

CROATIAN INTERNATIONAL PUBLICATIONS

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Duvnjak L, Blaslov K. Dipeptidyl peptidase-4 inhibitors improve arterial stiffness, blood pressure, lipid profile and inflammation parameters in patients with type 2 diabetes mellitus. *Diabetol Metab Syndr.* 2016;8:26.

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BACKGROUND: This uncontrolled open label study evaluated the effect of dipeptidyl peptidase-4 inhibitors (DPP-4i): sitagliptin and vildagliptin on augmentation index standardized for 75 beats per minute (cAIx@75), blood pressure (BP), lipid profile and high-sensitivity C-reactive protein (hs-CRP) in patients with type 2 diabetes mellitus (T2DM). **METHODS:** Fifty-one well-regulated T2DM patients were randomly assigned to either sitagliptin or vildagliptin (100 mg/day) for 3 months continuing their previous treatment. Lipid profile, cAIx@75, hsCRP, glycated hemoglobin (HbA1c) were measured at baseline at 4, 8 and 12th week were accessed. cAIx@75 and pulse wave velocity (PWV) were determined by SphygmoCor device. **RESULTS:** Following DPP-4 treatment there was a significant reduction in total serum cholesterol (5.18 vs 4.62 mmol/L), low-density lipoprotein (2.89 vs 2.54 mmol/L), hsCRP (3.21 vs 1.95 mg/L), cAIx@75 (24.5 vs 22.3) and central systolic BP (131.8 vs 119.5 mmHg). The sitagliptin treated group reached cAIx@75 reduction earlier in the study period while neither sitagliptin or vildagliptin use resulted in the significant HbA1c reduction. **CONCLUSION:** The treatment with DPP-4i: sitagliptin and vildagliptin provides favorable metabolic and vascular effects beyond glucose-control. Further studies are required to elucidate their implication in metabolic pathways.

Gregurić T, Trkulja V, Baudoin T, Grgić M, Šmigovec I, Kalogjera L. Differences in the Sino-Nasal Outcome Test 22 and visual analog scale symptom scores in chronic rhinosinusitis with and without nasal polyps. *Am J Rhinol Allergy.* 2016;30:107-12.

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BACKGROUND: Chronic rhinosinusitis (CRS) with and without polyps has a high impact on health-related quality of life (HRQL), but the difference in HRQL and symptom presentation between two clinical phenotypes of CRS has not been specifically evaluated before now. **OBJECTIVE:** To evaluate patterns of symptoms and HRQL disease-specific domains affected in patients with CRS by comparing differences between two clinical phenotypes, adjusted for demographics, major risk factors, comorbidities, current medical treatment, and previous surgery. **METHODS:** A group of 251 patients with CRS completed the visual analog scale (VAS) symptom severity score and the Sino-Nasal Outcome Test 22 (SNOT-22) questionnaire. Data sets were analyzed by using principal component analysis (PCA) to identify a set of symptom components, together with the items excluded from PCA, which were then analyzed for differences between patients with CRS with nasal polyps (CRSwNP) and patients with CRS without nasal polyps (CRSsNP). **RESULTS:** PCA of SNOT-22 items identified six components, three referred to CRS-specific symptoms termed "nasal"; "extranasal, rhinologic"; and "olfactory/cough"; and three referred to HRQL impairment termed "sleep disturbance," "functional disturbance," and "emotional disturbance." Nasal obstruction, ear pain, ear fullness, and fatigue were excluded from PCA and treated as separate outcomes. Patients with CRSwNP had significantly worse nasal symptoms, olfactory/cough symptoms, and nasal obstruction. Patients with CRSsNP scored significantly worse with regard to fatigue and to sleep and functional disturbances. The PCA results for VAS scores identified three symptom components: pain, nasal symptoms, and pharyngeal symptoms. Patients with CRSwNP had significantly worse VAS nasal symptoms but less pronounced VAS pain symptoms than patients with CRSsNP. The total SNOT-22 score between the groups was not significantly different. **CONCLUSION:** With controlling of covariates that may influence the severity of the disease, this study showed significant differences in symptom patterns and different aspects of HRQL impairment between pati-

ents with CRSwNP and patients with CRSsNP, however, with no difference in the total HRQL score.

