identified from previous literature, were evaluated.

**RESULTS:** Sixteen studies were included in our qualitative synthesis. Most trials were performed in primary care (n = 7) or hospitals (n = 6) and included atrial fibrillation (AF) patients (n = 9). Recommendations mainly focused on anticoagulation underuse (n = 11) and warfarin-drug interactions (n = 5). Most CDSS were integrated in electronic records or prescribing and provided support automatically at the time and location of decision-making. Significant improvements in practitioner performance were found in 9 out of 16 studies, while clinical outcomes were poorly reported. CDSS features seemed slightly more common in studies that demonstrated improvement.

**CONCLUSIONS:** CDSS might positively impact the use of oral anticoagulants in AF patients at high risk of stroke. The scope of CDSS should now evolve to assist prescribers in selecting the most appropriate and tailored medication. Efforts should nevertheless be made to improve the relevance of notifications and to address implementation outcomes.



## Mots-clefs

Clinical decision support systems; Drug prescribing; Oral anticoagulants; Quality improvement

# Biotin interferences: Have we neglected the impact on serological markers?

Bayart JL, Favresse J, Stoefs A, **Closset M**, Roy T, Fillée C, Rodriguez-Villalobos H, Kabamba-Mukadi B, Gruson D.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Chim Acta. 2020 Apr;503:107-112* | *10.1016/j.cca.2020.01.012* | *2,735* |




## Abstract

**BACKGROUND:** Biotin has been reported to be a leading cause of interference on several immunoassay platforms using the streptavidin-biotin immobilization system. While biotin interferences have now been well characterized for several assays, only few data are available on their impact on serological markers of infectious viral diseases.

**METHODS:** Overall, 10 healthy volunteers (HVs) received a single 100 mg dose of biotin to evaluate its effect on hepatitis B serological markers. Blood samples were taken several times before and after biotin intake. In addition, spiking experiments were applied to investigate biotin's impact on anti-HIV/p24 Ag and anti-HCV antibody levels. Several procedures designed to overcome this interference were evaluated.

**RESULTS:** Biotin intake resulted in a false-negative anti-HBs immunological status (‹10 mIU/mL) in 40.0% of cases. According to our anti-HBc and anti-HBe results, biotin intake was associated with 90.0% and 80.0% of false positive results, respectively. At the theoretical biotin peak concentration following a 100 mg intake, 50.0% and 66.6% of anti-HIV and anti-HCV results were false negatives, respectively. All the procedures evaluated to overcome the interference were proven effective.

**CONCLUSION:** HBV, HCV, and HIV serological markers are likely to be highly sensitive to biotin. Our data confirm that the scope of biotin interference is broader than commonly described.



## Mots-clefs

AIDS; Biotin; Hepatitis; Interference; Serology; Virology

# Parallel Guidewire for Catheter Stabilization in Interventional Radiology: The Anchoring Wire Technique

Moslemi I, Derbel H, Chiaradia M, **Deprez F**, Vitellius M, Kobeiter H, Tacher V.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Belg Soc Radiol. 2020 Jan 15;104(1):2* | *10.5334/jbsr.1890* | *0,150* |



**Abstract**

This technical note describes the parallel guidewire method: the anchoring technique as a strategy to ease difficult catheterization in various endovascular interventions. Sixteen patients were included in 2017 in whom this technique was used. The type of intervention, the nature of the target and anchored vessels and possible complications on the anchored vessel were reported. This study included thirteen various embolization cases and four visceral vessels angioplasties cases. The success of catheterization by using this technique was achieved in all cases, without complication on the anchored vessels.

**Mots-clefs**

Catheters; Chemoembolization; Education; Embolization; Interventional-Vascular

# Serotonin Syndrome Mimicking Intrathecal Baclofen Withdrawal In A Patient With Hereditary Spastic Paraparesis

Goffin N, **Nguyen V**, **Fostier M**, **Gustin T**, **Deltombe T**.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Rheabil Med Clin Comm, 2020 ;vol3* | *10.2340/20030711-1000026* | |



**Abstract**

Context: Serotonin syndrome is a drug-induced condition related to an increased level of serotonin in the brain, which may induce neuromuscular, autonomic and mental symptoms. Case report: A 40-year-old woman with hereditary spastic paraparesis (Strumpell-Lorrain disease) with an implanted intrathecal baclofen pump for severe spasticity. Two days after starting a medication known to inhibit serotonin re-uptake (paroxetine), she developed a sudden increase in lower limb spasticity with continuous spasms, fever, tachycardia and hypertension. Intrathecal baclofen withdrawal was excluded, confirming serotonin syndrome. Conclusion: Medications that inhibit serotonin reuptake may induce serotonin syndrome, resulting in increased spasticity in patients with spinal cord lesions, and should be prescribed with caution.

**Mots-clefs**

serotonin syndrome; hereditary spastic paraparesis; intrathecal baclofen; paroxetine

# Adult T-cell acute lymphoblastic leukemias with IL7R pathway mutations are slow-responders who do not benefit from allogeneic stem-cell transplantation

Kim R, Boissel N, Touzart A, Leguay T, Thonier F, Thomas X, Raffoux E, Huguet F, Villarese P, Fourrage C, Passini L, Hunault M, Lepretre S, Chevallier P, Braun T, Lhéritier V, Chantepie S, Maury S, Escoffre M, Tavernier E, Chalandon Y, **Graux C**, Macintyre E, Ifrah N, Asnafi V, Dombret H, Lhermitte L; on behalf the GRAALL group.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Leukemia. 2020 Jan 28 [Epub ahead of print]* | *10.1038/s41375-019-0685-4* | *9,944* |



**Abstract**

The prognostic value of IL7-receptor pathway (IL7Rp) mutations in T-cell acute lymphoblastic leukemia (T-ALL) remains unclear. We performed a comprehensive study of 200 adult patients with T-ALL included in the GRAALL2003/2005 protocols to address the clinical significance of IL7Rp mutations. Next-generation sequencing of the IL7Rp (IL7R/JAK1/JAK3/STAT5B) revealed that IL7Rp mutations were frequent in adult T-ALL (28%) particularly in immature/early T-cell progenitor (ETP)-ALL. They were associated with mutations of NOTCH-pathway, PHF6, and PRC2 components but not with K/NRAS. IL7Rp mutated (IL7Rpmut) T-ALL were slow-responders, with a high rate of M2/M3 day-8 marrow compared with IL7Rp non-mutated (IL7RpWT) T-ALL (p = 0.002) and minimal residual disease positivity at 6-weeks (MRD1) (p = 0.008) but no difference in MRD2 positivity at 12-weeks. Despite this, no adverse prognosis was evidenced when censored for allogeneic hematopoietic stem cell transplantation (HSCT). In time-dependent analysis, HSCT did not benefit IL7Rpmut patients whereas it was of marked benefit to IL7RpWT cases. IL7Rp-mutations identify a subgroup of slow-responder T-ALLs which benefit from post-induction chemotherapy regimens but not from HSCT. Our data suggest that prior knowledge of the mutation status of IL7Rp may influence HSCT decision and help to guide therapy reduction.

**Mots-clefs**

# Cross-cultural validation of the French version of the Lymphedema Functioning, Disability and Health Questionnaire for Upper Limb Lymphedema (Lymph-ICF-UL)

De Vrieze T, **Frippiat J, Deltombe T**, Gebruers N, Tjalma WAA, Nevelsteen I, Thomis S, Vandermeeren L, Belgrado JP, De Groef A, Devoogdt N.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Disabil Rehabil. 2020 Jan 28:1-8 [Epub ahead of print]* | *10.1080/09638288.2020.1716271* | *2,054* |




## Abstract

**PURPOSE:** Upper limb lymphedema is a vexing morbidity that can occur after the treatment for breast cancer. The Lymphedema Functioning, Disability and Health Questionnaire for Upper Limb Lymphedema (Lymph-ICF-UL) is a valid and reliable tool assessing problems in functioning in patients with breast cancer-related lymphedema. Until now, a French-language version was lacking. The aim of this study was to perform a cross-cultural validation of the French version of the Lymph-ICF-UL questionnaire.
**METHODS:** A forward-backward translation process between the original language (Dutch) and the target language (French) was performed. Psychometric properties of this final French version were examined in 50 participants.
**RESULTS:** Intraclass correlation coefficients for test-retest reliability ranged from 0.66 to 0.95. Cronbach's alpha coefficients for internal consistency were higher than 0.77. Face and content validity were very good because the scoring system was clear for all participants (100%), questions were understandable (100%), and all complaints due to BCRL were mentioned by 78% of the participants. Construct validity was moderate. Convergent validity was established since 3 out of 5 expected domains of the Lymph-ICF-UL showed a moderate correlation with expected domains of the 36-item Short-Form Health Survey. There was satisfactory divergent validity as 6 out of 9 hypotheses assessing divergent validity were accepted.
**CONCLUSION:** The French version of the Lymph-ICF-UL is a reliable and valid questionnaire and ready for use in clinical as well as in scientific practice.Implications for rehabilitationSince the introduction of more effective treatment modalities increasing the number of breast cancer survivors, the amount of patients dealing with lymphedema is rising likewise up to a pooled incidence rate of more than 16% of the women treated for breast cancer.The French version of the Lymph-ICF-UL is a reliable and valid questionnaire for assessing problems in functioning of patients with breast cancer-related lymphedema of the arm and/or hand.As the questionnaire provides patient information in the different domains of the International Classification of Functioning, Disability and Health, it facilitates evaluating the impact of breast cancer-related lymphedema on daily functioning.Based on the outcomes of the Lymph-ICF-UL treatment goals can be set, where after the questionnaire can be used to monitor long-term results of this treatment and self-care.



## Mots-clefs

Breast neoplasms; lymphedema; rehabilitation; reliability and validity; surveys and questionnaires

# Impact of donor lung quality on post-transplant recipient outcome in the Lung Allocation Score era in Eurotransplant - a historical prospective study

Smits JM, Gottlieb J, Verschuuren E, **Evrard P**, Hoek R, Knoop C, Lang G, Kwakkel-van Erp JM, Vos R, Verleden G, **Rondelet B**, Hoefer D, Langer F, Schramm R, Hoetzenecker K, Van Kessel D, Luijk B, Seghers L, Deuse T, Buhl R, Witt C, Strelniece A, Green D, de Vries E, Laufer G, Van Raemdonck D.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Transpl Int. 2020 Jan 26. [Epub ahead of print]* | *10.1111/tri.13582* | *3,526* |



**Abstract**

The aim of this study was to investigate whether there is an impact of donation rates on the quality of lungs used for transplantation and whether donor lung quality affects post-transplant outcome in the current Lung Allocation Score era. All consecutive adult LTx performed in Eurotransplant (ET) between January 2012 and December 2016 were included (N = 3053). Donors used for LTx in countries with high donation rate were younger (42% vs. 33% ≤45 years, P ‹ 0.0001), were less often smokers (35% vs. 46%, P ‹ 0.0001), had more often clear chest X-rays (82% vs. 72%, P ‹ 0.0001), had better donor oxygenation ratios (20% vs. 26% with PaO2 /FiO2 ≤ 300 mmHg, P ‹ 0.0001), and had better lung donor score values (LDS; 28% vs. 17% with LDS = 6, P ‹ 0.0001) compared with donors used for LTx in countries with low donation rate. Survival rates for the groups LDS = 6 and ≥7 at 5 years were 69.7% and 60.9% (P = 0.007). Lung donor quality significantly impacts on long-term patient survival. Countries with a low donation rate are more oriented to using donor lungs with a lesser quality compared to countries with a high donation rate. Instead of further stretching donor eligibility criteria, the full potential of the donor pool should be realized.

**Mots-clefs**

donation; donor; expanded donor pool; lung clinical; outcome

# Propositions du GIHP et du GFHT pour le diagnostic et la prise en charge d'une thrombopénie induite par l'héparine

Gruel Y, De Maistre E, Plouplard C, **Mullier F,** Susen S, Godier A, et al.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Soc Fr Anest Rea 2020 [Epub ahead of print]* | | |



**Abstract**

La Thrombopénie Induite par l'Héparine (TIH) est une pathologie rare, iatrogène, caractérisée par sa gravité potentielle, essentiellement liée aux thromboses, et par ses difficultés diagnostiques et thérapeutiques. En 2002, une conférence d'experts mobilisée par la SFAR avait rédigé des recommandations de prise en charge de la TIH (1). Depuis lors, les médicaments disponibles pour traiter les malades ont évolué, avec notamment la disparition de la lépirudine, la prescription croissante du fondaparinux et des anticoagulants oraux directs, et les tests biologiques nécessaires au diagnostic sont plus performants. Ces évolutions ont conduit le Groupe d'Intérêt en Hémostase Périopératoire (GIHP) et le Groupe Français d'Etudes sur l'Hémostase et la Thrombose (GFHT) en collaboration avec la Société Française d'Anesthésie-Réanimation (SFAR) à définir des propositions actualisées pour le diagnostic et la prise en charge des TIH.

