CROATIAN INTERNATIONAL PUBLICATIONS

by Ivan Bohaček
ibohacek@hiim.hr

Kljajić Z[1], Roje Ž[2], Bečić K[3], Čapkun V[4], Vilović K[5], Ivanišević P[1], Marušić E[6]. Formula for the prediction of apnea/hypopnea index in children with obstructive sleep apnea without polysomnography according to the clinical parameters: Is it reliable? Int J Pediatr Otorhinolaryngol. 2017;100:168-173.

[1]University Department of ENT, University Hospital Center Split, Split, Croatia; [2]Private ENT Practice dr. Željka Roje, Split, Croatia; [3]School of Medicine, University of Split, Split, Croatia; [4]Department of Nuclear Medicine, University Hospital Center Split, Split, Croatia; [5]Department of Pathology, University Hospital Center Split, Split, Croatia; [6]Department of Pediatrics, University Hospital Center Split, Split, Croatia

PURPOSE OF THE STUDY: The aim of the study was to propose "the risk formula" for obstructive sleep apnea in children according to the general and local clinical parameters and findings relevant for obstructive sleep apnea (OSA) severity. The unmet need for this formula arises from the economic burden of polysomnography (device, staff, training, special sleep centers, etc) as the golden standard for the diagnostics. MATERIALS AND METHODS USED: The study was performed from January 2013 until January 2016 in the Sleep Center, Department for Neuroscience, School of Medicine of the University of Split, Department of Pediatrics, University Hospital Split, Croatia and ENT Dept. University Hospital in Split, Croatia. Inclusion criteria were: age > two years, AHI >1 diagnosed by polysomnography. Exclusion criteria were: chronic lung disease, active tonsillitis/pharyngitis at the time of the physical exam and syndromes that affect breathing. All polysomnograms were scored by a qualified sleep technologist and interpreted by two board certified sleep physicians independently. Age, sex, BMI, Mallampati score, tonsillar size and adenoids size were recorded. All statistical calculations were performed using SPSS 20. RESULTS: In total 60 children were included in the study. The median of age was 5 years (range 2-9). There were 19 (32%) girls and 41 (68%) boys. Of all evaluated predictors, there were statistically significant differences in the values of AHI among children with different modified Mallampati score ($\chi 2 = 28.2$; $p < 0.001$), different size of tonsils ($\chi 2 = 25.3$; $p < 0.001$) and different size of adenoids ($z = 2.7$; $p = 0{,}006$) in univariate regression analysis. Strong positive association of AHI with modified Mallampati score (standardized B = 0.51; partial correlation = 0.542, r = 0.631) was found, as well as positive correlation of AHI with tonsillar size (standardized B = 0.246; partial correlation = 0.295,R = 0.489) in the multivariate forward stepwise regression analysis. CONCLUSION: Even though we are aware that PSG is the gold standard for diagnostics of SDB there is a significant financial burden for this diagnostic procedure. That is why there is a necessity for establishing good clinical standards and possible formula for OSA severity evaluation. We propose formula which includes Mallampati score and tonsillar size for OSA -risk calculation in order to perform early therapeutic intervention thereby reducing the risk of long-term negative consequences. We recommend this formula as the screening formula in circumstances where PSG is not available, in cases when the "waiting list" is too long or when a child can not cooperate to perform it. In developing countries like Croatia on time intervention with reduced procedure-associated costs is of the utmost importance.

Jukic A[1,2], Bozic D[3,4], Kardum D[5,6], Becic T[1,2], Luksic B[7,8], Vrsalovic M[9,10], Ljubkovic M[11], Fabijanic D[1,2]. Helicobacter pylori infection and severity of coronary atherosclerosis in patients with chronic coronary artery disease. Ther Clin Risk Manag. 2017;13:933-938.

[1]Department of Cardiology, University Hospital of Split; [2]Department of Cardiology, University of Split School of Medicine; [3]Department of Gastroenterology, University

Hospital of Split; [4]Department of Gastroenterology, University of Split School of Medicine, Split; [5]Department of Gastroenterology, University Hospital Dubrava, Zagreb; [6]Department of Gastroenterology, University of Osijek School of Medicine, Osijek; [7]Department of Surgery, University Hospital of Split; [8]Department of Surgery, University of Split School of Medicine, Split; [9]Department of Vascular Medicine, Cardiovascular Center, Sestre Milosrdnice University Hospital; [10]Department of Vascular Medicine, University of Zagreb School of Medicine, Zagreb; [11]Department of Integrative Physiology, University of Split School of Medicine, Split, Croatia

