

CROATIAN INTERNATIONAL PUBLICATIONS

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Grošić V, Folnegović Grošić P, Kalember P, Bajs Janović M, Radoš M, Mihanović M, Henigsberg N. The effect of atypical antipsychotics on brain N-acetylaspartate levels in antipsychotic-naïve first-episode patients with schizophrenia: a preliminary study. *Neuropsychiatr Dis Treat.* 2014;10:1243-53.

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PURPOSE: To investigate the correlates of a clinical therapeutic response by using the parameters measured by proton magnetic resonance spectroscopy after the administration of atypical antipsychotics. **PATIENTS AND METHODS:** Twenty-five antipsychotic-naïve first-episode patients with schizophrenia were monitored for 12 months. The patients were evaluated using (1)H magnetic resonance spectroscopy in the dorsolateral prefrontal cortex and Positive and Negative Syndrome Scale, Clinical Global Impression Scale of Severity, Tower of London - Drexel University, Letter-Number Span Test, Trail Making Test A, and Personal and Social Performance Scale. They were administered atypical antipsychotics, starting with quetiapine. In the absence of a therapeutic response, another antipsychotic was introduced. **RESULTS:** After 12 study months, the N-acetylaspartate/creatinine (NAA/Cr) level did not significantly change at the whole-group level. Additional analysis revealed a significant rise in the NAA/Cr level in

the study group that stayed on the same antipsychotic throughout the study course ($P=0.008$) and a significant drop in NAA/Cr in the study group that switched antipsychotics ($P=0.005$). On the whole-group level, no significant correlations between NAA/Cr values and other scores were found at either baseline or after 12 study months. **CONCLUSION:** One-year treatment with atypical antipsychotics administered to antipsychotic-naïve patients didn't result in a significant rise in the NAA/Cr ratio. However, a significant rise was witnessed in the study group in which a satisfactory therapeutic response had been achieved with a single antipsychotic administration.

Miljković A, Stipčić A, Braš M, Dorđević V, Brajković L, Hayward C, Pavić A, Kolčić I, Polašek O. Is experimentally induced pain associated with socioeconomic status? Do poor people hurt more? *Med Sci Monit.* 2014;20:1232-8.

Medical School, University of Split, Split, Croatia; University Department for Health Care Studies, University of Split, Split, Croatia; Centre for Palliative Medicine, Medical Ethics and Communication Skills, Medical School, University of Zagreb, Zagreb, Croatia; Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom; Surgery Clinic, Clinical Hospital Centre Split, Split, Croatia.

BACKGROUND The association of pain and socioeconomic status is widely reported, yet much less clearly understood. The aim of this study was to investigate the association of experimentally induced pain threshold and tolerance with socioeconomic status. **MATERIAL AND METHODS** The study sample consisted of 319 adult

subjects from the population of the island of Vis, Croatia, which was previously shown to have a high level of social homogeneity. A manual dolorimeter was used to measure mechanical pressure pain threshold (least stimulus intensity) and pain tolerance (maximum tolerance stimulus intensity) on both hands. Pain tolerance interval was defined as the difference between pain tolerance and threshold. Years of schooling and material status were used as socioeconomic estimates. RESULTS Both of the socioeconomic estimates were significantly correlated with pain threshold, tolerance, and tolerance interval ($P < 0.001$). The mixed modeling analysis, controlled for the effects of age, gender, and 4 psychological variables, indicated that education was not a significant predictor in any of the 3 models. However, lower material status was significantly associated with lower pain tolerance ($P = 0.038$) and narrower pain tolerance interval ($P = 0.032$), but not with pain threshold ($P = 0.506$). The overall percentages of explained variance were lower in the tolerance interval model (20.2%) than in pain tolerance (23.1%) and threshold (33.1%), suggesting the increasing share of other confounding variables in pain tolerance and even more so in tolerance interval model. CONCLUSIONS These results suggest a significant association between experimentally induced pain tolerance and tolerance interval with material status, suggesting that poor people indeed do hurt more.

Kranjčević K, Bergman Marković B, Ivezić Lalić D, Vrdoljak D, Vučak J. Is a targeted and planned GP intervention effective in cardiovascular disease prevention? A randomized controlled trial. Med Sci Monit. 2014;20:1180-7.

General Practice Office, Zagreb-Zapad Health Care Center, Zagreb, Croatia; Department of Family Medicine, University of Zagreb, School of Medicine, Zagreb, Croatia; General Practice Office, Kutina Health Care Center, Novska, Croatia; Department of Family Medicine, University of Split, School of Medicine, Split, Croatia; General Practice Office, Sukošan, Zadar, Croatia.