**Mots-clefs**

# Transcranial electric stimulation optimizes the balance of visual attention across space

Andres M, Masson N, Larigaldie N, Bonato M, **Vandermeeren Y**, Dormal V.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Neurophysiol. 2020 Jan 31;131(4):912-920* | *10.1016/j.clinph.2019.12.415* | *3,614* |




## Abstract

**OBJECTIVE:** Transcranial direct current stimulation (tDCS) provides a way to modulate spatial attention by enhancing the ratio of neural activity between the left and right hemispheres, with a potential benefit for the rehabilitation of visual neglect.
**METHODS:** We tested the effect of bilateral tDCS in healthy individuals performing a visual detection task. This protocol consists in the positioning of the anode and cathode on mirror positions over the left and right parietal areas. The stimulation was repeated over three days to maximize the chance to observe a bias to the hemispace controlateral to the anode.
**RESULTS:** Compared to a sham treatment, left anodal - right cathodal stimulation enhanced attention across the full range of space, since the first day with no build-up effect on the next days, and modified the balance of left-right omissions when stimuli appeared at the same time.
**CONCLUSION:** Bilateral tDCS improved detection in both visual fields, with no privileged processing of one side, except when concurrent stimuli were presented. The results provide partial support to the hemispheric rivalry hypothesis.
**SIGNIFICANCE:** The technique has the potential to boost attention in neglect patients but should be used as an adjuvant rather than as an alternative to functional rehabilitation.



## Mots-clefs

Attention; Awareness; Hemineglect; Parietal; Stroke; tDCS

# The Impact of Work-Related Rhinitis on Quality of Life and Work Productivity: A General Workforce-Based Survey

**Vandenplas O,** Suarthana E, Rifflart C, Lemière C, Le Moual N, Bousquet J.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Allergy Clin Immunol Pract. 2020 Jan 28 [Epub ahead of print]* | *10.1016/j.jaip.2019.12.033* | *7,550* |




## Abstract

**BACKGROUND:** The specific burden of work-related rhinitis (WRR) on quality of life (QoL) and work productivity has received little attention.
**OBJECTIVE:** The aim of this study was to investigate to what extent WRR affects QoL and work productivity as compared with subjects with rhinitis unrelated to work and those without rhinitis.
**METHODS:** This cross-sectional survey was conducted among workers randomly recruited at the time of their periodic occupational health visit in the French-speaking part of Belgium. The survey instruments consisted of rhinitis-specific and generic questionnaires: Mini-Rhinitis QoL Questionnaire, Medical Outcome Study Short Form-8, and Work Productivity and Activity Impairment-General Health questionnaire. Eligible participants were categorized into 3 groups: non-WRR (current nasal symptoms not related to work, n = 329); WRR (current rhinitis with ≥2 nasal symptoms at work, n = 161); and controls (no nasal symptom; n = 1155).
**RESULTS:** WRR showed significantly lower scores in all domains of the Mini-Rhinitis QoL Questionnaire compared with non-WRR. Multivariate analysis confirmed that WRR exerted an independent adverse effect on rhinitis-specific QoL. Both WRR and non-WRR were associated with greater impairment in the physical and mental health components of the Medical Outcome Study Short Form-8 instrument and the overall work productivity compared with controls, whereas these outcomes were more impacted in WRR than non-WRR. Multivariate analyses demonstrated that both WRR and non-WRR had an independent adverse impact on the physical and mental health status and overall work productivity.
**CONCLUSION:** WRR has an incremental adverse impact on QoL and work productivity that should be addressed in order to reduce the global burden of rhinitis.



## Mots-clefs

Quality of life; Rhinitis; Work productivity; Work-related rhinitis

# European Position Paper on Rhinosinusitis and Nasal Polyps 2020

Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, Toppila-Salmi S, Bernal-Sprekelsen M, Mullol J, Alobid I, Terezinha Anselmo-Lima W, Bachert C, Baroody F, von Buchwald C, Cervin A, Cohen N, Constantinidis J, De Gabory L, Desrosiers M, Diamant Z, Douglas RG, Gevaert PH, Hafner A, Harvey RJ, Joos GF, Kalogjera L, Knill A, Kocks JH, Landis BN, Limpens J, Lebeer S, Lourenco O, Matricardi PM, Meco C, O Mahony L, Philpott CM, Ryan D, Schlosser R, Senior B, Smith TL, Teeling T, Tomazic PV, Wang DY, Wang D, Zhang L, Agius AM, Ahlstrom-Emanuelsson C, Alabri R, Albu S, Alhabash S, Aleksic A, Aloulah M, Al-Qudah M, Alsaleh S, Baban MA, Baudoin T, Balvers T, Battaglia T, Bedoya JD67, Beule A, Bofares KM, Braverman I, Brozek-Madry E, Richard B, Callejas C, Carrie S, Caulley L, Chussi D, de Corso E, Coste A, Lal D, El Hadi U, Elfarouk A, **Eloy PH**, Farrokhi S, Felisati G, Ferrari MD, Fishchuk R, Grayson W, Goncalves PM, Grdinic B, Grgic V, Hamizan AW, Heinichen JV, Husain S, Ping TI, Ivaska J, Jakimovska F, Jovancevic L, Kakande E, Kamel R, Karpischenko S, Kariyawasam HH, Kjeldsen A, Klimek L, Kim SW, Letort JJ, Lopatin A, Mahdjoubi A, Netkovski J, Nyenbue Tshipukane D, Obando-Valverde A, Okano M, Onerci M, Ong YK, Orlandi R, Ouennoughy K, Ozkan M, Peric A, Plzak J, Prokopakis E, Prepageran N, Psaltis A, Pugin B, Raftopulos M, Rombaux P, Sahtout S, Sarafoleanu CC, Searyoh K, Rhee CS, Shi J, Shkoukani M, Shukuryan AK, Sicak M, Smyth D, Snidvongs K, Soklic Kosak T, Stjarne P.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Rhinology. 2020 Feb 20;58(Suppl S29):1-464* | *10.4193/Rhin20.600* | *3,350* |



## Abstract

The European Position Paper on Rhinosinusitis and Nasal Polyps 2020 is the update of similar evidence based position papers published in 2005 and 2007 and 2012. The core objective of the EPOS2020 guideline is to provide revised, up-to-date and clear evidence-based recommendations and integrated care pathways in ARS and CRS. EPOS2020 provides an update on the literature published and studies undertaken in the eight years since the EPOS2012 position paper was published and addresses areas not extensively covered in EPOS2012 such as paediatric CRS and sinus surgery. EPOS2020 also involves new stakeholders, including pharmacists and patients, and addresses new target users who have become more involved in the management and treatment of rhinosinusitis since the publication of the last EPOS document, including pharmacists, nurses, specialised care givers and indeed patients themselves, who employ increasing self-management of their condition using over the counter treatments. The document provides suggestions for future research in this area and offers updated guidance for definitions and outcome measurements in research in different settings. EPOS2020 contains chapters on definitions and classification where we have defined a large number of terms and indicated preferred terms. A new classification of CRS into primary and secondary CRS and further division into localized and diffuse disease, based on anatomic distribution is proposed. There are extensive chapters on epidemiology and predisposing factors, inflammatory mechanisms, (differential) diagnosis of facial pain, allergic rhinitis, genetics, cystic fibrosis, aspirin exacerbated respiratory disease, immunodeficiencies, allergic fungal rhinosinusitis and the relationship between upper and lower airways. The chapters on paediatric acute and chronic rhinosinusitis are totally rewritten. All available evidence for the management of acute rhinosinusitis and chronic rhinosinusitis with or without nasal polyps in adults and children is systematically reviewed and integrated care pathways based on the evidence are proposed. Despite considerable increases in the amount of quality publications in recent years, a large number of practical clinical questions remain. It was agreed that the best way to address these was to conduct a Delphi exercise . The results have been integrated into the respective sections. Last but not least, advice for patients and pharmacists and a new list of research needs are included. The full document can be downloaded for free on the website of this journal: http://www.rhinologyjournal.com.

## Mots-clefs

# MDA5+ Dermatomyositis Is Associated with Stronger Skin Type I Interferon Transcriptomic Signature with Upregulation of IFN-κ Transcript

**Cassius C,** Amode R, Delord M, Battistella M, Poirot J, How-Kit A, Lepelletier C, Jachiet M, de Masson A, Frumholtz L, Cordoliani F, Boccara D, Lehmann-Che J, Wong J, Dubanchet S, Alberdi AJ, Merandet M, Bagot M, Bensussan A, Bouaziz JD, Le Buanec H.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Invest Dermatol. 2020 Jan 10 [Epub ahead of print]* | *10.1016/j.jid.2019.10.020* | *6,290* |



## Abstract

## Mots-clefs

# A survey of Belgian practice for non-malignant diseases

Van Houtte P, **Remouchamps V**, Lievens Y; Belgian College for Physicians in Radiation Oncology.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Cancer Radiother. 2020 Jan 21 [Epub ahead of print]* | *10.1016/j.canrad.2019.09.004* | *1,263* |



**Abstract**

Two prior surveys were carried out in 1995 and 1999 to evaluate the use of radiotherapy in the treatment of non-malignant disease. In 2016, the same questionnaire was used and sent to the 24 centers of the country: 22 responded. A major decrease was observed in the number of patients treated: 360 in 2016 in contrast to 954 in 1999 and 1113 in 1995. The most frequent indications remain the prevention of heterotopic bone formation, keloids or gynecomastia. A new indication was observed: trigeminal nevralgia treated with radiosurgery. Two frequent indications in the past disappeared: the prevention of coronary restenosis and the macular degeneration. A great agreement was observed regarding the possible indications for radiotherapy but also to avoid it for inflammatory pathologies.

**Mots-clefs**

Affections bénignes; Benign diseases; Enquête; Pattern of care; Radiotherapy; Radiothérapie

# Assessment of Mandibular Movement Monitoring With Machine Learning Analysis for the Diagnosis of Obstructive Sleep Apnea

Pépin JL, Letesson C, Le-Dong NN, Dedave A, Denison S, **Cuthbert V, Martinot JB,** Gozal D.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *JAMA Netw Open. 2020 Jan 3;3(1):e1919657* | *10.1001/jamanetworkopen.2019.1965* | |




## Abstract

**IMPORTANCE:** Given the high prevalence of obstructive sleep apnea (OSA), there is a need for simpler and automated diagnostic approaches.

OBJECTIVE: To evaluate whether mandibular movement (MM) monitoring during sleep coupled with an automated analysis by machine learning is appropriate for OSA diagnosis.

**DESIGN, SETTING, AND PARTICIPANTS:** Diagnostic study of adults undergoing overnight in-laboratory polysomnography (PSG) as the reference method compared with simultaneous MM monitoring at a sleep clinic in an academic institution (Sleep Laboratory, Centre Hospitalier Universitaire Université Catholique de Louvain Namur Site Sainte-Elisabeth, Namur, Belgium). Patients with suspected OSA were enrolled from July 5, 2017, to October 31, 2018.

**MAIN OUTCOMES AND MEASURES:** Obstructive sleep apnea diagnosis required either evoking signs or symptoms or related medical or psychiatric comorbidities coupled with a PSG-derived respiratory disturbance index (PSG-RDI) of at least 5 events/h. A PSG-RDI of at least 15 events/h satisfied the diagnosis criteria even in the absence of associated symptoms or comorbidities. Patients who did not meet these criteria were classified as not having OSA. Agreement analysis and diagnostic performance were assessed by Bland-Altman plot comparing PSG-RDI and the Sunrise system RDI (Sr-RDI) with diagnosis threshold optimization via receiver operating characteristic curves, allowing for evaluation of the device sensitivity and specificity in detecting OSA at 5 events/h and 15 events/h.

**RESULTS:** Among 376 consecutive adults with suspected OSA, the mean (SD) age was 49.7 (13.2) years, the mean (SD) body mass index was 31.0 (7.1), and 207 (55.1%) were men. Reliable agreement was found between PSG-RDI and Sr-RDI in patients without OSA (n = 46; mean difference, 1.31; 95% CI, -1.05 to 3.66 events/h) and in patients with OSA with a PSG-RDI of at least 5 events/h with symptoms (n = 107; mean difference, -0.69; 95% CI, -3.77 to 2.38 events/h). An Sr-RDI underestimation of -11.74 (95% CI, -20.83 to -2.67) events/h in patients with OSA with a PSG-RDI of at least 15 events/h was detected and corrected by optimization of the Sunrise system diagnostic threshold. The Sr-RDI showed diagnostic capability, with areas under the receiver operating characteristic curve of 0.95 (95% CI, 0.92-0.96) and 0.93 (95% CI, 0.90-0.93) for corresponding PSG-RDIs of 5 events/h and 15 events/h, respectively. At the 2 optimal cutoffs of 7.63 events/h and 12.65 events/h, Sr-RDI had accuracy of 0.92 (95% CI, 0.90-0.94) and 0.88 (95% CI, 0.86-0.90) as well as posttest probabilities of 0.99 (95% CI, 0.99-0.99) and 0.89 (95% CI, 0.88-0.91) at PSG-RDIs of at least 5 events/h and at least 15 events/h, respectively, corresponding to positive likelihood ratios of 14.86 (95% CI, 9.86-30.12) and 5.63 (95% CI, 4.92-7.27), respectively.

**CONCLUSIONS AND RELEVANCE:** Automatic analysis of MM patterns provided reliable performance in RDI calculation. The use of this index in OSA diagnosis appears to be promising.