AIM: Controversy exists concerning the relation between Helicobacter pylori (HP) infection and coronary artery disease (CAD). We aimed to examine the relationship between HP infection and severity of coronary atherosclerosis in patients with chronic CAD. PATIENTS AND METHODS: A total of 150 patients (109 [73%] men; mean age 62.61±10.23 years) scheduled for coronary artery bypass grafting surgery were consecutively enrolled in the cross-sectional study. According to rapid urease test and/or gastric biopsy samples stained with hematoxylin and eosin and according to Giemsa, patients were classified as HP positive (n=87; 58%) or HP negative (n=63; 42%). Coronary angiograms were scored by quantitative assessment, using multiple angiographic scoring system: 1) vessel score (number of coronary arteries stenosed ≥50%), 2) Gensini score (assigning a severity score to each coronary stenosis according to the degree of luminal narrowing and its topographic importance) and 3) angiographic severity score (number of coronary artery segments stenosed ≥50%). RESULTS: In comparison to HP-negative patients, HP-positive patients were more frequently hypertensive (P=0.014), had higher values of systolic (P=0.043) and diastolic (P=0.005) blood pressure and total cholesterol (P=0.013) and had lower values of high-density lipoprotein-cholesterol (HDL-C; P=0.010). There were no significant differences between the groups in the severity of coronary atherosclerosis: vessel score (P=0.152), Gensini score (P=0.870) and angiographic severity score (P=0.734). CONCLUSION: It is likely that HP infection is not a risk factor for the severity of coronary atherosclerosis in chronic CAD patients.

Bijelić N[1], Belovari T[1], Stolnik D[2], Lovrić I[1], Baus Lončar M[3]. Histomorphometric Parameters of the Growth Plate and Trabecular Bone in Wild-Type and Trefoil Factor Family 3 (Tff3)-Deficient Mice Analyzed by Free and Open-Source Image Processing Software. Microsc Microanal. 2017;23:818-825.

[1]Department of Histology and Embryology, Faculty of Medicine, University of Osijek, Osijek, Croatia; [2]Public Health Centre Vinkovci, Vinkovci, Croatia; [3]Department of Molecular Medicine, Institute Ruđer Bošković, Zagreb, Croatia

Trefoil factor family 3 (Tff3) peptide is present during intrauterine endochondral ossification in mice, and its deficiency affects cancellous bone quality in secondary ossification centers of mouse tibiae. The aim of this study was to quantitatively analyze parameters describing the growth plate and primary ossification centers in tibiae of 1-month-old wild-type and Tff3 knock-out mice (n=5 per genotype) by using free and open-source software. Digital photographs of the growth plates and trabecular bone were processed by open-source computer programs GIMP and FIJI. Histomorphometric parameters were calculated using measurements made with FIJI. Tff3 knock-out mice had significantly smaller trabecular number and significantly larger trabecular separation. Trabecular bone volume, trabecular bone surface, and trabecular thickness showed no significant difference between the two groups. Although such histomorphological differences were found in the cancellous bone structure, no significant differences were found in the epiphyseal plate histomorphology. Tff3 peptide probably has an effect on the formation and quality of the cancellous bone in the primary ossification centers, but not through disrupting the epiphyseal plate morphology. This work emphasizes the benefits of using free and open-source programs for morphological studies in life sciences.

Juranić B[1], Rakošec Ž[2], Jakab J[1], Mikšić Š[1], Vuletić S[3], Ivandić M[4], Blažević I[1]. Prevalence, habits and personal attitudes towards smoking among health care professionals. J Occup Med Toxicol. 2017;12:20.

[1]Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [2]Department of Culturology, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [3]Catholic Faculty of Theology in Đakovo, Josip Juraj Strossmayer University of Osijek, Đakovo, Croatia; [4]Public Health Centre Osijek, Osijek, Croatia

BACKGROUND: Tobacco use is the second major cause of morbidity and the 4th most common health

risk factor in the world. Medical professionals have a critical role in the process of smoking cessation both as advisers and behavioural models for the citizens. The aim of this study was to investigate the prevalence of smoking among health care professionals, their smoking habits and personal attitudes toward smoking, role and the responsibility of health care professionals in the prevention of smoking. RESULTS: Out of the total number of examinees, 175 (35,1%) are active smokers, 29 (5,8%) are former smokers, and 295 (59,1%) are non-smokers. Nurses with secondary education disagree the most with the claim that passive smoking is more harmful to health ($\chi 2$ test, $p = .008$), also with the claim that the introduced Smoking Act is fair to smokers ($\chi 2$ test, $p = .021$). More nurses with secondary education disagree completely or partially that one should pay attention to smoking in the presence of non-smokers ($\chi 2$ test, $p = .012$). CONCLUSION: Training programs for health care workers are needed to improve their ability in smoking cessation techniques to provide active support to their patients.

Brčić L[1], Gračan S[2], Barić A[2], Gunjača I[1], Torlak Lovrić V[2], Kolčić I[3], Zemunik T[1], Polašek O[3], Barbalić M[1], Punda A[2], Boraska Perica V[1]. Association of Established Thyroid-stimulating Hormone and Free Thyroxine Genetic Variants with Hashimoto's Thyroiditis. Immunol Invest. 2017;46:625-638.

