

CROATIAN INTERNATIONAL PUBLICATIONS

by Ivan Bohacek

ibohacek@hiim.hr



Opačić D, Rustemović N, Kalauz M, Markoš P, Ostojić Z, Majerović M, Ledinsky I, Višnjic A, Krznarić J, Opačić M. Endoscopic ultrasound elastography strain histograms in the evaluation of patients with pancreatic masses. *World J Gastroenterol.* 2015;21(13):4014-9.

Clinical Hospital Center Zagreb, Zagreb, Croatia

AIM: To investigate the accuracy of the strain histogram endoscopic ultrasound (EUS)-based method for the diagnostic differentiation of patients with pancreatic masses. **METHODS:** In a prospective single center study, 149 patients were analyzed, 105 with pancreatic masses and 44 controls. Elastography images were recorded using commercially available ultrasound equipment in combination with EUS linear probes. Strain histograms (SHs) were calculated by machine integrated software in regions of interest and mean values of the strain histograms were expressed as Mode 1 (over the mass) and Mode 2 (over an adjacent part of pancreatic tissue, representing the reference area). The ratio between Mode 2 and Mode 1 was calculated later, representing a new variable, the strain histogram ratio. After the final diagnosis was established, two groups of patients were formed: a pancreatic cancer group with positive cytology achieved by fine needle aspiration puncture or histology after surgery (58 patients), and a mass-forming pancreatitis group with negative cytology and follow-up after 3 and 6 mo (47 patients). All statistical analyses were conducted in SPSS 14.0 (SPSS Inc., Chicago, IL, United States). **RESULTS:** Results were obtained with software for strain histograms with reversed hue scale (0 represents the hardest tissue structure and 255 the softest). Based on the receiver operating characteristics (ROC) curve coordinates, the cut-off point for Mode 1 was set at the value of 86. Values under the cut-off point indicated the presence of pancreatic malignancy. Mode 1 reached 100% sensitivity and 45% specificity with overall accuracy of 66% (95%CI: 61%-66%) in detection of pancreatic malignant tumors among the patients with pancreatic masses. The positive and negative predictive values were 54% and

100%, respectively. The cut-off for the new calculated variable, the SH ratio, was set at the value 1.153 based on the ROC curve coordinates. Values equal or above the cut-off value were indicative of pancreatic malignancy. The SH ratio reached 98% sensitivity, 50% specificity and an overall accuracy of 69% (95%CI: 63%-70%). The positive and negative predictive values were 92% and 100%, respectively. **CONCLUSION:** SH showed high sensitivity in pancreatic malignant tumor detection but disappointingly low specificity. Slight improvements in specificity and accuracy were achieved using the SH ratio.

Yilmaz G¹, Oto M¹, Thabet AM², Rogers KJ¹, Anticevic D³, Thacker MM¹, Mackenzie WG¹. Correction of lower extremity angular deformities in skeletal dysplasia with hemiepiphysiodesis: a preliminary report. *J Pediatr Orthop.* 2014;34(3):336-45.

¹Nemours/Alfred I. du Pont Hospital for Children, Wilmington, DE; ²Benha Medical School, Benha, Egypt; ³Department of Orthopaedic Surgery, Clinical Hospital Centre Zagreb, School of Medicine, University of Zagreb, Zagreb, Croatia.

BACKGROUND: Lower extremity angular deformities are common in children with skeletal dysplasia and can be treated with various surgical options. Both acute correction by osteotomy with internal fixation and gradual correction by external fixation have been used with acceptable results. Recently, the Guided Growth concept using temporary hemiepiphysiodesis for correction of angular deformities in the growing child has been proposed. This study presents the results of temporary hemiepiphysiodesis using eight-Plates and medial malleolus transphyseal screws in children with skeletal dysplasia with lower extremity angular deformities. **METHODS:** Twenty-nine patients (50 lower extremities) with skeletal dysplasia of different types were treated for varus or valgus deformities at 2 centers. The mean age at the time of hemiepiphysiodesis was 10±2.9 years. A to-