BACKGROUND: The optimal intensity and duration of the intervention to achieve sustained risk reduction in patients at high and very high cardiovascular (CV) risk still need to be established. The aim of this study was to evaluate the impact of general practitioner's (GP's) systematic and planned intervention on total CV risk reduction and a change in individual CV risk factors. MATERI-

AL AND METHODS: This was a cluster-randomized trial (ISRCTN31857696) including 64 practices and 3245 patients aged ≥ 40 . The participating GPs and their examinees were randomized into an intervention or to a control group (standard care). Intervention group practitioners followed up their examinees during 1, 3, 6, 12, and 18 months. The main outcome measures were change in proportion of patients with low, moderate, high, and very high CV risk, and change in individual CV risk factors from the first to the second registration. RESULTS: The proportion of patients with very high CV risk was lower in the intervention group, the same as of patients with high blood pressure, total and LDL cholesterol, and increased intake of alcohol. The mean systolic (-1.49 mmHg) and diastolic (-1.57 mmHg) blood pressure, triglycerides (-0.18 mmol/L), body mass index (-0.22), and waist (-0.4 cm) and hip circumference (-1.08 cm) was reduced significantly in the intervention group. There was no additional impact in the intervention group of other tested CV risk factors. CONCLUSIONS: Systematic and planned GP's intervention in CVD prevention reduces the number of patients with very high total CV risk and influences a change in lifestyle habits.

Ivekovic H, Rustemovic N, Brkic T, Ostojic R, Monkemuller K. Endoscopic ligation ("Loop-And-Let-Go") is effective treatment for large colonic lipomas: a prospective validation study. BMC Gastroenterol. 2014;14(1):122.

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BACKGROUND: Colonic lipomas (CL) are rare benign adipose tumours usually found incidentally during colonoscopy. Endoscopic resection of symptomatic large CL remains controversial, since significant rates of perforation have been reported. In recent years, a novel technique for removal of large CL has been described, consisting of looping and ligating the lipoma with a nylon snare. The aim of our study was to evaluate the safety and efficacy of the "loop and let go" technique for large colon lipomas in a large case series. METHODS: Consecutive patients referred to our institution for colonoscopy were eligible for the study. The diagnosis of CL was confirmed endoscopically by "pillow" and "naked fat" signs. Following diagnosis, lipomas were looped and ligated by endoloop. Follow-up colonoscopies were scheduled at 1- and 3-months interval. RESULTS: A total of 11 patients with large CL were

enrolled in study. The indications for the colonoscopy included altered bowel habits (7 patients, 64%), screening for colorectal neoplasm (3 pts, 27%) and lower gastrointestinal bleeding (1 pts, 9%). The median lesion size was 3 cm (range 2,5-6 cm). Lesions were located at the hepatic flexure in 4 patients (36%), cecum and ascending colon (4 pts, 36%), rectosigmoid (2 pts, 18%) and transverse colon (1 pts, 9%). There were no immediate and late complications. On follow-up (median follow-up time 11,9 months, range 8-24), there was one small residual lipoma (<1 cm). CONCLUSION: The results of this study confirm that "loop-and-let-go" technique is safe and efficacious treatment of large colonic lipomas.

Mikolasevic I, Orlic L, Milic S, Zaputovic L, Lukenda V, Racki S. Non-Alcoholic Fatty Liver Disease Proven by Transient Elastography in Hemodialysis Patients: Is It a New Risk Factor for Adverse Cardiovascular Events? Blood Purif. 2014;37(4):259-265.

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BACKGROUND/AIMS: Cardiovascular diseases (CVD) are the leading cause of mortality in hemodialysis (HD) patients. Recently, non-alcoholic fatty liver disease (NAFLD) has been recognized as a new risk factor for adverse CVD events in the general population. Our aim was to analyze the incidence of NAFLD in HD patients by using transient elastography and to analyze whether the presence of NAFLD is associated with a higher CVD risk in HD patients. METHODS: The subjects were 72 HD patients and 50 sex- and age-matched controls. RESULTS: NAFLD was found in 52.8% of HD patients. HD patients with NAFLD showed more carotid atherosclerosis and more adverse CVD events than HD patients without NAFLD and control subjects. CONCLUSION: We showed for the first time that HD patients have a high prevalence of NAFLD. HD patients with NAFLD show an advanced carotid atherosclerosis. Detection of NAFLD by transient elastography should alert to the existence of an increased cardiovascular risk in HD patients.

Kutleša M, Lepur D, Baršić B. Therapeutic hypothermia for adult community-acquired bacterial meningitis-Historical control study. Clin Neurol Neurosurg. 2014;123:181-6.