[1]Department of Medical Biology, University of Split, School of Medicine, Split, Croatia; [2]Department of Nuclear Medicine, University Hospital Split, Split, Croatia; [3]Department of Epidemiology, University of Split, School of Medicine, Split, Croatia

Hashimoto's thyroiditis (HT), the most frequent autoimmune thyroid disease (AITD), is characterized by chronic inflammation of the thyroid gland that usually results in hypothyroidism. Thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels are used as clinical determinants of thyroid function. The main aim of this study was to explore the association of established TSH and FT4 genetic variants with HT. We performed a case-control analysis using 23 genetic markers in 200 HT patients and 304 controls. Additionally, we tested the association of selected variants with several thyroid-related quantitative traits in HT cases only. Two genetic variants showed nominal association with HT: rs11935941 near NR3C2 gene ($p = 0.0034$, OR = 0.57, 95% CI = 0.39-0.83) and rs1537424 near MBIP gene ($p = 0.0169$, OR = 0.72, 95% CI = 0.55-0.94). Additionally, three SNPs showed nominal association with thyroglobulin antibody (TgAb) levels: rs4804416 in INSR gene ($p = 0.0073$, $\beta = -0.51$), rs6435953 near IGFBP5 gene ($p = 0.0081$, $\beta = 0.75$), and rs1537424 near MBIP gene ($p = 0.0117$, $\beta = 0.49$). GLIS3 genetic variant rs10974423 showed nominal association with thyroid peroxidase antibody (TPOAb) levels ($p = 0.0465$, $\beta = -0.56$) and NRG1 genetic variant rs7825175 was nominally associated with thyroid gland volume ($p = 0.0272$, $\beta = -0.18$). All detected loci were previously related to thyroid function or pathology. Findings from our study suggest biological relevance of NR3C2 and MBIP with HT, although these loci require additional confirmation in a larger replication study.

Ladavac R[1], Bedenić B[2], Vranić-Ladavac M[3], Barišić N[3], Karčić N[3], Pompe K[4], Ferenčić A[5], Stojanović A[3], Seifert H[6], Katić S[7], Higgins PG[6]. Emergence of different Acinetobacter baumannii clones in a Croatian hospital and correlation with antibiotic susceptibility. J Glob Antimicrob Resist. 2017;10:213-218.

[1]Department for Nephrology, General Hospital Pula, Pula, Croatia; [2]Department for Microbiology, School of Medicine, University of Zagreb, Zagreb, Croatia; Clinical Department for Clinical and Molecular Microbiology, University Hospital Centre Zagreb, Zagreb, Croatia; [3]Department for Microbiology, Public Health Institute of Istria County, Pula, Croatia; [4]Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Cologne, Germany; [5]School of Medicine, University of Rijeka, Rijeka, Croatia; [6]Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Cologne, Germany; German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany;

[7]Clinical Department for Clinical and Molecular Microbiology, University Hospital Center Zagreb, Zagreb, Croatia.

OBJECTIVES: During routine diagnostic laboratory work, the clinical microbiologist observed an increase of Acinetobacter baumannii isolates with three different carbapenem susceptibility patterns: susceptible, intermediate and resistant. Isolates belonging to the same carbapenem susceptibility phenotype exhibited identical susceptibility/resistance patterns to non-β-lactam antibiotics. This prompted us to analyse the mechanisms of carbapenem-resistance and the molecular epidemiology of the iso-

lates. A total of 59 A. baumannii isolates were analysed and grouped according to their susceptibility to imipenem: group 1 were susceptible (N=24), group 2 were intermediate (N=8) and group 3 were resistant (N=27) to imipenem. MATERIAL AND METHODS: PCR and sequencing was used to detect resistance genes. Genotyping of the isolates was performed by PFGE and MLST. RESULTS: Out of 27 resistant isolates, 20 harboured blaOXA-40-like and 7 blaOXA-23 -like genes. ISAba1 was found upstream of blaOXA-51 and blaOXA-23 genes. PFGE genotyping demonstrated the existence of three major A. baumannii clones in GH Pula and determination of sequence groups showed that the isolates belonged to international clones commonly associated with multidrug-resistance. MLST (performed on six isolates) showed diverse population structure of isolates belonging to the same cluster, including ST 195, ST 231, ST 775 and ST 1095. CONCLUSIONS: A previous study conducted in 2009-2010 showed that reduced susceptibility to carbapenems in GH Pula was only associated with upregulation of the intrinsic OXA-51 β-lactamase. In this study a shift to isolates with acquired oxacillinases, belonging to two major clones was reported.