Cerina V¹, Kruljac I³, Radosevic JM³, Kirigin LS³, Stipic D¹, Pecina HI², Vrkljan M³. Diagnostic Accuracy of Perioperative Measurement of Basal Anterior Pituitary and Target Gland Hormones in Predicting Adrenal Insufficiency After Pituitary Surgery. *Medicine (Baltimore)*. 2016;95(9):e2898.

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The insulin tolerance test (ITT) is the gold standard for diagnosing adrenal insufficiency (AI) after pituitary surgery. The ITT is unpleasant for patients, requires close medical supervision and is contraindicated in several comorbidities. The aim of this study was to analyze whether tumor size, remission rate, preoperative, and early postoperative baseline hormone concentrations could serve as predictors of AI in order to increase the diagnostic accuracy of morning serum cortisol. This prospective study enrolled 70 consecutive patients with newly diagnosed pituitary adenomas. Thirty-seven patients had nonfunctioning pituitary adenomas (NPA), 28 had prolactinomas and 5 had somatotropinomas. Thyroxin (T4), thyrotropin (TSH), prolactin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and insulin-like growth factor 1 (IGF-I) were measured preoperatively and on the sixth postoperative day. Serum morning cortisol was measured on the third postoperative day (CORT3) as well as the sixth postoperative day (CORT6). Tumor mass was measured preoperatively and remission was assessed 3 months after surgery. An ITT was performed 3 to 6 months postoperatively. Remission was achieved in 48% of patients and AI occurred in 51%. Remission rates and tumor type were not associated with AI. CORT3 had the best predictive value for AI (area under the curve (AUC) 0.868, sensitivity 82.4%, specificity 83.3%). Tumor size, preoperative T4, postoperative T4, and TSH were also associated with AI in a multivariate regression model. A combination of all preoperative and postoperative variables (excluding serum cortisol) had a sensitivity of 75.0% and specificity of 77.8%. The predictive power of CORT3 substantially improved by adding those variables into the model (AUC 0.921, sensi-

tivity 94.1%, specificity 78.3%, PPV 81.9%, NPV of 92.7%). In a subgroup analysis that included only female patients with NPA, LH had exactly the same predictive value as CORT3. The addition of baseline LH to CORT3, increased sensitivity to 100.0%, specificity to 88.9%, PPV to 90.4%, and NPV to 100.0%. Besides CORT3, tumor size, thyroid hormones, and gonadotropins can serve as predictors of AI. LH in postmenopausal female patients with NPA has similar diagnostic accuracy as CORT3. Further studies are needed in order to validate the scoring system proposed by this study.

Canecki-Varžić S, Prpić-Križevac I, Bilić-Čurčić I. Plasminogen activator inhibitor-1 concentrations and bone mineral density in postmenopausal women with type 2 diabetes mellitus. *BMC Endocr Disord*. 2016;16(1):14.

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BACKGROUND: Women with type 2 diabetes mellitus (T2DM) have a higher risk of fractures despite increased bone mineral density (BMD). In experimental studies a potential role of plasminogen activator inhibitor-1 (PAI-1) in bone remodeling is suggested but studies in humans are lacking. This is a first study in humans investigating whether circulated levels of PAI-1 in postmenopausal women with T2DM are related to BMD and adiposity. **METHODS:** Anthropometric variables, PAI-1 and insulin levels, serum lipids and bone turnover markers were measured in 127 postmenopausal women with T2DM. A total of 117 female patients were divided according to lumbar spine BMD measurements via dual-energy x-ray absorptiometry in three groups: 47 with osteopenia, 21 with osteoporosis and 49 with normal BMD. **RESULTS:** Diabetic patients with normal BMD had significantly higher BMI, greater waist circumference and lower bone turnover markers than diabetics with osteopenia and osteoporosis. PAI-1 was lower in diabetics with osteoporosis and osteopenia compared with diabetics with normal BMD. Multiple regression analysis revealed insulin, triglycerides levels, pyrilinks and beta blocker therapy to be the strongest predictors of PAI-1 levels. PAI-1 levels correlated with both L-BMD and hip BMD, but after adjustment for age and BMI association was no longer significant. **CONCLUSION:** Our findings suggest that elevated PAI-1 levels are associated with higher BMD in obese diabetic patients but the possible implications of this finding and underlying mechanisms

still remain unclear. Obviously, metabolic parameters, may affect both BMD and PAI-levels, and association of PAI-1 and BMD could be indirect. However, as pyrilinks is also independently and significantly negatively correlated to PAI-1 its direct involvement in bone metabolism is also plausible. Further investigations are needed to elucidate the nature of interaction of this matrix modulator in relation to energy and bone metabolism in humans.