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OBJECTIVE: Despite advances in antibiotic therapy and critical care, community-acquired bacterial meningitis (CABM) continues to have poor outcome in a significant portion of patients. This study was designed to assess the efficacy of therapeutic hypothermia (TH) in the treatment of CABM. MATERIAL AND METHODS: In a period from January 2009 to January 2013, 41 enrolled patients with CABM were treated with TH. Their outcome was compared to 90 patients in the historical control group that were recruited from the existing database and included patients in a period between 1994 and 2008 with Glasgow coma scale score (GCS) ≤ 9 and respiratory failure. TH was indicated in patients with GCS ≤ 9 , respiratory failure, and breath holding index ≤ 0.835 (measured with transcranial Doppler). If the acoustic window was absent, GCS ≤ 9 plus optic nerve sheath diameter of ≥ 6 mm plus respiratory failure were indications for TH. RESULTS: Outcome variables were mortality and neurologic recovery measured with the Glasgow outcome scale (GOS). The incidence of hospital mortality (19.5% vs 48.9%, $p=0.002$) and adverse neurological outcome (GOS 1-3) (43.9% vs 65.6%, $p=0.023$) were significantly lower in patients treated with TH. Multivariate analysis confirmed the positive effect of TH on hospital mortality (OR=0.059, 95% CI 0.017-0.211) and risk of adverse neurological outcome (OR=0.209, 95% CI 0.082-0.534) after an adjustment for other risk factors of unfavorable patients' outcome. CONCLUSIONS: The new therapeutic concept based on hypothermia significantly improves the outcome in adult patients with severe CABM.

Supe S, Božina N, Matijević V, Bazina A, Mišmaš A, Ljevak J, Alvir D, Habek M, Poljaković Z. Prevalence of genetic polymorphisms of CYP2C9 and VKORC1 - Implications for warfarin management and outcome in Croatian patients with acute stroke. J Neurol Sci. 2014;343(1-2):30-5.

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Laboratory Diagnosis, Zagreb University Hospital Center, Department of Pharmacology, Zagreb, Croatia; University of Zagreb, School of Medicine, Croatia.

BACKGROUND: Data on the prevalence of CYP2C9 and VKORC1 genes and their influence on anticoagulant effect and warfarin dose in stroke patients are scarce. The aim of this study was to determine the occurrence and significance of these gene polymorphisms and to establish pharmacogenetic algorithm to estimate the dose of introduction. Also, the goal was to determine tailored safety and intensity of anticoagulation response depending on the allelic variants and their impact on the clinical outcome in acute stroke patients in Croatia. **METHODS:** A total of 106 consented acute stroke patients were tested for CYP2C9*2,*3 and VKORC1 1173C>T gene polymorphisms. We estimated the dose of introduction and monitored anticoagulant effect obtained by INR values, time to reach stable dose, stable maintenance dose, time spent within the therapeutic/supratherapeutic INR range, occurrence of dosage side effects and clinical outcome depending on genotypes. **RESULTS:** We found that 83% of stroke patients in our study were carriers of multiple allelic variants. The predicted initial dose correlated with the stable warfarin maintenance dose ($p=0.0311$) and we correctly estimated the dose for 81.5% of 61.3% of study patients who required higher/lower doses than average. Warfarin dosage complications were slightly more frequent among the carriers of CYP2C9*2,*3 compared to the carriers of VKORC1 1173T alleles (68.9% versus 62.5%), but their occurrence did not affect the final clinical outcome. **CONCLUSION:** Our data indicated rapid and safe anticoagulation achieved by using pharmacogenetically-predicted warfarin dose in high-risk acute stroke patients without increasing the risk of warfarin dosage complications in an elderly population.

Orešković D, Klarica M. A new look at cerebrospinal fluid movement. *Fluids Barriers CNS.* 2014;11:16.

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Brinker et al. extensively reviewed recent findings about CSF circulation in a recent article: "A new look at cerebrospinal circulation", but did not analyze some important available data in sufficient detail. For example, our findings as well as some clinical data and experimental results obtained from different animal species, do not support unidirectional CSF circulation but strongly suggest that there are cardiac cycle-dependent systolic-diastolic to-and-fro cranio-spinal CSF movements. These are based on: a) physiological oscillations of arterial and venous blood during cranio-spinal blood circulation; b) respiratory activity, and c) body activity and posture. That kind of complex CSF movement could explain the observed distribution of many different substances in all directions along the CSF system and within central nervous system tissue. It seems that efflux transport systems at capillary endothelium may be more important for brain homeostasis than the removal of metabolites by CSF flow. Thus, when discussing the CSF dynamics we suggest that a more appropriate term would be CSF movement rather than CSF circulation.