

## CROATIAN INTERNATIONAL PUBLICATIONS

by Ivan Boháček

[ibohacek@hiim.hr](mailto:ibohacek@hiim.hr)



**Bozek T<sup>1</sup>, Blazekovic A<sup>2</sup>, Perkovic MN<sup>3</sup>, Jercic KG<sup>2</sup>, Sustar A<sup>4</sup>, Smircic-Duvnjak L<sup>1</sup>, Outeiro TF<sup>5,6</sup>, Pivac N<sup>3</sup>, Borovecki F<sup>2</sup>. The influence of dopamine-beta-hydroxylase and catechol O-methyltransferase gene polymorphism on the efficacy of insulin detemir therapy in patients with type 2 diabetes mellitus. *Diabetol Metab Syndr.* 2017;9:97.**

<sup>1</sup>Vuk Vrhovac University Clinic, Merkur University Hospital, Zagreb, Croatia; <sup>2</sup>Department for Functional Genomics, Center for Translational and Clinical Research, University of Zagreb School of Medicine, University Hospital Center Zagreb, Zagreb, Croatia; <sup>3</sup>Division of Molecular Medicine, Rudjer Boskovic Institute, Zagreb, Croatia; <sup>4</sup>Department of Cardiology, University Hospital Center Rijeka, Rijeka, Croatia; <sup>5</sup>Department of Experimental Neurodegeneration, Center for Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), Center for Biostructural Imaging of Neurodegeneration, University Medical Center Göttingen, Göttingen, Germany; <sup>6</sup>Max Planck Institute for Experimental Medicine, Göttingen, Germany

**BACKGROUND:** Type II diabetes is an important health problem with a complex connection to obesity, leading to a broad range of cardiovascular complications. Insulin therapy often results in weight gain and does not always ensure adequate glycemic control. However, previous studies reported that insulin detemir is an efficient long-acting insulin with a weight sparing effect. The aim of this study was to determine the association of catechol O-methyltransferase (COMT) Val108/158Met and dopamine-beta-hydroxylase (DBH) 1021C/T polymorphisms with the effectiveness of insulin detemir in achieving glucose control and body weight control. **Participants and methods:** This 52-week observational study included 185 patients with inadequate glycemic control treated with premix insulin analogues, which were replaced with insulin aspart and insulin detemir, and 156 healthy controls. After DNA isolation from blood samples, genotyping of DBH-1021C/T polymorphism (rs1611115) and COMT

Val108/158Met polymorphism (rs4680) was performed. **RESULTS:** Our results confirmed that insulin detemir did not lead to weight gain. The most significant finding was that A carriers (the combined AG and AA genotype) of the COMT Val108/158Met achieved significantly better hemoglobin A1c (HbA1c) values compared to patients carrying GG genotype. No association between DBH-1021C/T genotypes and weight and/or glucose control was detected in diabetes patients or in healthy control subjects. **CONCLUSIONS:** This study showed that the presence of one or two A allele of the COMT Val108/158Met was associated with improved glycemic response, and with a better response to insulin detemir therapy in patients with type II diabetes, separating them as best candidates for detemir therapy.

**Gobić D, Tomulić V, Lulić D, Židan D, Brusich S, Jakljević T, Zaputović L. Drug-Coated Balloon Versus Drug-Eluting Stent in Primary Percutaneous Coronary Intervention: A Feasibility Study. *Am J Med Sci.* 2017;354(6):553-560.**

*Department of Cardiovascular Disease, University Hospital Rijeka, Rijeka, Croatia*