Ostojić V. Increased specific immunoglobulin G4 antibodies induced by natural exposure to ambrosia pollen in patients with allergy. Allergy Asthma Proc. 2016;37(2):115-20.

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BACKGROUND: Induction of specific immunoglobulin G4 (slgG4) response (so-called blocking antibodies) in patients who receive specific immunotherapy (SIT) has been observed for many years. Although many other mechanisms have been identified as key regulators of immunologic processes in peripheral tolerance to allergens, the rise of slgG4 during immunotherapy, together with the clinical improvement, is still believed to be one of the most important mechanisms through which SIT reaches its clinical efficacy. **OBJECTIVE:** The aim of this prospective study was to measure levels of IgG4 and slgE in subjects allergic to *Ambrosia elatior* pollen (common ragweed), before and during natural exposure to *A. elatior* pollen. Healthy controls were also included. **METHODS:** Twenty-four patients with allergic diseases of the respiratory tract and 24 healthy controls entered the study. The slgG4 and slgE levels were measured by using the enzyme-linked immunosorbent assay method before and during *A. elatior* pollination season. **RESULTS:** A significant increase of the slgG4 level in subjects with allergy during natural exposure to an allergen (0.676 increased to 0.937; $p < 0.05$) was shown. An increase in slgE levels was also observed. Healthy subjects had comparable levels of slgG4 as in subjects with allergy before the pollination season and no change in slgG4 and slgE levels during the pollination season. **CONCLUSION:** Increases of slgG4 and slgE levels were induced by natural allergen exposure in subjects with allergy but not in healthy individuals. This result support further reevaluation of the "blocking" antibodies concept as one concept responsible for allergen tolerance in patients who receive SIT.

Baric M¹, Sever AZ², Vuletic LB², Rasic Z¹, Sever M¹, Drmic D³, Pavelic-Turudic T⁴, Sucic M⁵, Vrcic H⁴, Seiwert S², Sikiric P³. Stable gastric pentadecapeptide BPC 157 heals rectovaginal fistula in rats. Life Sci. 2016;148:63-70.

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AIM: Rectovaginal fistula is a devastating condition providing more than 99% of patients for surgical treatment. We hypothesized that rectovaginal fistula may be healed by therapy with stable gastric pentadecapeptide BPC 157, in consistence with its initial clinical application and effect on external fistulas. **MAIN METHODS:** BPC 157 (10µg/kg or 10ng/kg) was given perorally, in drinking water (0.16µg/ml or 0.16ng/ml, 12ml/rat/day) till sacrifice, or alternatively, intraperitoneally, first application at 30min after surgery, last at 24h before sacrifice. Controls simultaneously received an equivolume of saline (5.0ml/kg ip) or water only (12ml/rat/day). The assessment (i.e., rectal and vaginal defect, fistula leakage, defecation through the fistula, adhesions and intestinal obstruction as healing processes) was at day 1, 3, 5, 7, 10, 14 and 21. **KEY FINDINGS:** Regularly, rectovaginal fistulas exhibited poor healing, with both of the defects persisting, continuous fistula leakage, defecation through the fistula, advanced adhesion formation and intestinal obstruction. By contrast, BPC 157 given perorally or intraperitoneally, in µg- and ng-regimens rapidly improved the whole presentation, with both rectal and vaginal defects simultaneously ameliorated and eventually healed. The maximal instilled volume was continuously raised till the values of healthy rats were achieved, there were no signs of defecation through the fistula. A counteraction of advanced adhesion formation and intestinal obstruction was achieved. Microscopic improvement was along with macroscopic findings. **SIGNIFICANCE:** BPC 157 effects appear to be suited to induce a full healing of rectovaginal fistulas in rats.