## Mots-clefs

# Development and Validation of a Quantification Method of Cotinine in Urine Using Two Innovative Technologies: Supported Liquid Extraction and QDa Detection

**Colsoul ML, Goderniaux N,** Vanpee D, **Galanti L.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *JAMA Netw Open. 2020 Jan 3;3(1):e1919657* | *10.1001/jamanetworkopen.2019.1965* | |




## Abstract

**IMPORTANCE:** Given the high prevalence of obstructive sleep apnea (OSA), there is a need for simpler and automated diagnostic approaches.
OBJECTIVE: To evaluate whether mandibular movement (MM) monitoring during sleep coupled with an automated analysis by machine learning is appropriate for OSA diagnosis.
**DESIGN, SETTING, AND PARTICIPANTS:** Diagnostic study of adults undergoing overnight in-laboratory polysomnography (PSG) as the reference method compared with simultaneous MM monitoring at a sleep clinic in an academic institution (Sleep Laboratory, Centre Hospitalier Universitaire Université Catholique de Louvain Namur Site Sainte-Elisabeth, Namur, Belgium). Patients with suspected OSA were enrolled from July 5, 2017, to October 31, 2018.
**MAIN OUTCOMES AND MEASURES:** Obstructive sleep apnea diagnosis required either evoking signs or symptoms or related medical or psychiatric comorbidities coupled with a PSG-derived respiratory disturbance index (PSG-RDI) of at least 5 events/h. A PSG-RDI of at least 15 events/h satisfied the diagnosis criteria even in the absence of associated symptoms or comorbidities. Patients who did not meet these criteria were classified as not having OSA. Agreement analysis and diagnostic performance were assessed by Bland-Altman plot comparing PSG-RDI and the Sunrise system RDI (Sr-RDI) with diagnosis threshold optimization via receiver operating characteristic curves, allowing for evaluation of the device sensitivity and specificity in detecting OSA at 5 events/h and 15 events/h.
**RESULTS:** Among 376 consecutive adults with suspected OSA, the mean (SD) age was 49.7 (13.2) years, the mean (SD) body mass index was 31.0 (7.1), and 207 (55.1%) were men. Reliable agreement was found between PSG-RDI and Sr-RDI in patients without OSA (n = 46; mean difference, 1.31; 95% CI, -1.05 to 3.66 events/h) and in patients with OSA with a PSG-RDI of at least 5 events/h with symptoms (n = 107; mean difference, -0.69; 95% CI, -3.77 to 2.38 events/h). An Sr-RDI underestimation of -11.74 (95% CI, -20.83 to -2.67) events/h in patients with OSA with a PSG-RDI of at least 15 events/h was detected and corrected by optimization of the Sunrise system diagnostic threshold. The Sr-RDI showed diagnostic capability, with areas under the receiver operating characteristic curve of 0.95 (95% CI, 0.92-0.96) and 0.93 (95% CI, 0.90-0.93) for corresponding PSG-RDIs of 5 events/h and 15 events/h, respectively. At the 2 optimal cutoffs of 7.63 events/h and 12.65 events/h, Sr-RDI had accuracy of 0.92 (95% CI, 0.90-0.94) and 0.88 (95% CI, 0.86-0.90) as well as posttest probabilities of 0.99 (95% CI, 0.99-0.99) and 0.89 (95% CI, 0.88-0.91) at PSG-RDIs of at least 5 events/h and at least 15 events/h, respectively, corresponding to positive likelihood ratios of 14.86 (95% CI, 9.86-30.12) and 5.63 (95% CI, 4.92-7.27), respectively.
**CONCLUSIONS AND RELEVANCE:** Automatic analysis of MM patterns provided reliable performance in RDI calculation. The use of this index in OSA diagnosis appears to be promising.



## Mots-clefs

# FEVRIER

# Evolving concepts on the management of dyslipidaemia

Descamps OS, Verhaegen A, **Demeure F,** Langlois M, Rietzschel E, Mertens A, De Sutter J, Wallemacq C, Lancellotti P, De Backer G.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Clin Belg. 2020 Feb;75(1):80-90* | *10.1080/17843286.2019.1702823* | *0,960* |



**Abstract**

It has been well established that low-density lipoproteins (LDL) and other apolipoprotein B-containing lipoproteins are causally related to atherosclerotic cardiovascular disease (ASCVD) and that lowering these lipoproteins reduces the risk of ASCVD. By lowering LDL particles as much as possible, ASCVD can be prevented. There seems to be no LDL-cholesterol (LDL-C) threshold below which no further ASCVD prevention can be achieved. Furthermore, a low (an even very low) LDL-C appears to be safe. The new ESC/EAS guidelines based on these concepts are a step towards a benefit-based strategy by focusing on the clinical benefit that can be achieved by treating the cause of ASCVD. It is recommended to lower LDL-C as much as possible to prevent ASCVD, especially in high and very high-risk patients. With these new recommendations come recognition of the importance of combination therapies in high and very high-risk patients, first with statins and ezetimibe, and if needed with a PCSK9 inhibitor. The present paper is a review of some new concepts arising during the past 10 years in the field of lipidology and the description of what is new in the 2019 EAS/ESC guidelines.

**Mots-clefs**

Cardiovascular prevention; atherosclerosis; cholesterol; coronary heart disease; genetic

# Pseudoaneurysm of the Superficial Temporal Artery After Blunt Trauma

**Balligand A, Mulquin N.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Mayo Clin Proc. 2020 Feb;95(2):226-227* | *10.1016/j.mayocp.2019.11.009* | *7,199* |



## Abstract

## Mots-clefs

# Intra-spinal iliac venous stent migration with lumbar nerve roots compression: a case report.

**Di Santo M, Belhaj A, Rondelet B, Gustin T.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *World Neurosurg. 2020 Feb 11 [Epub ahead of print]* | *10.1016/j.wneu.2020.02.028* | *1,723* |




## Abstract

**BACKGROUND:** Venous stenting is a common treatment for chronic peripheral venous disease. The most frequent complications caused by this technique are stent misplacement and intra-cardiac or intra-vascular stent migration. In this publication, we will describe the first case of an intra-spinal stent misplacement, leading to lumbar nerve root compression.

**CASE DESCRIPTION:** Our patient is a 20-year-old woman with a bilateral pulmonary embolism caused by a right common iliac vein thrombosis and a severe compression of the left common iliac vein by the right common iliac artery (May-Thurner or Cockett syndrome). She underwent an endovascular stenting of the left iliac vein. A few days later, she reported some pain in the right L5 radicular, showed signs of hypoesthesia of the left leg and of paresis of the left extensor hallucis longus muscle. A lumbar computed tomography scan showed a stent misplacement into the spinal canal through the left L5 foramen with nerve root compression. She underwent a surgical removal of the stent through a unilateral L5-S1 laminarthrectomy. The postoperative follow-up showed a complete clinical recovery and a control lumbar CT-scan confirmed the L5 nerve roots decompression.

**CONCLUSION:** The intra-spinal misplacement of a venous stent is a rare complication which may cause nerve root injury. It requires a prompt treatment. Surgically removing the stent by a posterior approach seems to be a simple and safe therapeutic option.



## Mots-clefs

Ectopic intra-spinal stent; endovascular stent; stent migration

# Kyste épidermoïde du testicule

**Tirraf I, Falticeanu A, Mulquin N.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Im Diag et Inter 2020;3(1):32-33* | *10.1016/j.jidi.2019.10.006* | |


## Abstract

**Mots-clefs**

# Real-Life Study of Mepolizumab in Idiopathic Chronic Eosinophilic Pneumonia

Brenard E, Pilette C, **Dahlqvist C**, Colinet B, Schleich F, Roufosse F, Froidure A.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Lung. 2020 Feb 12 [Epub ahead of print]* | *10.1007/s00408-020-00336-3* | *2,149* |




## Abstract

**INTRODUCTION:** Idiopathic chronic eosinophilic pneumonia (ICEP) is an orphan lung disease characterized by concomitant systemic and local eosinophilia, along with bilateral lung infiltrates. Symptoms include dyspnea of subacute/chronic onset, cough, and general systemic signs. Although all patients do respond to oral corticosteroids, relapse rate is very high, which highlights the need for alternative therapies in case of relapsing ICEP. Mepolizumab is a fully humanized antibody directed against interleukin 5, a key growth factor of eosinophils. In the present study, we retrospectively studied the effect of off-label use of mepolizumab for relapsing ICEP.

**MATERIALS AND METHODS:** All data from patients treated with mepolizumab for relapsing ICEP were included in our database and diagnoses were reviewed. We analyzed the effect of treatment on relapse rate, oral corticosteroids (OCS) use, and lung lesions on high-resolution computed tomography (HRCT).

**RESULTS:** We included ten patients in the final analysis, with a median follow-up of 9 months after initiation of mepolizumab. Beside its expected effect on circulating eosinophils, treatment with mepolizumab was associated with a significant reduction of annual rate of exacerbations and a reduced consumption of corticosteroids. We also observed a remission of lung lesions on follow-up HRCT.

**CONCLUSIONS:** In this open-label retrospective study, treatment of ICEP with mepolizumab was associated with a reduction of relapses, OCS use, and the disappearance of lung infiltrates.



## Mots-clefs

Idiopathic chronic eosinophilic pneumonia; Interstitial lung diseases; Mepolizumab

# Reduction of Preoperative Waiting Time before Urgent Surgery for Patients on P2Y12 Inhibitors Using Multiple Electrode Aggregometry: A Retrospective Study

**Hardy M, Dupuis C, Dincq AS, Jacqmin H,** Lecompte T, **Mullier F, Lessire S.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Clin Med. 2020 Feb 4;9(2)* | *10.3390/jcm9020424* | *5,688* |




## Abstract

P2Y12 inhibitor discontinuation is essential before most surgical interventions to limit bleeding complications. Based on pharmacokinetic data, fixed discontinuation durations have been recommended. However, as platelet function recovery is highly variable among patients, a more individualized approach based on platelet function testing (PFT) has been proposed. The aim of this retrospective single-centre study was to determine whether PFT using whole blood adenosine diphosphate-multiple electrode aggregometry (ADP-MEA) was associated with a safe reduction of preoperative waiting time. Preoperative ADP-MEA was performed for 29 patients on P2Y12 inhibitors. Among those, 17 patients underwent a coronary artery bypass graft. Twenty one were operated with an ADP-MEA ≥ 19 U (quantification of the area under the aggregation curve), and the waiting time was shorter by 1.6 days (median 1.8 days, IQR 0.5-2.9), by comparison with the current recommendations (five days for clopidogrel and ticagrelor, seven days for prasugrel). Platelet function recovery was indeed highly variable among individuals. With the 19 U threshold, high residual platelet inhibition was associated with perioperative platelet transfusion. These results suggest that preoperative PFT with ADP-MEA could help reduce waiting time before urgent surgery for patients on P2Y12 inhibitors



## Mots-clefs

P2Y12 inhibitors; clopidogrel; multiplate; multiple electrode aggregometry; perioperative; prasugrel; preoperative; ticagrelor; urgent surgery

# European Position Paper on Rhinosinusitis and Nasal Polyps 2020

Fokkens WJ, **Eloy P,** et al.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Rhinology. 2020 Feb 20;58(Suppl S29):1-464* | *10.4193/Rhin20.600* | *3,350* |




## Abstract

The European Position Paper on Rhinosinusitis and Nasal Polyps 2020 is the update of similar evidence based position papers published in 2005 and 2007 and 2012. The core objective of the EPOS2020 guideline is to provide revised, up-to-date and clear evidence-based recommendations and integrated care pathways in ARS and CRS. EPOS2020 provides an update on the literature published and studies undertaken in the eight years since the EPOS2012 position paper was published and addresses areas not extensively covered in EPOS2012 such as paediatric CRS and sinus surgery. EPOS2020 also involves new stakeholders, including pharmacists and patients, and addresses new target users who have become more involved in the management and treatment of rhinosinusitis since the publication of the last EPOS document, including pharmacists, nurses, specialised care givers and indeed patients themselves, who employ increasing self-management of their condition using over the counter treatments. The document provides suggestions for future research in this area and offers updated guidance for definitions and outcome measurements in research in different settings. EPOS2020 contains chapters on definitions and classification where we have defined a large number of terms and indicated preferred terms. A new classification of CRS into primary and secondary CRS and further division into localized and diffuse disease, based on anatomic distribution is proposed. There are extensive chapters on epidemiology and predisposing factors, inflammatory mechanisms, (differential) diagnosis of facial pain, allergic rhinitis, genetics, cystic fibrosis, aspirin exacerbated respiratory disease, immunodeficiencies, allergic fungal rhinosinusitis and the relationship between upper and lower airways. The chapters on paediatric acute and chronic rhinosinusitis are totally rewritten. All available evidence for the management of acute rhinosinusitis and chronic rhinosinusitis with or without nasal polyps in adults and children is systematically reviewed and integrated care pathways based on the evidence are proposed. Despite considerable increases in the amount of quality publications in recent years, a large number of practical clinical questions remain. It was agreed that the best way to address these was to conduct a Delphi exercise . The results have been integrated into the respective sections. Last but not least, advice for patients and pharmacists and a new list of research needs are included. The full document can be downloaded for free on the website of this journal: http://www.rhinologyjournal.com


**Mots-clefs**

# Predicting, Preventing, and Managing Treatment-related Complications in Patients With Inflammatory Bowel Diseases

Beaugerie L, **Rahier JF,** Kirchgesner J.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Gastroenterol Hepatol. 2020 Feb 11 [Epub ahead of print]* | *10.1016/j.cgh.2020.02.009* | *7,958* |




## Abstract

Risk of complications from specific classes of drugs for inflammatory bowel diseases (IBD) can be kept low by respecting contra-indications. Patients with IBD frequently develop serious infections, due to the disease itself or its treatment. At the time of diagnosis, patients' vaccination calendars should be updated according to IBD guidelines-live vaccines should be postponed for patients receiving immunosuppressive drugs. Opportunistic infections should be detected and the vaccine against Pneumococcus should be given before patients begin immunosuppressive therapy. Thiopurines promote serious viral infections, in particular, whereas tumor necrosis factor (TNF) antagonists promote all types of serious and opportunistic infections. Severe forms of varicella can be prevented by vaccinating seronegative patients against varicella zoster virus. Detection and treatment of latent tuberculosis is mandatory before starting anti-TNF therapy and other new IBD drugs. Tofacitinib promotes herpes zoster infection in a dose- and age-dependent manner. Physicians should consider giving patients live vaccines against herpes zoster before they begin immunosuppressive therapy or a recombinant vaccine, when available, at any time point during treatment. Risk of thiopurine-induced lymphomas can be lowered by limiting the use of thiopurines in patients who are seronegative for Epstein-Barr virus (especially young men) and in older men. The risk of lymphoma related to monotherapy with anti-TNF agents is still unclear. There are no robust data on carcinogenic effects of recently developed IBD drugs. For patients with previous cancer at substantial risk of recurrence, physicians should try to implement a pause in the use of immunosuppressive therapy (except in patients with severe disease and no therapeutic alternative) and prioritize use of IBD drugs with lowest carcinogenic effects. Finally, sun protection and skin surveillance from the time of diagnosis are recommended.