**BACKGROUND:** Drug-eluting stents (DES) represent a significant evolution in the treatment of patients with acute myocardial infarction with ST elevation. However, stent-related adverse events have led to an introduction of drug-coated balloons (DCB) applied particularly to bifurcation lesions, in-stent restenosis and small vessel disease. The aim of this study was to determine whether a DCB-only strategy has a similar safety profile and equal angiographic and clinical outcomes to DES implantation in primary percutaneous coronary intervention (pPCI). **MATERIALS AND METHODS:** Seventy-five patients with acute myocardial infarction with ST elevation were randomized into DES and DCB groups of 37 and 38 patients, respectively. The study end-points were major adverse cardiac events and late lumen loss during

the 6 months following the pPCI. RESULTS: Reinfarction occurred in 5.4% of patients in the DES and 5.3% of patients in the DCB group after 1 month (risk ratio = 1.03, 95% CI [0.15-6.91],  $P = 0.98$ ). After 6 months, major adverse cardiac events were reported in 5.4% of patients in the DES group and none in the DCB group (risk ratio = 5.13, 95% CI [0.25-103.42],  $P = 0.29$ ). Late lumen loss in the DES group was  $0.10 \pm 0.19$ mm and  $-0.09 \pm 0.09$ mm in the DCB group ( $P < 0.05$ ). CONCLUSIONS: A DCB-only strategy is safe and feasible in the pPCI setting and showed good clinical and angiographic outcomes in a 6-month follow-up period.

**Boban M<sup>1,2</sup>, Pesa V<sup>1</sup>, Gabric ID<sup>3</sup>, Manola S<sup>3</sup>, Persic V<sup>1,2</sup>, Antic-Kauzlaric H<sup>1</sup>, Zulj M<sup>2</sup>, Vcev A<sup>2</sup>. Auxiliary diagnostic potential of ventricle geometry and late gadolinium enhancement in left ventricular non-compaction; non-randomized case control study. BMC Cardiovasc Disord. 2017;17(1):286.**

<sup>1</sup>Department of Cardiology, University hospital "Thalassotherapia Opatija"; Faculty of Medicine, University of Rijeka, Opatija, Croatia; <sup>2</sup>Department of Internal medicine, Faculty of Medicine, "J.J. Strossmayer" University of Osijek, Osijek, Croatia; <sup>3</sup>Department of Cardiology, University Hospital "Sestre Milosrdnice" Zagreb, Zagreb, Croatia

BACKGROUND: There are still ambiguities existing in regard to left ventricular non-compaction (LVNC) diagnostic imaging. The aim of our study was to analyze diagnostic potential of late gadolinium enhancement (LGE) and ventricle geometry in patients with LVNC and controls. METHODS: Data on cardiac magnetic resonance imaging (CMR) studies for LVNC were reassessed from the hospital's database (3.75 years;  $n=1975$  exams). Matching sample of controls included cases with no structural heart disease, hypertrophic or dilative cardiomyopathy, arrhythmogenic right ventricular dysplasia or subacute myocarditis. Eccentricity of the left ventricle was measured at end diastole in the region with pronounced NC and maximal to minimal ratio (MaxMinEDDR) was calculated. RESULTS: Study included 255 patients referred for CMR, 100 (39.2%) with LVNC (prevalence in the studied period 5.01%) and 155 (60.8%) controls. Existing LGE had sensitivity of 52.5% (95%-CI:42.3-62.5), specificity of 80.4% (95%-CI:73.2-86.5) for LVNC, area under curve (AUC) 0.664 (95%-CI:0.603-0.722);  $p < 0.001$ . MaxMinEDDR  $> 1.10$  had sensitivity of 95.0% (95%-CI:88.7-98.4), specificity of 82.6% (95%-CI: 75.7-88.2) for LVNC, AUC 0.917 (95%-CI:0.876-0.948);  $p < 0.001$ . LGE correlated with

Max-Min-EDD-R ( $\text{Rho}=0.130$ ;  $p=0.038$ ) and there was significant difference in ROC analysis  $\Delta\text{AUC}0.244$  (95%-CI:0.175-0.314);  $p < 0.001$ . LGE also correlated negatively with stroke volume and systolic function (both  $p < 0.05$ , respectively). CONCLUSIONS: LGE was found to be frequently expressed in patients with LVNC, but without sufficient power to be used as a discriminative diagnostic parameter. Both LGE and eccentricity of the left ventricle were found to be relatively solid diagnostic landmarks of complex infrastructural and functional changes within the failing heart.

