# CROATIAN INTERNATIONAL PUBLICATIONS

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**Kozić Dokmanović S[1], Kolovrat K[1], Laškaj R[1], Jukić V[1], Vrkić N[2], Begovac J[3]. Effect of extra virgin olive oil on biomarkers of inflammation in HIV-infected patients: a randomized, crossover, controlled clinical trial. Med Sci Monit. 2015;21:2406-13.**

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BACKGROUND Premature atherosclerosis in HIV-infected patients is associated with chronic infection by itself and adverse effects of antiretroviral treatment (ART). Extra virgin olive oil (EVOO) has a beneficial effect on the cardiovascular system because of its anti-inflammatory properties. The objective of this study was to determine whether the consumption of EVOO improves inflammation and atherosclerosis biomarkers in HIV-infected patients receiving ART. MATERIAL AND METHODS This randomized, crossover, controlled trial included 39 HIV-positive male participants who consumed 50 mL of EVOO or refined olive oil (ROO) daily. Four participants dropped out of the study. Leukocyte count, erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hsCRP), interleukin-6, fibrinogen, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, malondialdehyde, glutathione-peroxidase, superoxide dismutase, oxidized LDL and von Willebrand factor were determined before the first and after each of the 2 intervention periods. Intervention and washout periods lasted for 20 and 14 days, respectively. RESULTS In participants with >90% compliance (N=30), hsCRP concentrations were lower after EVOO intervention (geometric mean [GM], 1.70 mg/L; 95% confidence interval [CI], 1.15-2.52) compared to ROO administration (GM, 2.92 mg/L; 95% CI, 1.95-4.37) (p=0.035). In participants using lopinavir/ritonavir, ESR and hsCRP concentrations decreased 62% and 151%, respectively, after EVOO administration. In the whole study population (N=35) we found no difference in analyzed biomarkers after EVOO administration. CONCLUSIONS Our exploratory study suggests that EVOO consumption could lower hsCRP in patients on ART.

**Nikolac N[1], Simundic AM[2], Kackov S[3], Serdar T[4], Dorotic A[5], Fumic K[6], Gudasic-Vrdoljak J[7], Klenkar K[8], Sambunjak J[9], Vidranski V[10]. The quality and scope of information provided by medical laboratories to patients before laboratory testing: survey of the working group for patient preparation of the Croatian society of medical biochemistry and laboratory medicine. Clin Chim Acta. 2015;450:104-109.**

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INTRODUCTION: The aim of this work was to evaluate to what extent the scope and content of information provided to patients is standardized across medical biochemistry laboratories in Croatia. MATERIALS AND METHODS: Two on-line self-report surveys were sent out: Survey A regarding attitudes on importance of patient preparation and Survey B on the contents of patient preparation instructions. RESULTS: 13/118 laboratories (11%) do not provide written instructions to patients on how to prepare for laboratory testing, and 36 (40%) do not include information about water intake in their instructions. Only half of laboratories provide instructions for prostate-specific antigen (53.8%), female sex hormones (53.7%) and therapeutic drug monitoring (TDM) (52.5%). Inadequate information about fasting status (55.0%) and 24hour urine collection (77.9%) were frequent errors with high severity and were associated with the greatest potential to cause patient harm. CONCLUSIONS: Laboratory professionals in Croatia have a positive attitude towards the importance of patient preparation for laboratory testing. However, the information for laboratory testing is not standardized and frequently lacks guidance for tests related to TDM, coagulation and endocrinology. This study highlights the need for standardized, updated and evidence-based recommendations for patient preparation in order to minimize the risk for patients.

**Matosevic P[1], Klepac-Pulanic T[2], Kinda E[1], Augustin G[1], Brcic I[3], Jakic-Razumovic J[3]. Immunohistochemical expression of 8-oxo-7,8-dihydro-2'-deoxyguanosine in cytoplasm of tumour and adjacent normal mucosa cells in patients with colorectal cancer. World J Surg Oncol. 2015;13(1):241.**

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BACKGROUND: The aim of this research was to study the levels of 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) in tumour tissue samples of colorectal carcinoma based upon immunohistochemical detection and compare those results with patients' outcome. METHODS: Tumour blocks of patients surgically treated for colorectal cancer were evaluated by 8-oxodG immunohistochemical staining. The expression was analysed in 500 tumour cells. The percentage of positive cells, as well as staining intensity, was recorded, and Allred score was calculated. For each patient, data of age, gender, tumour size and location, margin status, histologic grade, tumour stage, lymph node status, vascular invasion, overall survival, and therapy protocols were collected. Tumour grade was divided into two groups as low and high grade. RESULTS: In this study, 146 consecutive patients with primary colorectal carcinoma were included. All data were available for 138 patients, and they were included in this research. There were 83 male and 55 female patients; the median age was 64 years (range 35-87 years). The results showed shorter 5- and 10-year survival in patients with 8-oxodG positive tumour cells (5-year survival, $n = 138$, Mantel-Cox, chi-square 4.116, degree of freedom (df) = 1, $p < 0.05$; 10-year survival, $n = 134$, Mantel-Cox, chi-square 4.374, $df = 1$, $p < 0.05$). The results showed a positive correlation between Allred score and high tumour grade (two-tailed Spearman's $\rho$ 0.184; $p < 0.05$), as well as with non-polypoid tumour growth (two-tailed Spearman's $\rho$ 0.198; $p < 0.05$). There was no significant difference of 8-oxodG expression related to age, sex, blood group, size and tumour site, distance from the edge of the resected tumour margin, lymph nodes involvement, and vascular invasion. CONCLUSIONS: In this study, the positive correlation between 8-oxodG presence in the tumour cells, worse clinical outcome, higher tumour grade, and flat morphology was found.