## Mots-clefs

Crohn’s disease; infliximab; side effect; ulcerative colitis

# Bleeding Complications After Transoral Robotic Surgery: A Meta-Analysis and Systematic Review

Stokes W, Ramadan J, **Lawson G,** Ferris FRL, Holsinger FC, Turner MT.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Laryngoscope. 2020 Feb 28 [Epub ahead of print]* | *10.1002/lary.28580* | *2,343* |




## Abstract

**OBJECTIVE:** Postoperative hemorrhage is the most common complication of transoral robotic surgery (TORS), the severity of which can range from minor bleeding treated with observation to catastrophic hemorrhage leading to death. To date, little is known about the incidence, risk factors, and management of post-TORS hemorrhage.
STUDY DESIGN: Systematic Review and Metanlysis.
**METHODS:** A systematic review of the published literature using the Cochrane Handbook for Systematic Reviews of Interventions was performed and examined TORS, postoperative hemorrhage, and the use of prophylactic transcervical arterial ligation (TAL).
**RESULTS:** A total of 13 articles were included in the analysis. To date, there have been 332 cases of hemorrhage following a total of 5748 TORS. The pooled median post-TORS hemorrhage rate was 6.47%. The overall incidence of minor and major hemorrhage was 5.29% and 2.90%. Patients with prior radiation (relative risk [RR] = 1.46, 95% confidence interval [CI] = 1.00-2.12), large tumors (RR = 2.11, 95% CI = 1.48-2.99), and those requiring perioperative coagulation (RR = 2.25, 95% CI = 1.54-3.28) had significantly higher relative risks of hemorrhage. There was no significant difference in the relative risk of overall hemorrhage with TAL. Looking at major hemorrhage, patients undergoing TAL had a large but insignificant relative risk reduction in post-TORS hemorrhage (RR = 0.40, 95% CI = 0.15-1.07).
**CONCLUSION:** The incidence of post-TORS hemorrhage is low (5.78%), and for major hemorrhage requiring emergent embolization, TAL, or tracheotomy to control hemorrhage it is even lower (2.90%). Large tumors, perioperative anticoagulation, and prior radiation were associated with significantly increased risk of post-TORS hemorrhage. TAL does not reduce the overall incidence of post-TORS hemorrhage but may lead to fewer severe hemorrhages.



## Mots-clefs

Hemorrhage; TORS; bleeding; complications; transcervical arterial ligation; transoral robotic surgery

# Glioblastoma in a fingolimod-treated multiple sclerosis patient: Causal or coincidental association?

**London F, Cambron B,** Jacobs S, **Delrée P, Gustin T.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Mult Scler Relat Disord. 2020 Feb 15;41:102012 [Epub ahead of print]* | *10.1016/j.msard.2020.102012* | *2,725* |



## Abstract

## Mots-clefs

# Comparison of two multiplex immunochromatographic assays for the rapid detection of major carbapenemases in Enterobacterales

**Bogaerts P, Berger AS, Evrard S1, Huang TD.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Antimicrob Chemother. 2020 Feb 21 [Epub ahead of print]* | *10.1093/jac/dkaa043* | *5,113* |




## Abstract

**OBJECTIVES:** Two commercially available lateral flow immunochromatographic assays (ICAs) for detection of the major carbapenemases were prospectively assessed for the detection of carbapenemases in Enterobacterales: RESIST-4 O.K.N.V. (Coris BioConcept) and NG-Test CARBA 5 (NG Biotech).

**METHODS:** These two assays were performed prospectively on consecutive Enterobacterales suspected of producing a carbapenemase that were referred to the Belgian National Reference Center for Monitoring Antimicrobial Resistance in Gram-Negative Bacteria between March and June 2018. The intensity of the band corresponding to a carbapenemase for each test was compared using ImageJ software.

**RESULTS:** Of the 161 isolates tested, a carbapenemase was detected in 91 (60 OXA-48-like, 15 VIM, 9 KPC, 5 NDM, 1 IMP and 1 IMP + OXA-48); in the remaining 70, no carbapenemases were detected. For both tests, the results were 100% concordant with the results of the PCR-sequencing reference method. Two IMP producers were only detected by NG-Test CARBA 5 as IMP is not targeted by RESIST-4 O.K.N.V. The mean intensity of the OXA-48, VIM and NDM bands displayed by NG-Test CARBA 5 was 3 to 3.7 times higher than for RESIST-4 O.K.N.V., while the KPC band was on average 1.7 times more intense with RESIST-4 O.K.N.V.

**CONCLUSIONS:** RESIST-4 O.K.N.V. and NG-Test CARBA 5 are two efficient assays for identification of the major carbapenemases. NG-Test CARBA 5 offers the advantage of detecting IMP, which remains rare in Western countries.


**Mots-clefs**

# Long-term Physicochemical Stability of Concentrated Solutions of Isosorbide Dinitrate in Polypropylene Syringes for Administration in the Intensive Care Unit

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



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Int J Pharm Compd. 2020 Jan-Feb;24(1):64-68.* | | *0,124* |



**Abstract**

In order to avoid fluid overload, more concentrated drug solutions in intensive care units are commonly used. This study evaluated the physicochemical stability of concentrated solution of isosorbide dinitrate in polypropylene syringes during 28 days at 5°C ± 3°C with protection from light. Five syringes of 50 mL, containing 0.60 mg/mL of isosorbide dinitrate in sodium chloride 0.9% were prepared and stored at 5°C ± 3°C with protection from light during 28 days. Immediately after preparation and periodically during the storage, isosorbide dinitrate concentration was measured by an ultra-performance liquid chromatography. Spectrophotometric absorbance at different wavelengths, pH measurements, and microscopic observations were also performed. All solutions were physicochemically stable during the whole period storage at 5°C ± 3°C. No color change, turbidity, precipitation or opacity, significant pH variations, or optic densities were observed in the solutions. Any crystals were seen by microscopic analysis. The concentration of isosorbide dinitrate remained above 90% of the initial concentration during the 28 days of storage. Solutions of isosorbide dinitrate 0.60 mg/mL in syringe of sodium chloride 0.9 % injection can be considered physically and chemically stable for 28 days when stored in syringes at 5°C ± 3°C with protection from light and may be prepared in advance by a centralized intravenous additive service.

**Mots-clefs**

# Randomized clinical trial on reduction of radiotherapy dose to the elective neck in head and neck squamous cell carcinoma; update of the long-term tumor outcome

Deschuymer S, Nevens D, **Duprez F,** Daisne JF, Dok R, Nuyts S, et al.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Rad and Oncol 2020 [Epub ahead of print]* | *10.1016/j.radonc.2020.01.005* | *5,252* |



**Abstract**

A multicenter prospective randomized controlled trial was performed to investigate whether dose reduction to the elective nodal volume (PTVelect) in head and neck carcinoma reduces radiation-induced dysphagia, primary endpoint, without compromising tumor control, secondary endpoint. Here, we report on the long-term follow-up of the secondary endpoint (NCT01812486). Two hundred patients treated with primary (chemo)radiotherapy (RT) were randomized (1:1) between the standard arm, irradiation to PTVelect up to an equivalent dose (EQD2) of 50 Gy and the experimental arm, irradiation to PTVelect up to EQD2 of 40 Gy. The primary tumor and involved nodes were treated according to the standard of care, EQD2 70 Gy (PTVhigh). Regional recurrences (RR) were projected on the initial RT planning-CT to identify the recurrence localization. The 5-year (5Y) RR was 14.0% (CI95% 7.9; 21.8) in the 40 Gy arm versus 7.5% (CI95% 3.3; 14.0) in the 50 Gy arm (p = 0.10). Majority of RR in the 40 Gy arm (9/13) were projected in PTVhigh and 2 RR were seen outside the treated RT volume. Only 2 RR occurred in PTVelect irradiated up to 40 Gy which was the same number as RR occurring in the 50 Gy PTVelect. The 5Y-overall survival (OS) was 56.5% (CI95% 45.7; 65.9) in the 40 Gy arm versus 49.6% (CI95% 39.0; 59.2) in the 50 Gy arm (p = 0.56). At 5-years, no statistically significant differences regarding OS, local recurrence, RR nor distant metastases were observed between both treatment arms. This study is underpowered to undoubtedly demonstrate non-inferiority. However, since in both arms only two RR in the PTVelect were observed, reducing the dose to PTVelect appears safe and should be further investigated.

**Mots-clefs**

# La déprescription chez la personne âgée

**Sibille FX**, Pétein C, Evrard P, **Mouzon A**, Thevelin S, **de Saint-Hubert M, Spinewine A.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Louvain Med 2020;139(2):71-77* | *10.1016/j.cmet.2019.02.002* | *0,010* |



**Abstract**

Deprescription is the process of stopping, reducing, or switching an inappropriate medication to another deemed more appropriate, which is supervised by a healthcare professional (either a physician, pharmacist, or nurse) in order to improve health and reduce costs. It has gradually become a major topic in the (appropriate) prescription domain, especially in the elderly and end-of-life patients. While its global security and benefits are commonly accepted, routine implementation and optimization still needs to be further investigated in many research paths. We will first review the viewpoints of actors involved in the deprescribing process, namely patients and relatives, as well as health care professionals. Evidences concerning a specific medication class, benzodiazepine receptor agonists, will be reviewed. Finally, the article will outlinehow deprescription can be implemented in nursing home residents and endof-life patients.

**Mots-clefs**

Deprescription ; barriers ; facilitators ; benzodiazepine receptor agonists ; nursing homes ; patients' attitudes ; older patients ; end-of-life care

# Localized Bullous Pemphigoid: Four Clinical Cases and a Literature Review

**Algoet C, Mostinckx S,** Theate I**, Vanhooteghem O.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Case Rep. 2020 Feb 11;8(3):516-519* | *10.1002/ccr3.2697* | *0,171* |



**Abstract**

Localized bullous pemphigoid (LBP) rarely evolves into the generalized form, and the prognosis is better. In our opinion, the occurrence of LBP is underestimated because of incorrect diagnoses. It is therefore important to perform a skin biopsy each time a bullous rash is concerned in order to make a definite diagnosis.

**Mots-clefs**

autoimmune disease; comorbidities; localized bullous pemphigoid; pemphigoid.

# 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. 2020 Jan;63(1):103620* | *10.1016/j.ejmg.2019.01.010* | *2,022* |



**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

# GERPAC Consensus Conference – Guidance on the Assignment of Microbiological Shelf-life for Hospital Pharmacy Aseptic Preparations

Crauste-Manciet S, Krämer I, Lagarce F, Sautou V, Beaney A, Smith J, V'Iain Fenton-May, **Hecq JD,** Sadeghipour F, Le Brun P.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Pharm Technol Hosp Pharm 2020; fev* | *10.1515/pthp-2020-0001* | *0,35* |



**Abstract**

All dosage forms prepared in hospital pharmacies should be labelled with an appropriate shelf-life. This shelflife should be validated taking chemical, physical andmicrobiological data into consideration. This guidance focuses on
parenteral aseptically prepared products, as they are highrisk preparations. The risk is exacerbated by a requirement
for longer shelf lives for reasons of economy and efficiency. The scope of this guidance includes individual patient preparations, preparations prepared in series (same type of preparation being repeatedly prepared) and batch preparations prepared from the same initial bulk admixture.

**Mots-clefs**

shelf-life, microbiological, consensus, guidance

# Lenalidomide Added to Standard Intensive Treatment for Older Patients With AML and High-Risk MDS.

Ossenkoppele G, Breems D, Stuessi G, van Norden Y, Bargetzi M, Biemond B, von dem Borne P, Chalandon Y, Cloos J, Deeren D, Fehr M, Gjertsen B, **Graux C,** Huls G, W Janssen J, Jaspers A, Jongen-Lavrencic M, de Jongh E, Klein S, van der Klift M, van Marwijk Kooy M, Maertens J, Micheaux L, van der Poel M, van Rhenen A, Tick L, Valk P, Vekemans M, van der Velden W, de Weerdt O, Pabst T, Manz M, Löwenberg B, Dutch-Belgian Hemato-Oncology Cooperative Group (HOVON) and Swiss Group for Clinical Cancer Research (SAKK)



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Leukemia. 2020 Feb 4. Online ahead of print* | *10.1038/s41375-020-0725-0* | *9,944* |



**Abstract**

More effective treatment modalities are urgently needed in patients with acute myeloid leukemia (AML) of older age. We hypothesized that adding lenalidomide to intensive standard chemotherapy might improve their outcome. After establishing a safe lenalidomide, dose elderly patients with AML were randomly assigned in this randomized Phase 2 study (n = 222) to receive standard chemotherapy ("3 + 7") with or without lenalidomide at a dose of 20 mg/day 1-21. In the second cycle, patients received cytarabine 1000 mg/m2 twice daily on days 1-6 with or without lenalidomide (20 mg/day 1-21). The CR/CRi rates in the two arms were not different (69 vs. 66%). Event-free survival (EFS) at 36 months was 19% for the standard arm versus 21% for the lenalidomide arm and overall survival (OS) 35% vs. 30%, respectively. The frequencies and grade of adverse events were not significantly different between the treatment arms. Cardiovascular toxicities were rare and equally distributed between the arms. The results of the present study show that the addition of lenalidomide to standard remission induction chemotherapy does not improve the therapeutic outcome of older AML patients. This trial is registered as number NTR2294 in The NederlandsTrial Register (www.trialregister.nl).