**Dumic A<sup>1</sup>, Miskulin I<sup>1</sup>, Matic Licanin M<sup>1</sup>, Mujkic A<sup>2</sup>, Cacic Kenjeric D<sup>3</sup>, Miskulin M<sup>1</sup>. Nutrition Counselling Practices among General Practitioners in Croatia. Int J Environ Res Public Health. 2017;14(12).**

<sup>1</sup>Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; <sup>2</sup>School of Medicine, University of Zagreb, Zagreb, Croatia; <sup>3</sup>Faculty of Food Technology, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia

Chronic non-communicable diseases are a significant public health problem and imbalanced nutrition is one of the most significant risk factor for them. The objective of this study was to examine Croatia's general practitioners' nutrition counselling practice and determine the factors that influence such practice. A cross-sectional study was conducted among 444 (17.0%) randomly selected general practitioners (GPs) in Croatia from May to July 2013 via a 32-item anonymous questionnaire. Study showed that 77.0% of participants had provided nutrition counselling exclusively to patients with specific health risks; 18.7% participants had provided nutrition counselling for all patients, regardless of their individual risks, while 4.3% had not provide nutrition counselling. As the most significant stimulating factor for implementing nutrition counselling in their daily work with patients, 55.6% of the participants identified personal interest regarding nutrition and the effects it has on health. The latter factor was more frequently emphasized among female general practitioners ( $p < 0.001$ ) and general practitioners without chronic diseases ( $p < 0.001$ ). The most significant barrier for nutrition counselling was lack of time (81.6%). It is necessary to make additional efforts to increase the frequency of nutrition counselling provided by general practitioners in Croatia. The majority of Croatian general practitioners could increase their nutrition counselling practice in order to promote balanced nutrition and improve the overall health status of their patients.

Budimir I<sup>1</sup>, Stojavljević S<sup>1</sup>, Baršić N<sup>1</sup>, Biščanin A<sup>1</sup>, Mirošević G<sup>2</sup>, Bohnec S<sup>3</sup>, Kirigin LS<sup>2</sup>, Pavić T<sup>1</sup>, Ljubičić N<sup>1</sup>. Scoring systems for peptic ulcer bleeding: Which one to use? *World J Gastroenterol.* 2017;23(41):7450-7458.

<sup>1</sup>Division of Gastroenterology, Department of Internal Medicine, "Sestre Milosrdnice" University Hospital Center, Zagreb, Croatia; <sup>2</sup>Division of Endocrinology, Department of Internal Medicine, "Sestre Milosrdnice" University Hospital Center, Medical and Dental Faculty, University of Zagreb, Zagreb, Croatia; <sup>3</sup>Gastroenterologie, Allgemeine Innere Medizin und Geriatrie, Rems-Murr Klinik Winnenden, Winnenden, Germany.

AIM: To compare the Glasgow-Blatchford score (GBS), Rockall score (RS) and Baylor bleeding score (BBS) in predicting clinical outcomes and need for interventions in patients with bleeding peptic ulcers. METHODS: Between January 2008 and December 2013, 1012 consecutive patients admitted with peptic ulcer bleeding (PUB) were prospectively followed. The pre-endoscopic RS, BBS and GBS, as well as the post-endoscopic diagnostic scores (RS and BBS) were calculated for all patients according to their urgent upper endoscopy findings. Area under the receiver-operating characteristics (AUROC) curves were calculated for the prediction of lethal outcome, rebleeding, needs for blood transfusion and/or surgical intervention, and the optimal cutoff values were evaluated. RESULTS: PUB accounted for 41.9% of all upper gastrointestinal tract bleeding, 5.2% patients died and 5.4% patients underwent surgery. By comparing the AUROC curves of the aforementioned pre-endoscopic scores, the RS best predicted lethal outcome (AUROC 0.82 vs 0.67 vs 0.63, respectively), but the GBS best predicted need for hospital-based intervention or 30-d mortality (AUROC 0.84 vs 0.57 vs 0.64), rebleeding (AUROC 0.75 vs 0.61 vs 0.53), need for blood transfusion (AUROC 0.83 vs 0.63 vs 0.58) and surgical intervention (0.82 vs 0.63 vs 0.52). The post-endoscopic RS was also better than the post-endoscopic BBS in predicting lethal outcome (AUROC 0.82 vs 0.69, respectively). CONCLUSION: The RS is the best predictor of mortality and the GBS is the best predictor of rebleeding, need for blood transfusion and/or surgical intervention in patients with PUB. There is no one 'perfect score' and we suggest that these two tests be used concomitantly.