Pećina-Šlaus N[1,2], Kafka A[1,2], Bukovac A[1,2], Vladušić T[3], Tomas D[4,5], Hrašćan R[3]. Genetic changes of MLH1 and MSH2 genes could explain constant findings on microsatellite instability in intracranial meningioma. Tumour Biol. 2017;39(7):1010428317705791.

[1]Laboratory of Neurooncology, Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Zagreb, Croatia; [2]Department of Biology, School of Medicine, University of Zagreb, Zagreb, Croatia; [3]Department of Biochemical Engineering, Faculty of Food Technology and Biotechnology, University of Zagreb, Zagreb, Croatia; [4]Department of Pathology, School of Medicine, University of Zagreb, Zagreb, Croatia; [5]University Hospital "Sisters of Charity," Zagreb, Croatia.

Postreplicative mismatch repair safeguards the stability of our genome. The defects in its functioning will give rise to microsatellite instability. In this study, 50 meningiomas were investigated for microsatellite instability. Two major mismatch repair genes, MLH1 and MSH2, were analyzed using microsatellite markers D1S1611 and BAT26 amplified by polymerase chain reaction and visualized by gel electrophoresis on high-resolution gels. Furthermore, genes DVL3 (D3S1262), AXIN1 (D16S3399), and CDH1 (D16S752) were also investigated for microsatellite instability. Our study revealed constant presence of microsatellite instability in meningioma patients when compared to their autologous blood DNA. Altogether 38% of meningiomas showed microsatellite instability at one microsatellite locus, 16% on two, and 13.3% on three loci. The percent of detected microsatellite instability for MSH2 gene was 14%, and for MLH1, it was 26%, for DVL3 22.9%, for AXIN1 17.8%, and for CDH1 8.3%. Since markers also allowed for the detection of loss of heterozygosity, gross deletions of MLH1 gene were found in 24% of meningiomas. Genetic changes between MLH1 and MSH2 were significantly positively correlated ($p = 0.032$). We also noted a positive correlation between genetic changes of MSH2 and DVL3 genes ($p = 0.034$). No significant associations were observed when MLH1 or MSH2 was tested against specific histopathological meningioma subtype or World Health Organization grade. However, genetic changes in DVL3 were strongly associated with anaplastic histology of meningioma ($\chi 2 = 9.14$; $p = 0.01$). Our study contributes to better understanding of the genetic profile of human intracranial meningiomas and suggests that meningiomas harbor defective cellular DNA mismatch repair mechanisms.

Crnogorac M[1], Horvatic I[1], Toric L[1], Galesic Ljubanovic D[2], Tisljar M[1], Galesic K[1]. Clinical, serological and histological determinants of patient and renal outcome in ANCA-associated vasculitis with renal involvement: an analysis from a referral centre. Int Urol Nephrol. 2017;49:1419-1431.

[1]Department of Nephrology and Dialysis, Dubrava University Hospital, Zagreb, Croatia; [2]Department of Pathology, Dubrava University Hospital, Zagreb, Croatia.

PURPOSE: To evaluate significance of clinical and histopathological prognostic factors for renal and patient outcome in AAV patient cohort. METHODS: Retrospective study included consecutive patients diagnosed with pauci-immune crescentic glomerulonephritis from January 2003 to December 2013. Primary outcome was combined endpoint patient death or progression to end-stage renal disease (ESRD). Secondary outcomes were patient survival and progression to ESRD (renal survival) singularly and disease relapse. Kaplan-Meyer survival analysis and multivariate Cox proportional hazard regression analysis were used to explore difference between phenotypes and finding significant predictors regarding outcomes.

RESULTS: Out of 81 patients, 40.7% patients reached primary endpoint, 22.2% died, 29.6% reached ESRD and 16% relapsed during follow-up. Multivariate Cox proportional hazards regression-adjusted analysis found higher BVAS (HR 1.08, 95% CI 1.01-1.17, p = 0.042), higher baseline maximal serum creatinine (HR 1.02, 95% CI 1.01-1.03, p = 0.04) and lower haemoglobin (HR 0.97, 95% CI 0.95-0.99, p = 0.011) significantly associated with primary endpoint. Higher BVAS (HR 1.25, 95% CI 1.01-1.43, p = 0.001) and lower haemoglobin (HR 0.95, 95% CI 0.91-0.99, p = 0.008) were significantly associated with patient survival, while for renal survival, lower haemoglobin (HR 0.97, 95% CI 0.94-0.99, p = 0.041) and the need for acute haemodialysis (HR 3.15, 95% CI 1.20-8.26, p = 0.02) were significant predictors. On multivariate-adjusted analysis, no significant predictors for disease relapse were found. Kaplan-Meier survival analysis found no difference between clinical, serological and pathohistological phenotypes for all of the endpoints. CONCLUSIONS: Renal function at presentation, anaemia and BVAS should be included in prediction models for the outcomes for the AAV patients.