**Mots-clefs**

# Second Look Surgery and Hyperthermic Intraperitoneal Chemotherapy for Patients with Colorectal Cancer at High Risk of Peritoneal Carcinomatosis: A Single Center Experience

**Kothonidis C, Dili A, Lemaire J, De Moor V, Rosiere A, Bertrand C**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Eur J Surg Oncol. 2020;46(2):e86-e87* | *10.1016/j.ejso.2019.11.205* | *3,959* |




## Abstract

**BACKGROUND:** Second look surgery, complete cytoreduction (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has the rational to treat patients with high recurrence risk, at an early stage with low peritoneal carcinomatosis index (PCI) score and give a better chance of cure. The purpose of this study is to evaluate our results in terms of morbidity and oncologic benefit for the patient.

**MATERIALS AND METHODS:** Data were retrospectively collected from all patients with second look surgery and HIPEC between April 2012 and May 2018. Twelve patients with limited carcinomatosis initially resected or perforated tumour (in the literature, 70% and 50% of risk for peritoneal recurrence respectively) were identified (colorectal n=8 and appendicular cancer n=4). At second look a HIPEC was systematically proposed, even if there was no evidence of macroscopic recurrence.

**RESULTS:** Median follow-up from initial diagnosis was 24,8 months (range 9 -67). The mean PCI score was 1 (range 0 – 8). Only 2 patients out of 12 had PCI score other than 0 but histopathology showed peritoneal disease in 3 patients. Three patients were explored by laparoscopy and HIPEC was performed by mini laparotomy. One 90 days, Dindo-Clavien grade IIIb complication occurred (8%) and no mortality. Mean hospital stay was 14 days (range 8 -29). All patients are alive in the follow up but 5 of them presented recurrent disease (42%): 1 peritoneal with redo HIPEC, 1 hepatic with partial hepatectomy, 1 pulmonary resected, 1 multisite recurrence.

**CONCLUSIONS:** In our series of 12 patients, with a theoretical risk of 50 to 70% of peritoneal relapse, we only identified 1 (8%) of peritoneal recurrence suggesting that this strategy can be considered as an essential weapon in the management of colorectal cancer and this with an acceptable morbidity.



## Mots-clefs

Surgery ; Oncology ; General Medicine

# MARS

# Two-site Evaluation of a New Workflow for the Detection of Malignant Cells on the Sysmex XN-1000 Body Fluid Analyzer

**Favresse J**, Boland L, Schellen M, **Fervaille C, Wuestenberghs F**, Camboni A, **Chatelain B, Mullier F**, Defour JP, **Jacqmin H.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Int J Lab Hematol. 2020 Mar 12. Online ahead of print.* | *10.1111/ijlh.13187* | *2,073* |




## Abstract

**INTRODUCTION:** The presence of high fluorescent cells high fluorescent cells (on the body fluid analyzer) (HF-BF) on the Sysmex XN-1000 hematology analyzers has gained interest regarding the prediction of malignant cells in body fluids, but lacks sensitivity. We aimed to increase this sensitivity by combining HF-BF value, automated results, and clinical information.

**METHODS:** We evaluated a new workflow for the management of body fluids in the hematology laboratory, including the HF-BF criterion and clinical information. In two laboratories, 1623 serous fluids were retrospectively analyzed on the XN-1000 BF mode. All samples were morphologically screened for malignant cells. Optimal HF-BF cutoffs were determined to predict their presence. Thereafter, the added value of clinical information was evaluated. Other reflex testing rules (eosinophilic count ›5% and presence of the WBC Abnormal Scattergram flag) were also used to refine our workflow.

**RESULTS:** Optimal HF-BF cutoffs in the two hematology centers were 108 and 45 cells/µL, yielding a sensitivity/specificity of 66.7/93.6% and 86.8/66.6% for malignant cell detection. When adding clinical information, sensitivity/specificity evolved to 100.0/68.9% and 100.0%/not determined. Of 104 samples containing malignant cells, 97 had positive clinical information; the remainder had a HF-BF › cutoff.

**CONCLUSION:** Combining clinical information and HF-BF reached 100% sensitivity for malignant cell detection in body fluid analysis. Lack of robustness of the optimal HF-BF cutoff deserves the use of local cutoffs. Rapid automated results reporting from the XN-1000 BF mode are also feasible in clinical practice. Prospective evaluation of the workflow is needed before its implementation in clinical practice.



## Mots-clefs

Sysmex XN-1000; body fluids; cell count; malignant cell detection; reflex testing rules.

# Radiologically Atypical Paraganglioma of the Filum Terminale as a Rare Cause of Superficial Siderosis of the Central Nervous System

**London F, Mulquin N, Fervaille C, Lebecque O, Jankovski A.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Neurol Belg. 2020 Mar 10. Online ahead of print.* | *10.1007/s13760-020-01321-6* | *1,612* |



## Abstract

## Mots-clefs

# Preserved Motor Skill Learning in Acute Stroke Patients

**Baguma M, Yeganeh Doost M, Riga A, Laloux P, Bihin B, Vandermeeren Y.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Neurol Belg. 2020 Apr;120(2):365-374* | *10.1007/s13760-020-01304-7* | *1,612* |




## Abstract

Recovery is dynamic during acute stroke, but whether new motor skills can be acquired with the paretic upper limb (UL) during this recovery period is unknown. Clarifying this unknown is important, because neurorehabilitation largely relies on motor learning. The aim was to investigate whether, during acute stroke, patients achieved motor skill learning and retention with the paretic UL. Over 3 consecutive days (D1-D3), 14 patients practiced with their paretic UL the CIRCUIT, a motor skill learning task with a speed/accuracy trade-off (SAT). A Learning Index (LI) was used to quantify normalised SAT changes in comparison with baseline. Spontaneous motor recovery was quantified by another task without SAT constraint (EASY), by grip force (GF), and the Box and Blocks test (BBT). In patients, CIRCUIT LI improved 98% ± 66.2 (mean ± SD). This improvement was similar to that of young healthy individuals (n = 30) who trained with a slightly different protocol for 3 consecutive days (83.8% ± 58.8%). Generalisation of SAT gains to an untrained circuit was observed in both groups. From D1 to D3, stroke patients improved their performance on EASY, while changes in GF and BBT were heterogeneous. During acute stroke, patients retained SAT gains for a motor skill learned with the paretic UL in a manner similar to that of healthy individuals. These results demonstrate acute stroke patients achieved motor skill learning and retention that exceeded paretic UL improvements explained by spontaneous recovery.



## Mots-clefs

Acute stroke; Hemiparesis; Motor recovery; Motor skill learning; Neurorehabilitation; Upper limb function

# Platelet Counting: Ugly Traps and Good Advice. Proposals From the French-Speaking Cellular Hematology Group (GFHC)

Baccini V, Geneviève F, **Jacqmin H, Chatelain B,** Girard S, Wuilleme S, Vedrenne A, Guiheneuf E, Toussaint-Hacquard M, Everaere F, Soulard M, Lesesve JF, Bardet V.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Clin Med. 2020 Mar 16;9(3):808* | *10.3390/jcm9030808* | *5,688* |



**Abstract**

Despite the ongoing development of automated hematology analyzers to optimize complete blood count results, platelet count still suffers from pre-analytical or analytical pitfalls, including EDTA-induced pseudothrombocytopenia. Although most of these interferences are widely known, laboratory practices remain highly heterogeneous. In order to harmonize and standardize cellular hematology practices, the French-speaking Cellular Hematology Group (GFHC) wants to focus on interferences that could affect the platelet count and to detail the verification steps with minimal recommendations, taking into account the different technologies employed nowadays. The conclusions of the GFHC presented here met with a "strong professional agreement" and are explained with their rationale to define the course of actions, in case thrombocytopenia or thrombocytosis is detected. They are proposed as minimum recommendations to be used by each specialist in laboratory medicine who remains free to use more restrictive guidelines based on the patient's condition.

**Mots-clefs**

platelet count; proposals; thrombocytopenia; thrombocytosis.

# Unusual Cause of Lymphadenopathy in a Patient With Systemic Sclerosis

**Montigny P,** Camboni A, Houssiau F.


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Exp Rheumatol. 2020 Mar 19. Online ahead of print.* | | *3,238* |


## Abstract

## Mots-clefs

# Atypical Termination of a Typical Arrhythmia

**Robaye B, Blommaert D, Collet B, Xhaët O.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Cardiol. 2020 Mar 18;1-2. Online ahead of print.* | *10.1080/00015385.2020.1741142* | *0,607* |



## Abstract

## Mots-clefs

# Leptospirosis-induced Purpura: An Atypical Manifestation of Weil's Disease

**Higny J, Forêt F,** Laterre PF.


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Clin Case Rep. 2020 Feb 5;8(3):572-573* | *10.1002/ccr3.2692* | |


**Abstract**

Purpura is a rare but documented presenting feature of severe leptospirosis. We describe a case of Weil's disease characterized by predominating coagulopathy and hepato-nephritis. We illustrate dynamic changes in cutaneous lesions.

**Mots-clefs**

Weil's syndrome; coagulopathy; hepato-nephritis; leptospirosis; purpura

# Intervention Protocol: OPtimising thERapy to Prevent Avoidable Hospital Admission in the Multi-morbid Elderly (OPERAM): A Structured Medication Review With Support of a Computerised Decision Support System

Crowley EK, Sallevelt B, Huibers C, Murphy K, Spruit M, Shen Z, Boland B, **Spinewine A**, Dalleur O, Moutzouri E, Löwe A, Feller M, Schwab N, Adam L, Wilting I, Knol W, Rodondi N, Byrne S, O'Mahony D



| *Références* | *Doi* | *IF* |
|---|---|---|
| *BMC Health Serv Res. 2020 Mar 17;20(1):220* | *10.1186/s12913-020-5056-3.* | *1,932* |



## Abstract

**BACKGROUND:** Several approaches to medication optimisation by identifying drug-related problems in older people have been described. Although some interventions have shown reductions in drug-related problems (DRPs), evidence supporting the effectiveness of medication reviews on clinical and economic outcomes is lacking. Application of the STOPP/START (version 2) explicit screening tool for inappropriate prescribing has decreased inappropriate prescribing and significantly reduced adverse drug reactions (ADRs) and associated healthcare costs in older patients with multi-morbidity and polypharmacy. Therefore, application of STOPP/START criteria during a medication review is likely to be beneficial. Incorporation of explicit screening tools into clinical decision support systems (CDSS) has gained traction as a means to improve both quality and efficiency in the rather time-consuming medication review process. Although CDSS can generate more potential inappropriate medication recommendations, some of these have been shown to be less clinically relevant, resulting in alert fatigue. Moreover, explicit tools such as STOPP/START do not cover all relevant DRPs on an individual patient level. The OPERAM study aims to assess the impact of a structured drug review on the quality of pharmacotherapy in older people with multi-morbidity and polypharmacy. The aim of this paper is to describe the structured, multi-component intervention of the OPERAM trial and compare it with the approach in the comparator arm.

**METHOD:** This paper describes a multi-component intervention, integrating interventions that have demonstrated effectiveness in defining DRPs. The intervention involves a structured history-taking of medication (SHiM), a medication review according to the systemic tool to reduce inappropriate prescribing (STRIP) method, assisted by a clinical decision support system (STRIP Assistant, STRIPA) with integrated STOPP/START criteria (version 2), followed by shared decision-making with both patient and attending physician. The developed method integrates patient input, patient data, involvement from other healthcare professionals and CDSS-assistance into one structured intervention.

**DISCUSSION:** The clinical and economical effectiveness of this experimental intervention will be evaluated in a cohort of hospitalised, older patients with multi-morbidity and polypharmacy in the multicentre, randomized controlled OPERAM trial (OPtimising thERapy to prevent Avoidable hospital admissions in the Multi-morbid elderly), which will be completed in the last quarter of 2019.

## Mots-clefs

Cluster randomised controlled trial; Geriatric patient; Inappropriate prescribing; STOPP/START

# Surgical Bed Stereotactic Radiotherapy of Brain Metastases: Clinical Outcome and Predictors of Local and Distant Brain Failure

Mousli A, **Bihin B, Gustin T,** Koerts G, Mouchamps M, **Daisne JF.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Cancer Radiother. 2020 Jul;24(4):298-305* | *10.1016/j.canrad.2019.12.002* | *1,263* |




## Abstract

**PURPOSE:** To retrospectively analyze the outcomes of stereotactic radiotherapy (SRT) targeted at surgical bed of brain metastases (BM) and identify patterns of local/distant brain relapses (LR/DBR).