**Komić D[1], Marušić SL[2], Marušić A[3]. Research integrity and research ethics in professional codes of ethics: survey of terminology used by professional organizations across research disciplines. PLoS One. 2015;10(7):e0133662.**

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Professional codes of ethics are social contracts among members of a professional group, which aim to instigate, encourage and nurture ethical behaviour and prevent professional misconduct, including research

and publication. Despite the existence of codes of ethics, research misconduct remains a serious problem. A survey of codes of ethics from 795 professional organizations from the Illinois Institute of Technology's Codes of Ethics Collection showed that 182 of them (23%) used research integrity and research ethics terminology in their codes, with differences across disciplines: while the terminology was common in professional organizations in social sciences (82%), mental health (71%), sciences (61%), other organizations had no statements (construction trades, fraternal social organizations, real estate) or a few of them (management, media, engineering). A subsample of 158 professional organizations we judged to be directly involved in research significantly more often had statements on research integrity/ethics terminology than the whole sample: an average of 10.4% of organizations with a statement (95% CI = 10.4-23-5%) on any of the 27 research integrity/ethics terms compared to 3.3% (95% CI = 2.1-4.6%), respectively (P<0.001). Overall, 62% of all statements addressing research integrity/ethics concepts used prescriptive language in describing the standard of practice. Professional organizations should define research integrity and research ethics issues in their ethics codes and collaborate within and across disciplines to adequately address responsible conduct of research and meet contemporary needs of their communities.

**Pibernik-Okanović M[1], Hermanns N[2], Ajduković D[1], Kos J[1], Prašek M[1], Šekerija M[3], Lovrenčić MV[1]. Does treatment of subsyndromal depression improve depression-related and diabetes-related outcomes? A randomised controlled comparison of psychoeducation, physical exercise and enhanced treatment as usual. Trials. 2015;16:305.**

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BACKGROUND: Elevated depressive symptoms that do not reach criteria for a clinical diagnosis of depression are highly prevalent in persons with diabetes. This study was aimed at determining the efficacy of psychoeducation and physical exercise compared with enhanced treatment as usual on 1-year changes in depressive symptoms, diabetes distress and self-management, and quality of life and metabolic control in type 2 diabetes patients with subsyndromal depression. METHODS: Adult type 2 diabetes patients who screened positively for depression and expressed a need for professional help with mood-related issues were eligible. Exclusion criteria were clinical depression, current psychiatric treatment and advanced diabetes complications. Out of 365 eligible patients 209 consented to either 6 weekly sessions of psychoeducation (A) and physical exercise (B), or to enhanced treatment as usual (C). Computer-generated sequences for block randomisation stratified by gender were used. Depressive symptoms (primary outcome) and diabetes distress, diabetes self-care, metabolic control and health-related quality of life (secondary outcomes) were analysed at 6-month and 12-month follow-up using repeated-measures ANOVAs. RESULTS: Out of the 74 patients randomised into group A, 66 into B and 69 into group C, 203 completed the interventions, and 179 patients with all 3 assessments were analysed. Depressive symptoms in participants from the psychoeducational, physical exercise and the enhanced treatment as usual groups improved equally from baseline to 12-month follow-up (time versus time x group effect; $F = 12.51$, $p < 0.001$, $\eta(2) = 0.07$ and $F = 0.609$, $p = 0.656$, $\eta(2) = 0.007$ respectively), as did diabetes distress and quality of life (all $p < 0.001$), diabetes self-care ($p < 0.001$ to $< 0.05$), triglycerides, and total cholesterol and LDL-cholesterol ($p < 0.001$). CONCLUSIONS: The employed interventions had comparable positive effects on 12-month psychological and diabetes-related outcomes suggesting that even minimal intervention addressing patients' diabetes-related problems and concerns had favourable clinical implications and might be sufficient to treat subsyndromal depression. Further investigation is warranted to clarify possible mechanisms of improvement. TRIAL REGISTRATION: Current Controlled Trials ISRCTN05673017.