Berkovic MC<sup>1</sup>, Bilic-Curcic I<sup>2</sup>, Herman Mahecic D<sup>1</sup>, Gradiser M<sup>3</sup>, Grgurevic M<sup>4</sup>, Bozek T<sup>4</sup>. Long-Term Effectiveness of Liraglutide in Association with Patients' Baseline Characteristics in Real-Life

Setting in Croatia: An Observational, Retrospective, Multicenter Study. *Diabetes Ther.* 2017;8(6):1297-1308.

<sup>1</sup>Department for Endocrinology, Diabetes and Metabolism University Hospital Centre, Sestre Milosrdnice, Zagreb, Croatia; <sup>2</sup>Department of Pharmacology, Faculty of Medicine, J.J. Strossmayer University Osijek, Clinical Hospital Center Osijek, Osijek, Croatia; <sup>3</sup>Department for Internal Medicine, General Hospital Čakovec, Čakovec, Croatia; <sup>4</sup>University Clinic for Diabetes Vuk Vrhovac, Zagreb, Croatia.

INTRODUCTION: Glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) are recommended therapy for type 2 diabetes (T2DM) and liraglutide is the most used worldwide. We assessed the glycemic efficacy and extra-glycemic effects of liraglutide during 36 months' follow-up of individuals with poorly regulated T2DM under routine clinical practice and sought to identify the phenotype of treatment responders. METHODS: A total of 207 individuals were included. The primary endpoint was the proportion of participants with HbA1c < 7.0% and/or weight reduction. Secondary endpoints included changes in lipids, blood pressure, fasting c-peptide, and antidiabetic treatment during follow-up of 3 years. RESULTS: Liraglutide was prescribed to 89.8% of participants already on at least two antidiabetic medications and 18% on insulin. Subject's mean age was 53.28 ± 9.42 years with duration of diabetes 8.29 ± 4.89 years. Baseline HbA1c was 8.5 ± 1.3% and body mass index (BMI) was 39 ± 4.5 kg/m<sup>2</sup>. Reduction of HbA1c was observed in 84.4% of participants, and 89.2% experienced average weight reduction of 5 kg. A composite outcome (reduction of HbA1c with any weight loss) was achieved in 76.2% of patients. After 6 months on liraglutide treatment, 38.1% of participants achieved target HbA1c level < 7%. This effect was maintained for 36 months in 50.8% of subjects. Increase in c-peptide was evident after 24 months (p = 0.030). Participants experienced a significant reduction in systolic blood pressure (BP) (p = 0.003), while there was no effect on diastolic BP, lipid profile, or liver enzymes. The number of participants treated with sulfonylurea decreased from 60.8% to 17.5%, while the number treated with insulin and sodium-glucose co-transporter-2 (SGLT-2) inhibitor increased (17.6% to 24.6% and 2.5% to 36.8%, respectively). Independent predictors of durability of HbA1c reduction were initial BMI (p = 0.004), HbA1c (p < 0.001), systolic BP (p = 0.007), and cholesterol (p = 0.020). Moreover, female gender and shorter duration of diabetes were independent predictors for HbA1c reduction. CONCLUSION: Liraglutide shows sustained glycemic and extra-glycemic effects when used for treatment of obese poorly regulated individuals with T2DM.