Patients/methods: Seventy patients were treated with SRT between 2008-2017. Marginal dose prescription on the 70% isodose line depended on the maximal diameter of the target volume and range between 15-18Gy for single fraction radiosurgery and 23.1-26Gy in 3-5 fractions for fractionated SRT.

**RESULTS:** At 12 months, the overall survival (OS) was 69% [CI 95%=59%-81%]. At 6 and 12 months, the cumulative incidence functions (CIF) of local relapse were 4% [1%-13%] and 15% [8%-26%], respectively. According to univariate analysis, factors associated with LR were an initial volume larger than 7cc (hazard ratio: 4.6 [1.0-20.8], P=0.046) and a positive resection margin [hazard ratio: 3.6 [1.1-12.0], P=0.037. DBR occurred in 54.3% of patients with a median time of 8 months. None of the variables tested (histology, location or number of lesions) were found correlated with the DBR. Leptomeningeal disease occurred in 12.9% of cases. Salvage whole brain radiotherapy (WBRT) was required in 45.7% of patients and delayed by a median time of 9.6 months. Symptomatic radionecrosis (RN) occurred in 7.1%.

**CONCLUSIONS:** Adjuvant SRT was an effective and well-tolerated treatment to control the postoperative risk of recurrence of BM without compromising OS. Positive resection margins and large volumes were predictors factor of local relapse.



## Mots-clefs

Brain metastases; Contrôle local; Local control; Métastases cérébrales; Postoperative; Postopératoire; Radiothérapie stéréotaxique; Stereotactic radiotherapy.

# Hereditary Hemorrhagic Telangiectasia: The ENT point of view

**Eloy P**, Musat G.


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Romanian J of Rhinol. 2020;10(37):4-12* | *10.2478/rjr-2020-0002* | *0,560* |



## Abstract

Hemorrhagic Hereditary Telangiectasia (HHT) disease, also called Osler-Weber-Rendu (OWR) disease, is a rare and underdiagnosed genetic disorder characterized by a multisystemic vascular dysplasia. Nosebleeds, acute or chronic digestive tract bleeding and various problems due to the involvement of major organs (liver, lungs, brain) characterize the disease. Although it was described at the beginning of the 20th century, many patients, GPs and specialists still ignore the disease, its morbidities and the modalities of the treatment. That is the reason why the authors have decided to publish this review on this familiar, evolving and potentially life-threatening disease, whose management can be sometimes a real nightmare for the clinician.



## Mots-clefs

hereditary hemorrhagic telangiectasia ; Osler-Weber-Rendu ; telangiectasia ; arterio-venous malformations ; nosebleeds

# Interactions Between Avibactam and Ceftazidime-Hydrolyzing Class D β-Lactamases

Frère JM, **Bogaerts P, Huang TD,** Stefanic P, Moray J, Bouillenne F, Brans A.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Biomolecules. 2020 Mar 23;10(3):483* | *10.3390/biom10030483.* | *4,694* |



**Abstract**

Class D β-lactamases exhibit very heterogeneous hydrolysis activity spectra against the various types of clinically useful β-lactams. Similarly, and according to the available data, their sensitivities to inactivation by avibactam can vary by a factor of more than 100. In this paper, we performed a detailed kinetic study of the interactions between two ceftazidime-hydrolyzing OXA enzymes and showed that they were significantly more susceptible to avibactam than several other class D enzymes that do not hydrolyze ceftazidime. From a clinical point of view, this result is rather interesting if one considers that avibactam is often administered in combination with ceftazidime.

**Mots-clefs**

OXA-163; OXA-24; OXA-427; OXA-β-lactamases; avibactam; ceftazidime; class D β-lactamases

# Collagenous Gastritis : About Two Paediatric Cases and Literature Review

**De Ronde O, Delos M, Jespers S, Gillain C, De Ronde Th.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Gastroenterol Belg. Jan-Mar 2020;83(1):41-45* | | *0,477* |



## Abstract

**BACKGROUND AND STUDY AIMS**: Collagenous gastritis is a rare entity divided in two subgroups (paediatric and adult). In the paediatric population, it often causes anaemia and abdominal pain. Therapy remains the most challenging part as no randomized clinical trial exists and long-term outcome is not well established.
Patients and methods: We reviewed the 43 paediatric patients with diagnosis of collagenous gastritis reported in Pubmed from 1989 to mid 2019 to analyse clinical and histological response depending on the treatment choice.
**RESULTS**: In 43 patients (M/F ratio 1:2), a clinical response was observed in 85.7% of patients and a histological response in 20.8% of patients. PPI treatment associated with oral iron supplement was the most frequent choice with clinical improvement in 78.5% of patients. Other treatments such as gluten-free diet or corticoids showed relatively good rates of clinical improvement. Histological remission seems difficult to achieve and recurrence of symptoms after treatment interruption was often reported.
**CONCLUSIONS**: Collagenous gastritis in children is mainly characterized by symptoms of anaemia, abdominal pain or diarrhea. Gastroscopy with fundic biopsies helps to confirm diagnosis and treatment with PPI's (associated with oral iron supplement in case of anaemia) seems to be the most efficient choice to achieve clinical and sometimes histological remission. Long-term outcome of these young patients is unknown. A better understanding of the pathogenesis could lead to new medications focusing on this histological remission.



## Mots-clefs

anaemia; collagenous gastritis; enteritis; paediatrics.

# Medico-psychological Aspects Relating to the Coronavirus Epidemic (Covid-19): The Contribution of the Theory of Signal Detection and the Concept of Place of Control

Naviaux AF, **Janne P, Gourdin M.**


| *Références* | *Doi* | *IF* |
|---|---|---|
| *Ann Med Psychol (Paris). 2020 Mar;178(3):223-225* | *10.1016/j.amp.2020.03.001.* | *0,221* |


## Abstract

**Mots-clefs**
Comportement; Coronavirus; Covid-19; Health locus of control; Pandemic; Signal detection theory.

# Bruxism Relieved Under CPAP Treatment in a Patient With OSA Syndrome

**Martinot JB,** Borel JC, Le-Dong NN, Silkoff PE, Denison S, Gozal D, Pépin JL.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Chest. 2020 Mar;157(3):e59-e62* | *10.1016/j.chest.2019.07.032* | *9,657* |



**Abstract**

Bruxism is a heterogeneous condition related to various underlying mechanisms, including the presence of OSA. This case report illustrates that sleep mandibular movement monitoring and analysis could provide a useful opportunity for detection of both sleep bruxism and respiratory effort. The current case suggests that tracking of respiratory effort could enable evaluation of bruxism and its potential interactions. Successful treatment of sleep-related respiratory effort may lead to improved or resolution of bruxism in cases where such a causal relationship does exist.

**Mots-clefs**

bruxism; mandibular movements; sleep apnea.

# How Does Physicians' Decisional Conflict Influence Their Ability to Address Treatment Outcomes in a Decision-Making Encounter With an Advanced-Stage Cancer Simulated Patient? A Descriptive Study

Libert Y, Peternelj L, Canivet D, Farvacques C, Liénard A, Ménard C, Merckaert I, **Reynaert C,** Slachmuylder JL, Razavi D.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Patient Educ Couns. 2020 Mar 28;S0738-3991(20)30142-7* | *10.1016/j.pec.2020.03.008.* | *9,657* |




## Abstract

**OBJECTIVE:** This descriptive study assesses how physicians' decisional conflict influences their ability to address treatment outcomes (TOs) in a decision-making encounter with an advanced-stage cancer simulated patient (SP).

**METHODS:** Physicians (N = 138) performed a decision-making encounter with the SP trained to ask for TOs information. The physicians' decisional conflict regarding patients' cancer treatments in general was assessed with the General Decisional Conflict Scale (Gen-DCS). The physicians' decisional conflict regarding the SP's cancer treatments was assessed with the Specific Decisional Conflict Scale (Spe-DCS). Physicians' ability to address TOs during the encounter was assessed with an interaction analysis system: the Multi-Dimensional Analysis of Patient Outcome Predictions (MD.POP). Weekly time spent with cancer patients was assessed with a questionnaire.

**RESULTS:** Physicians' Spe-DCS (β = -.21 ; p = .014) and weekly time spent with cancer patients (β = .22 ; p = .008) predicted the number of TOs addressed during the encounter. Spe-DCS scores predicted nearly all MD.POP dimensions (r = -.18 ; p = .040 to r = -.30 to p ‹ .001) whereas Gen-DCS scores predicted nearly none MD.POP dimensions.

**CONCLUSION:** Physicians' specific decisional conflict interferes with their ability to address TOs in a decision-making encounter with an advanced-stage cancer SP.

**PRACTICE IMPLICATIONS:** Physicians should be trained to address TOs according to patient preferences, despite their own decisional conflict.



## Mots-clefs

Cancer; Communication; Decisional conflict; Physicians; Simulated patient; Treatment outcomes.

# Radiolucent lines around knee arthroplasty components : a narrative review

**Wautier D,** Ftaïta S, Thienpont E.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Orthop Belg. 2020 Mar;86(1):82-94.* | | *0,390* |



**Abstract**

Aseptic loosening of total knee arthroplasty (TKA) components is one of the frequent reasons for early revision together with infection and instability. Aseptic loosening is usually preceded by the observation of radiolucent lines (RLL) on radiographs. Radiolucent lines have conventionally been considered a sign of osteolysis due to particles disease of either polyethylene or cement wear. However, RLL can be observed quite early after TKA, way before wear and osteolysis can even occur. Immediate postoperative RLL are secondary to surgical technique with either inadequate cement penetration in sclerotic bone, insufficient preparation of the bone or malpositioning of the component relative to the bone cuts. This type of RLL can be observed radiologically but remains often without clinical symptoms. Early development of RLL, on an initially satisfying radiograph, is secondary to changes to the cement-bone interface. These are most often related to micromotion because of constraint, malalignment, remaining mechanical deformity, erroneous bone cuts or osteoporosis. This type of RLL are observed progressively on follow-up radiographs and can be accompanied by pain complaints despite of initial good outcome. Young age, male sex or osteoporotic bones often found in elderly females, are all risk factors. A special form of aseptic loosening is tibial debonding that has been observed for different types of implants and different types of cement. It occurs at the cement-implant interface with cement remaining well attached to the trabecular bone. Probably it is a lack of cement adhesion between the high viscosity cement and the component. Revision is proposed upon diagnosis to avoid component's displacement with secondary destruction of the proximal tibial bone. Finally, RLL can develop over time secondary to polyethylene wear. These lines appear because of osteolysis and bone loss and will lead at the end to aseptic loosening of the components. Symptoms are related to failure of the implant-bone construct. Radiolucent lines without clinical symptoms should be analysed according to their potential reason of development and followed up closely with adequate radiological techniques. If symptoms develop or radiological imaging objectivizes failure and component mobility, revision knee arthroplasty might be necessary.

**Mots-clefs**

# AVRIL

# The Validity of the Canadian Clinical Scores for Occupational Asthma in European Populations

Suarthana E, Taghiakbari M, Saha-Chaudhuri P, **Rifflart C**, Suojalehto H, Hölttä P, Walusiak-Skorupa J, Wiszniewska M, Muñoz X, Romero-Mesones C, Sastre J, Rial MJ, Henneberger PK, **Vandenplas O.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Allergy. 2020 Apr 3. Online ahead of print.* | *10.1111/all.14294* | *3,81* |



## Abstract

**Mots-clefs**
asthma; epidemiology; occupational allergies; prevention

# Mepolizumab for Allergic Bronchopulmonary Aspergillosis: Report of 20 Cases From the Belgian Severe Asthma Registry and Review of the Literature

Schleich F, Vaia ES, Pilette C, **Vandenplas O,** Halloy JL, Michils A, Peche R, Hanon S, LouisR, Michel O.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Allergy Clin Immunol Pract. 2020 Apr 5;S2213-2198(20)30283-X. Online ahead of print.* | *10.1016/j.jaip.2020.03.023* | *7,550* |



## Abstract

## Mots-clefs

# A Novel Phenotype Combining Primary Ovarian Insufficiency Growth Retardation and Pilomatricomas With MCM8 Mutation

Heddar A, **Beckers D**, Fouquet B, Roland D, Misrahi M.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Clin Endocrinol Metab. 2020 Jun 1;105(6):dgaa155* | *10.1210/clinem/dgaa155* | *5,605* |




## Abstract

**CONTEXT:** Primary Ovarian insufficiency (POI) affects 1% of women aged ‹40 years and leads most often to definitive infertility with adverse health outcomes. Very recently, genes involved in deoxyribonucleic acid (DNA) repair have been shown to cause POI. Objective: To identify the cause of a familial POI in a consanguineous Turkish family. Design: Exome sequencing was performed in the proposita and her mother. Chromosomal breaks were studied in lymphoblastoid cell lines treated with mitomycin (MMC).
**SETTING AND PATIENTS:** The proposita presented intrauterine and postnatal growth retardation, multiple pilomatricomas in childhood, and primary amenorrhea. She was treated with growth hormone (GH) from age 14 to 18 years.
**RESULTS:** We identified a novel nonsense variant in exon 9 of the minichromosome maintenance complex component 8 gene (MCM8) NM_001281522.1: c.925C › T/p.R309* yielding either a truncated protein or nonsense-mediated messenger ribonucleic acid decay.The variant was homozygous in the daughter and heterozygous in the mother. MMC induced DNA breaks and aberrant metaphases in the patient's lymphoblastoid cells. The mother's cells had intermediate but significantly higher chromosomal breaks compared with a control.
**CONCLUSION:** We describe a novel phenotype of syndromic POI related to a novel truncating MCM8 variant. We show for the first time that spontaneous tumors (pilomatricomas) are associated with an MCM8 genetic defect, making the screening of this gene necessary before starting GH therapy in patients with POI with short stature, especially in a familial or consanguineous context. Appropriate familial monitoring in the long term is necessary, and fertility preservation should be considered in heterozygous siblings to avoid rapid follicular atresia.