**Jelavić TB, Miše BP, Strikic A, Ban M, Vrdoljak E. Adjuvant chemotherapy in locally advanced cervical cancer after treatment with concomitant chemoradiotherapy - room for improvement? Anticancer Res. 2015;35(7):4161-5.**

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BACKGROUND: The standard treatment for locally advanced cervical cancer (LACC) is concomitant chemoradiotherapy. In the majority of patients with LACC after pro-

perly executed concomitant chemoradiotherapy local control of the disease is achieved, and consequently distant relapse becomes the main cause of death for these patients. In an attempt to improve the outcome of patients with LACC, we designed a regimen of concomitant chemobrachyradiotherapy with cisplatin and ifosfamide followed by consolidation chemotherapy. PATIENTS AND METHODS: Between 1999 and 2012, 118 patients diagnosed with LACC, The International Federation of Gynecology and Obstetrics (FIGO) stages IB2-IVA, regardless of histology, were treated with concomitant chemobrachyradiotherapy and consolidation chemotherapy at our Institution. Chemotherapy consisted of two cycles of cisplatin and ifosfamide applied concomitantly with two intracavitary low-dose rate brachytherapy applications, and of four cycles of the same drug combination as an adjuvant/consolidation part of the treatment. The primary outcome in this analysis was distant disease-specific survival. RESULTS: A total of 18 patients had documented relapse of cervical cancer, with only three local recurrences observed; 15 patients developed only distant recurrence, and one patient developed both local and distant recurrence. The distant disease-specific survival after a median follow-up of 96 months was 86.4%. CONCLUSION: Consolidation or adjuvant chemotherapy that follows concomitant chemoradiotherapy has a potential role in further improving control of the disease, especially distant control of the disease.

**Mikolasevic I, Racki S, Spanjol J, Zupan Z, Jakopcic I, Devcic B, Orlic L. Outcomes following renal transplantation in older renal transplant recipients: a single-center experience and "Croatian senior program". Int Urol Nephrol. 2015;47(8):1415-22.**

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BACKGROUND/OBJECTIVE: Outcomes of kidney transplantation in older patients have not, however, been fully defined. The aims of this study were to analyze the number of new end-stage renal disease (ESRD) patients ≥65 years of age who were managed with kidney transplantation and their survival through the study period. In addition, we have analyzed post-transplantation outcomes in younger and older renal transplant recipients (RTRs). METHODS: We have analyzed the mean age of 505 RTRs transplanted between January 1990 and December 2013. Older people were defined as aging 65 years or older. Of 505 RTRs, there were 73 (14.5 %) patients who were ≥65 years of age. Therefore, in further analysis, patients were divided into two subgroups: younger recipients (younger than 65 years) and older recipients (aging 65 years or older). RESULTS: In the period from 1990 to 2001, patients who were 65 years of age and older were only sporadically treated with kidney transplantation in Croatia. Since 2002, the number of patients older than 65 years undergoing renal transplantation has been increasing. The older recipients were more likely to receive organs from older donors (52.6 ± 16.8 vs. 45.8 ± 13.2; p = 0.0001). There were no significant differences due to HLA mismatch between the two groups of analyzed patients. There was no difference in the rates of DGF between the older and younger recipients. Older recipients were less likely than younger recipients to have acute rejection crisis during the first-ear after transplantation (16.4 vs. 34.7 %; p = 0.03). There were no significant differences due to readmission rates in the first-year post-transplantation between the two groups. There was no significant difference due to graft function and 1-year graft and patient's survival between young and older recipients. Serum creatinine values at 1 year were higher in older recipients who received kidneys from elderly donor. CONCLUSION: Our experience supports the use of kidney transplantation in the population of older ESRD patients. We can increase patients and graft survivals in elderly individuals with careful pre-transplant evaluation and HLA matching. "Croatian senior program" that includes HLA matching represents a good approach for kidney transplantation in older ESRD patients.

**Kapuralin K[1], Ćurlin M[1], Mitrečić D[1], Kosi N[1], Schwarzer C[2], Glavan G[3], Gajović S[1]. STAM2, a member of the endosome-associated complex ESCRT-0 is highly expressed in neurons. Mol Cell Neurosci. 2015;67:104-15.**

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STAM2 (signal transducing adaptor molecule 2), a subunit of the ESCRT-0 complex, is an endosomal protein

acting as a regulator of receptor signaling and trafficking. To analyze STAM2 in the nervous system, its gene expression and protein localization in the mouse brain were identified using three methods: mRNA in situ hybridization, immunohistochemistry, and via lacZ reporter in frame with Stam2 gene using the gene trap mouse line Stam2(Gt1Gaj). STAM2 intracellular localization was analyzed by subcellular fractionation and co-immunofluorescence using confocal microscopy. Stam2 was strongly expressed in the cerebral and cerebellar cortex, hippocampal formation, olfactory bulb, and medial habenula. The majority of STAM2-positive cells co-stained with the neuronal markers. In neurons STAM2 was found in the early endosomes and also in the nucleus. The other members of the ESCRT-0 complex co-localized with STAM2 in the cytoplasm, but they were not present in the nucleus. The newly identified neuron-specific nuclear localization of STAM2, together with its high expression in the brain indicated that STAM2 might have a specific function in the mouse nervous system.