## Mots-clefs

MCM8; Primary ovarian insufficiency; chromosomal breakage syndrome; fertility preservation; growth hormone therapy; pilomatricoma.

# Diagnosis and Management of Heparin-Induced Thrombocytopenia

Gruel Y, De Maistre E, Pouplard C, **Mullier F,** Susen S, Roullet S, Blais N, Le Gal G, Vincentelli A, Lasne D, Lecompte T, Albaladejo P, Godier A, Members of the French Working Group on Perioperative Haemostasis Groupe d'intérêt en hémostase périopératoire GIHP.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Anaesth Crit Care Pain Med. 2020 Apr;39(2):291-310.* | *10.1016/j.accpm.2020.03.012* | *2,734* |



## Abstract

**Mots-clefs**

# Assessment of Low Plasma Concentrations of Apixaban in the Periprocedural Setting

**Lessire S, Dincq AS,** Siriez R, Pochet L, **Sennesael AL, Vornicu O, Hardy M, Deceuninck O,** Douxfils J, **Mullier F.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Int J Lab Hematol. 2020 Apr 16. Online ahead of print.* | *10.1111/ijlh.13202* | *2,073* |




## Abstract

**INTRODUCTION:** Estimation of residual apixaban plasma concentrations may be requested in the management of emergencies. This study aims at assessing the performance of specific anti-Xa assays calibrated with apixaban on real-life samples with low apixaban plasma concentrations (‹30 ng/mL) and on-treatment ranges, with and without interference of low-molecular-weight heparin (LMWH).
**METHODS:** The performance of the STA® -Liquid Anti-Xa assay (STA® LAX) and the low and normal procedures of the Biophen® Direct Factor Xa Inhibitors (DiXaI) assay was tested on 134 blood samples, collected from patients on apixaban, wherefrom 74 patients received LMWH after apixaban cessation. The results were compared with the liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) measurements.
**RESULTS:** The Biophen® DiXaI, Biophen® DiXaI LOW, and STA® LAX showed very good correlation with LC-MS/MS measurements in patients without LMWH administration (Spearman r .95, .99, and .98, respectively). Their limits of quantitation were defined at 48, 24, and 12 ng/mL, respectively. The Bland-Altman test measured mean bias (SD) at 5.6 (13.1), -2.5 (5.0), and -0.8 (6.1) ng/ml, respectively. The Spearman r of the Biophen® DiXaI decreased to 0.64 in presence of low apixaban concentrations. The Spearman r of the Biophen® DiXaI LOW and STA® LAX decreased to 0.39 and 0.26, respectively, in presence of LMWH.
**CONCLUSIONS:** The accuracy of the low methodologies (Biophen® DiXaI LOW and STA® LAX) is slightly improved for low apixaban plasma concentrations, compared with the normal procedure of Biophen® DiXaI. The interference of LMWH on the low methodologies is measurable, however, less important than the previously reported interference of LMWH on rivaroxaban calibrated specific anti-Xa assays.



## Mots-clefs

anticoagulants; apixaban; drug monitoring; heparin; low-molecular-weight heparin; perioperative; periprocedural.

# Individualized Prophylactic Neck Irradiation in cNo Head and Neck Cancer Patients Based on Sentinel Lymph Node(s) Identification: Definitive Results of a Prospective Phase I-II Study

**Longton M, Lawson G, Bihin B, Mathieu I, Hanin FX, Deheneffe S, Vander Borght T, Laloux M, Daisne JF.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Int J Radiat Oncol Biol Phys. 2020 Apr 12;S0360-3016(20)30949-4.* | *10.1016/j.ijrobp.2020.03.021.* | *6,203* |




## Abstract

**PURPOSE:** This prospective, non-randomized, interventional phase I-II study investigated the individualization of the elective node irradiation in clinically No (cNo) head and neck squamous cell carcinoma (HSNCC) by sentinel lymph node (SLN) mapping with SPECT/CT and its impact on tumor control and radiation-related toxicity.

**MATERIALS AND METHODS**: Forty-four cNo HNSCC patients treated with definitive (chemo-)radiotherapy were imaged with SPECT/CT after 99mTc nanocolloid injection around the tumor. The neck levels containing up to the four hottest SLN were selected for prophylactic irradiation (CTVn-LS). A comparative virtual planning was performed with the selection of neck levels based on the current international guidelines (CTVn-IG). The regional control was monitored in function of the selected volume. Dosimetric data to the organs-at-risk (OAR) were compared between both plans. Normal tissue complication probability (NTCP) rates were derived for xerostomia, dysphagia and hypothyroidism to predict the clinical benefit and correlated to quality of life (QoL) assessments at 6 months.

**RESULTS:** Sixteen percent of patients presented unpredicted lymphatic drainage and 48% drained unilaterally. CTVn-LS were smaller than the CTVn-IG by a factor of two ($p < 0.0001$). After a median follow-up of 46 months, only 1 patient experienced a regional relapse in a non-irradiated area. Significant median dose reductions to OAR were observed, particularly to contralateral salivary glands in patients with unilateral drainage [14.6 Gy-28.1 Gy] and to the thyroid gland in all patients [22.4 Gy-48.9 Gy]. Median NTCP reductions were observed for xerostomia [0.3%-13.7%], dysphagia [1.7%-10.8%] and hypothyroidism [14.0%-36.1%]. QoL at 6 months was improved, particularly in patients irradiated unilaterally.

**CONCLUSIONS:** Neck SLN mapping with SPECT/CT individualizes and reduces the elective nodal target volumes without compromising the regional control. The NTCP rates were reduced and favorable QoL were observed in all patients, particularly in case of unilateral irradiation.



## Mots-clefs

Head and neck cancer; Individualized radiotherapy; SPECT/CT; Sentinel lymph node; Target volume selection.

# Splenosis Mimicking Peritoneal Carcinomatosis

Pichon L, **Lebecque O, Mulquin N.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Belg Soc Radiol. 2020 Apr 6;104(1):14* | *10.5334/jbsr.2089.* | *0,150* |




## Abstract

**TEACHING POINT:** Splenosis must be considered in patients with history of splenectomy or splenic trauma, later presenting with multiple peritoneal nodules.



## Mots-clefs

computed tomography; scintigraphy; splenectomy; splenosis.

# The Daily Impact of COVID-19 in Gastroenterology

Magro F, Abreu C, **Rahier JF.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *United European Gastroenterol J. 2020 Jun;8(5):520-527.* | *10.1177/2050640620920157* | *3,54* |



**Abstract**

A new strain of coronavirus, called SARS-CoV-2, emerged in Wuhan, China, in December 2019, probably originating from a wild-animal contamination. Since then, the situation rapidly evolved from a cluster of patients with pneumonia, to a regional epidemic and now to a pandemic called COrona VIrus Disease 2019 (COVID-19). This evolution is related to the peculiar modes of transmission of the disease and to the globalization and lifestyle of the 21st century that created the perfect scenario for virus spread. Even though research has not evidenced particular susceptibility of inflammatory bowel disease (IBD) patients to SARS-CoV-2 infection, immunosuppressive and immunomodulatory treatments were considered potential risk factors. In this context, initiating treatments with these agents should be cautiously weighted and regular ongoing treatments shall be continued, while the dose of corticosteroids should be reduced whenever possible. Due to the increased risk of contamination, elective endoscopic procedures and surgeries should be postponed and IBD online appointments shall be considered. IBD patients shall also follow the recommendations provided to the general population, such as minimization of contact with infected or suspected patients and to wash hands frequently. In the absence of effective treatments and vaccines, this pandemic can only be controlled through prevention of SARS-CoV-2 transmission with the main objectives of providing patients the best healthcare possible and reduce mortality.

**Mots-clefs**

Gastroenterology; endoscopy; epidemiology; immunology; inflammatory bowel disease.

# The Role of Physical and Rehabilitation Medicine in the COVID-19 Pandemic: The Clinician's View

Carda S, Invernizzi M, Bavikatte G, Bensmaïl D, Bianchi F, **Deltombe T,** Draulans N, Esquenazi A, Francisco GE, Gross R, Jacinto LJ, Pérez SM, O'Dell MW, Reebye R, Verduzco-Gutierrez M, Wissel J, Molteni F.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Ann Phys Rehabil Med. 2020 Apr 18;S1877-0657(20)30076-2* | *10.1016/j.rehab.2020.04.001.* | *4,196* |



## Abstract

**Mots-clefs**

# Detection of Platelet-Activating Antibodies Associated With Heparin-Induced Thrombocytopenia

Tardy B, Lecompte T, **Mullier F,** Vayne C, Pouplard C.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Clin Med. 2020 Apr 24;9(4):1226* | *10.3390/jcm9041226.* | *5,688* |




## Abstract

Heparin-induced thrombocytopenia (HIT) is a prothrombotic immune drug reaction caused by platelet-activating antibodies that in most instances recognize platelet factor 4 (PF4)/polyanion complexes. Platelet activation assays (i.e., functional assays) are more specific than immunoassays, since they are able to discern clinically relevant heparin-induced antibodies. All functional assays used for HIT diagnosis share the same principle, as they assess the ability of serum/plasma from suspected HIT patients to activate fresh platelets from healthy donors in the presence of several concentrations of heparin. Depending on the assay, donors' platelets are stimulated either in whole blood (WB), platelet-rich plasma (PRP), or in a buffer medium (washed platelets, WP). In addition, the activation endpoint studied varies from one assay to another: platelet aggregation, membrane expression of markers of platelet activation, release of platelet granules. Tests with WP are more sensitive and serotonin release assay (SRA) is considered to be the current gold standard, but functional assays suffer from certain limitations regarding their sensitivity, specificity, complexity, and/or accessibility. However, the strict adherence to adequate preanalytical conditions, the use of selected platelet donors and the inclusion of positive and negative controls in each run are key points that ensure their performances.



## Mots-clefs

diagnosis; functional assays; heparin-induced thrombocytopenia

# COVID-19 Pandemic: Overview of Protective-Ventilation Strategy in ARDS Patients

**Higny J, Feye F, Forêt F.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Clin Belg. 2020 Apr 27;1-3. Online ahead of print.* | *10.1080/17843286.2020.1761162* | *0,960* |




## Abstract

**OBJECTIVES:** In the context of COVID-19 pandemic, the aim of this manuscript is to provide a standard of care of patients with ARDS for non-emergency medicine trained physicians who are not customary with mechanical ventilation.
**METHODS**: We conducted a systematic review of the literature to investigate the best practice recommendations regarding the mechanical ventilation of patients with ARDS.
**CONCLUSION:** We summarized the principal strategies for lung-protective ventilation of patients with ARDS. This focus is particularly addressed to physicians who are not experienced in the invasive respiratory management of ARDS patients. Nevertheless, it remains fundamental to acknowledge that new insights concerning this quickly spreading illness become available on a regular base.



## Mots-clefs

COVID-19; SARS-CoV-2; acute respiratory distress syndrome; mechanical ventilation; protective ventilation

# Corrigendum to "A Validated UHPLC-MS/MS Method for Simultaneous Quantification of 9 Exocyclic DNA Adducts Induced by 8 Aldehydes"

[J. Pharm. Biomed. Anal. 179 (2020) Article Number 1499]

Alamil H, Lechevrel M, Lagadu S, **Galanti L**, Dagher Z, Delépée R.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Pharm Biomed Anal. 2020 Jun 5;185:113248.* | *10.1016/j.jpba.2020.113248* | *2,983* |



## Abstract

## Mots-clefs

# Worldwide Clinical Practices in Perioperative Antibiotic Therapy for Lung Transplantation

Coiffard B, Prud'Homme E, Hraiech S, Cassir N, Le Pavec J, Kessler R, Meloni F, Leone M, Thomas PA, Reynaud-Gaubert M, Papazian L, **Evrard P.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *BMC Pulm Med. 2020 Apr 29;20(1):109.* | *10.1186/s12890-020-1151-9* | *2,209* |




## Abstract

**BACKGROUND:** Infection is the most common cause of mortality within the first year after lung transplantation (LTx). The management of perioperative antibiotic therapy is a major issue, but little is known about worldwide practices.

**METHODS**: We sent by email a survey dealing with 5 daily clinical vignettes concerning perioperative antibiotic therapy to 180 LTx centers around the world. The invitation and a weekly reminder were sent to lung transplant specialists for a single consensus answer per center during a 3-month period.

**RESULTS:** We received a total of 99 responses from 24 countries, mostly from Western Europe (n = 46) and the USA (n = 34). Systematic screening for bronchial recipient colonization before LTx was mostly performed with sputum samples (72%), regardless of the underlying lung disease. In recipients without colonization, antibiotics with activity against gram-negative bacteria resistant strains (piperacillin / tazobactam, cefepime, ceftazidime, carbapenems) were reported in 72% of the centers, and antibiotics with activity against methicillin-resistant Staphylococcus aureus (mainly vancomycin) were reported in 38% of the centers. For these recipients, the duration of antibiotics reported was 7 days (33%) or less (26%) or stopped when cultures of donor and recipients were reported negatives (12%). In recipients with previous colonization, antibiotics were adapted to the susceptibility of the most resistant strain and given for at least 14 days (67%).

**CONCLUSION:** Practices vary widely around the world, but resistant bacterial strains are mostly targeted even if no colonization occurs. The antibiotic duration reported was longer for colonized recipients.



## Mots-clefs

Antibiotic therapy; Bronchial colonization; Lung transplantation; Perioperative; Survey

# Tumor Sequencing Is Useful to Refine the Analysis of Germline Variants in Unexplained High-Risk Breast Cancer Families

Van Marcke C, Helaers R, De Leener A, Merhi A, Schoonjans CA, Ambroise J, Galant C, Delrée P, Rothé F, Bar I, Khoury E, Brouillard P, Canon JL, **Vuylsteke P,** Machiels JP, Berlière M, Limaye N, Vikkula M, Duhoux FP.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Breast Cancer Res. 2020 Apr 15;22(1):36* | *10.1186/s13058-020-01273-y* | *5,676* |



## Abstract

**BACKGROUND:** Multigene panels are routinely used to assess for predisposing germline mutations in families at high breast cancer risk. The number of variants of unknown significance thereby identified increases with the number of sequenced genes. We aimed to determine whether tumor sequencing can help refine the analysis of germline variants based on second somatic genetic events in the same gene.

**METHODS**: Whole-exome sequencing (WES) was performed on whole blood DNA from 70 unrelated breast cancer patients referred for genetic testing and without a BRCA1, BRCA2, TP53, or CHEK2 mutation. Rare variants were retained in a list of 735 genes. WES was performed on matched tumor DNA to identify somatic second hits (copy number alterations (CNAs) or mutations) in the same genes. Distinct methods (among which immunohistochemistry, mutational signatures, homologous recombination deficiency, and tumor mutation burden analyses) were used to further study the role of the variants in tumor development, as appropriate.

**RESULTS:** Sixty-eight patients (97%) carried at least one germline variant (4.7 ± 2.0 variants per patient). Of the 329 variants, 55 (17%) presented a second hit in paired tumor tissue. Of these, 53 were CNAs, resulting in tumor enrichment (28 variants) or depletion (25 variants) of the germline variant. Eleven patients received variant disclosure, with clinical measures for five of them. Seven variants in breast cancer-predisposing genes were considered not implicated in oncogenesis. One patient presented significant tumor enrichment of a germline variant in the oncogene ERBB2, in vitro expression of which caused downstream signaling pathway activation.

**CONCLUSION**: Tumor sequencing is a powerful approach to refine variant interpretation in cancer-predisposing genes in high-risk breast cancer patients. In this series, the strategy provided clinically relevant information for 11 out of 70 patients (16%), adapted to the considered gene and the familial clinical phenotype.

**Mots-clefs**

Breast cancer; Germline; Mutational signatures; Predisposition; Second hit; Variant of unknown significance.

# The Use of Cadaveric Fascia Lata in Single-Stage Implant-Based Breast Reconstruction: A Two-Center Experience

Schettini AV, **Servaes M, Berners A,** Lafosse A, **Fosseprez P.**



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Plast Reconstr Aesthet Surg. 2020 Apr 15;S1748-6815(20)30144-3* | *10.1016/j.bjps.2020.03.013* | *2,228* |



## Abstract

## Mots-clefs

# The Prognostic Value of Patient-Reported Health-Related Quality of Life and Geriatric Assessment in Predicting Early Death in 6769 Older (≥70 Years) Patients With Different Cancer Tumors

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

| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Geriatr Oncol. 2020 Apr 16;S1879-4068(19)31646-7* | *10.1016/j.jgo.2020.03.017.* | *3,164* |

## Abstract

**OBJECTIVES:** We aimed to determine the prognostic value of baseline Health-Related Quality Of Life (HRQOL) and geriatric assessment (GA) to predict three-month mortality in older patients with cancer undergoing treatment.

**METHODS:** Logistic regressions analysed HRQOL, as measured with the EORTC Global Health Status (GHS) scale, and geriatric information prognostic for early mortality controlling for oncology variables. The assessment was established with the odds ratio (OR), 95% confidence interval (CI) and level of significance set at $p < 0.05$. Discriminative power was evaluated with area under the curve (AUC).

**RESULTS:** In total, 6769 patients were included in the study, of whom 1259 (18.60%) died at three months. Our model showed higher odds of early death for patients with lower HRQOL (GHS, OR 0.98, 95% CI 0.98-0.99; $p < 0.001$), a geriatric risk profile (G8 Screening Tool, 1.94, 1.14-3.29; $p = 0.014$), cognitive decline (Mini Mental State Examination, 1.41, 1.15-1.72; $p = 0.001$), being at risk for malnutrition (Mini Nutritional Assessment-Short Form, 1.54, 1.21-1.98; $p = 0.001$), fatigue (Visual Analogue Scale for Fatigue, 1.45, 1.16-1.82; $p = 0.012$) and comorbidities (Charlson Comorbidity index, 1.23, 1.02-1.49; $p = 0.033$). Additionally, older age, poor ECOG PS and being male increased the odds of early death, although the magnitude differed depending on tumor site and stage, and treatment (all $p < 0.05$). Predictive accuracy increased with 3.7% when including HRQOL and GA in the model.

**CONCLUSION:** The results suggest that, in addition to traditional clinical measures, HRQOL and GA provide additional prognostic information for early death, but the odds differ by patient and tumor characteristics.

## Mots-clefs

# Tapering of biological antirheumatic drugs in rheumatoid arthritis patients is achievable and cost-effective in daily clinical practice: data from the Brussels UCLouvain RA Cohort

**Dierckx S,** Sokolova T, Lauwerys B, Avramovska A, Meric de Bellefon L, Nzeusseu Toukap A, Stoenoiu M, Houssiau F and Durez P.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Arthritis Res Ther. 2020 Apr 28;22(1):96* | *10.1186/s13075-020-02165-4* | *4,15* |




## Abstract

**BACKGROUND/PURPOSE:** Studies have demonstrated that rheumatoid arthritis (RA) patients who achieve low disease activity or remission are able to taper biological disease-modifying antirheumatic drugs (bDMARDs). The aim of this study was to evaluate the proportion of patients in whom bDMARDs can be tapered in daily practice and to analyse the characteristics of these patients. Other objectives were to analyse which bDMARDs are more suitable for dose reduction and the cost savings.

**RESULTS:** Data from 332 eligible RA patients from our Brussels UCLouvain cohort were retrospectively analysed; 140 patients (42.1%) received a tapered regimen, and 192 received stable doses of bDMARDs. The age at diagnosis (43.1 vs 38.7 years, p = 0.04), health assessment questionnaire (HAQ) score (1.3 vs 1.5, p = 0.048), RF positivity rate (83.3 vs 72.9%, p = 0.04) and disease duration at the time of bDMARD introduction (9.7 vs 12.1 years, p = 0.034) were significantly different between the reduced-dose and stable-dose groups. Interestingly, relatively more patients receiving a tapered dose were treated with a combination of bDMARDs and methotrexate (MTX) (86.7% vs 73.8%, p = 0.005). In our cohort, anti-TNF agents were the most commonly prescribed medications (68%). Only 15 patients experienced a flare during follow-up. Adalimumab, etanercept and rituximab were the most common bDMARDs in the reduced-dose group and were associated with the most important reductions in annual cost.

**CONCLUSION:** In daily practice, tapering bDMARDs in RA patients who have achieved low disease activity or remission is an achievable goal in a large proportion of patients, thereby reducing potential side effects and annual drug-associated costs. The combination of bDMARDs with MTX could improve the success of dose reduction attempts.

**TRIAL REGISTRATION:** This retrospective non-interventional study was retrospectively registered with local ethics approval.



## Mots-clefs

Dose tapering; Remission; Rheumatoid arthritis; bioDMARDs

# La Belgian CAP48 RA Cohort: l'importance de la rémission précoce

**Dierckx S ,** Sapart E, Sokolova T , Malaise O , Avramovska A, Sidiras P, Kleimberg S , Meric de Bellefon L , Ribbens C , Di Romana S , Badot V , Lauwerys B , Durez P.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Revue ortho-rhumato 02-03/2020; vol 18, n°1* | | |



## Abstract

**Mots-clefs**

# Standard Anthracycline Based Versus Docetaxel-Capecitabine in Early High Clinical and/or Genomic Risk Breast Cancer in the EORTC 10041/BIG 3-04 MINDACT Phase III Trial

Delaloge S, Piccart M, Rutgers E, Litière S, van 't Veer LJ, van den Berkmortel F, Brain E, Dudek-Peric A, Gil-Gil M, Gomez P, Hilbers FS, Khalil Z, Knox S, Kuemmel S, Kunz G, Lesur A, Pierga JY, Ravdin P, Rubio IT, Saghatchian M, Smilde TJ, Thompson AM, Viale G, Zoppoli G, **Vuylsteke P,** Tryfonidis K, Poncet C, Bogaerts J, Cardoso F, MINDACT investigators and the TRANSBIG Consortium



| *Références* | *Doi* | *IF* |
|---|---|---|
| *J Clin Oncol. 2020 Apr 10;38(11):1186-1197* | *10.1200/JCO.19.01371* | *32,956* |




## Abstract

**PURPOSE:** MINDACT demonstrated that 46% of patients with early breast cancer at high clinical but low genomic risk on the basis of MammaPrint may safely avoid adjuvant chemotherapy. A second random assignment (R-C) compared docetaxel-capecitabine with an anthracycline-based regimen.
**PATIENTS AND METHODS:** R-C randomly assigned patients 1:1 between standard anthracycline-based regimens, with or without taxanes (control) and experimental docetaxel 75 mg/m2 intravenously plus oral capecitabine 825 mg/m2 two times per day for 14 days (DC) every 3 weeks for 6 cycles. The primary end point was disease-free survival (DFS). Secondary end points included overall survival and safety.
**RESULTS:** Of 2,832 patients, 1,301 (45%) were randomly assigned, and 97% complied with R-C assignment. In the control arm, 29.6% only received taxanes (0.5% of No patients). DFS events (n = 148) were much less than required (n = 422) as a result of a lower-than-expected accrual and event rate. At 5 years of median follow-up, DFS was not different between DC (n = 652) and control (n = 649; 90.7% [95% CI, 88% to 92.8%] v 88.8% [95% CI, 85.9% to 91.1%]; hazard ratio [HR], 0.83 [95% CI, 0.60 to 1.15]; P = .26). Overall survival (HR, 0.91 [95% CI, 0.54 to 1.53]) and DFS in the clinical high and genomic high-risk subgroup (86.1% v 88.1%; HR, 0.83 [95% CI, 0.58 to 1.21]) were similar in both arms. DC led to more grade 1 neuropathy (27.1% v 11.2%) and more grade 2 hand/foot syndrome (28.5% v 3.3%) and diarrhea (13.7% v 5.8%). Serious cardiac events occurred in 9 patients (control, n = 4; DC, n = 5). Fifty-three patients developed second cancers (control, n = 32; DC, n = 21; leukemia: 2 v 1). Five treatment-related deaths occurred (control, 2 [0.3%]; DC, 3 [0.5%]).
**CONCLUSION:** Although underpowered, this second randomization in MINDACT did not show any improvement in outcome or safety with the use of DC compared with anthracycline-based chemotherapy.



## Mots-clefs

# Atrial fibrillation and cardiac rehabilitation: an overview

**Robaye B**, Lakiss N, Dumont F, Laruelle C.



| *Références* | *Doi* | *IF* |
|---|---|---|
| *Acta Cardiol. 2020 Apr;75(2):116-120* | *10.1080/00015385.2019.1565663* | *0,951* |




## Abstract

**BACKGROUND:** Atrial fibrillation (AF) is the most common cardiac arrhythmia, and its frequency will only continue to increase in the future. Despite available drug and electrophysical treatments, death and functional restrictions due to AF are still common. More comprehensive standards of care are therefore needed.
Purpose: After a foreword regarding the link between physical activity and AF, this article aims to give to the clinician an overview of the benefits he may expect or not when including patients suffering from AF in a cardiac rehabilitation programme.
**METHOD:** We selected prospective, randomised controlled trials published during the past 10 years and referenced in the PubMed Database evaluating the safety of rehabilitation and/or its impact on AF incidence or tolerance, and tried to summarise them to propose a narrative review.
**CONCLUSION:** Cardiac rehabilitation, along with moderate and regular physical activity, has been proven to reduce the time in arrhythmia of patients with paroxysmal and persistent AF. In chronic AF, cardiac rehabilitation may decrease the resting ventricular response rate in patients and therefore improve symptoms linked to arrhythmia. These studies have managed to demonstrate cardiac rehabilitation as a safe and manageable option for AF patients, without serious risk of additional side effects. Its efficiency to limit the occurrence of serious undesirable outcomes, such as mortality and hospitalisation, has not been adequately demonstrated, likely due to the small scale of most studies and lack of long-term follow-up. Large-scale and long-term studies are thus desirable.



## Mots-clefs

Atrial fibrillation; cardiac arrythmia; cardiac rehabilitation; exercice training.

## Site Dinant

+32 (0)82 21 24 11
Rue Saint Jacques,501 - 5500 Dinant

## Site Godinne

+32 (0)81 42 21 11
Avenue Dr Gaston-Therasse 1, 5530 Yvoir

## Site Sainte-Elisabeth

+32 (0)81 72 04 11
Place Louise Godin 15 - 5000 Namur

www.chuuclnamur.be

Editeur responsable : Benoît Libert, CHU UCL Namur asbl, | Av. Docteur G. Thérasse, 1 - B5530 Yvoir (Belgique) | RPM BE 641.733.885 | Réalisation : Unité de Support Scientifique

Dinant • Godinne • Sainte-Elisabeth

CHU UCL NAMUR