tal of 66 eight-Plates and 12 medial malleolus screws were used. The average follow-up time between the index surgery and the latest follow-up with the eight-Plate in was 25 ± 13.4 months. Erect long-standing anteroposterior and lateral view radiographs were obtained for deformity planning before the procedure. Angular deformities on radiograph were evaluated by mechanical axis deviation, mechanical lateral distal femoral angle, medial proximal tibial angle, and lateral distal tibial angle. Mechanical axis deviation was also expressed as a percentage to one half of the width of the tibial plateau, and the magnitude of the deformity was classified by determining the zones through which the mechanical axis of the lower extremity passed. Four zones were determined on both the medial and lateral side of the knee and the zones were labeled 1, 2, 3, and 4, corresponding to the severity of the deformity. A positive value was assigned for valgus alignment and a negative for varus alignment. RESULTS: Patients were analyzed in valgus and varus groups. There was correction in 34 of 38 valgus legs and 7 of 12 varus legs. In the valgus group, the mean preoperative and postoperative mechanical lateral distal femoral angles were 82.1 ± 3.7 and 91.1 ± 4.9 degrees, respectively ($P < 0.001$). The mean preoperative and postoperative medial proximal tibial angles were 98.5 ± 8 and 87.8 ± 7.1 degrees, respectively ($P < 0.001$). Six patients with bilateral ankle valgus deformities (12 ankles) underwent single-screw medial malleolus hemiepiphysiodesis. The mean preoperative and postoperative lateral distal tibial angles were 73.9 ± 8.7 and 86.1 ± 6.8 degrees, respectively ($P < 0.001$). The numbers of plates in each anatomic location were not enough to make statistical conclusions in varus legs. Four patients in the valgus group and 3 patients in the varus group did not benefit from the procedure. Mechanical axes were in zone 2 or over in 94% of the legs preoperatively, whereas postoperatively, only 23% of the legs had mechanical axes in zone 2 or over in varus and valgus groups. CONCLUSIONS: Growth modulation with an eight-Plate is a relatively simple surgery and has low risk of mechanical failure or physeal damage. It can be performed in very young patients, which is an important advantage in skeletal dysplasia. Screw purchase is reliable even in the abnormal epiphysis and metaphysis. Our results show that Guided Growth using eight-Plates in skeletal dysplasia is safe and effective.

Plestina-Borjan I¹, Katusic D², Medvidovic-Grubisic M³, Supe-Domic D⁴, Bucan K¹, Tandara L⁴, Rogosic V¹. Association of age-related macular degeneration

with erythrocyte antioxidant enzymes activity and serum total antioxidant status. *Oxid Med Cell Longev*. 2015;2015:804054.

¹Department of Ophthalmology, University of Split School of Medicine; ²Department of Ophthalmology, University of Zagreb School of Medicine; ³Department of Ophthalmology, Institute of Navy Medicine, Split; ⁴Department of Medical Laboratory Diagnostics, University of Split School of Medicine, Croatia.

The aim was to estimate association of the oxidative stress with the occurrence of age-related macular degeneration (AMD). The activities of erythrocyte antioxidant enzymes: superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) and additionally serum total antioxidant status (TAS) were used as indicators of the oxidative stress level. 57 AMD patients (32 early and 25 late AMD) and 50 healthy, age and gender matched controls were included. GPx activity ($P < 0.001$) and serum TAS ($P = 0.015$) were significantly lower in AMD patients. The difference was not significant for SOD or CAT activities. Significant interaction between GPx and SOD was detected ($P = 0.003$). At high levels of SOD activity (over 75th percentile), one standard deviation decrease in GPx increases the odds for AMD for six times ($OR = 6.22$; $P < 0.001$). ROC analysis revealed that combined values of GPx activity and TAS are significant determinants of AMD status. Accuracy, sensitivity, specificity, and positive and negative predictive values were 75%, 95%, 52%, 69%, and 90%, respectively. The study showed that low GPx activity and TAS are associated with AMD. SOD modulates the association of GPx and AMD. The results suggest that erythrocyte antioxidant enzymes activity and serum TAS could be promising markers for the prediction of AMD.

Knezovic A, Osmanovic-Barilar J, Curlin M, Hof PR, Simic G, Riederer P, Salkovic-Petrisic M. Staging of cognitive deficits and neuropathological and ultrastructural changes in streptozotocin-induced rat model of Alzheimer's disease. *J Neural Transm*. 2015;122(4):577-92.

Department of Pharmacology and Croatian Institute for Brain Research, University of Zagreb School of Medicine, Zagreb, Croatia.

Sporadic Alzheimer's disease (sAD) is the most common form of dementia. Rats injected intracere-

broventricularly with streptozotocin (STZ-icv) develop insulin-resistant brain state and represent a non-transgenic sAD model with a number of AD-like cognitive and neurochemical features. We explored cognitive, structural and ultrastructural changes in the brain of the STZ-icv rat model over a course of 9 months. Cognitive functions were measured in the STZ-icv- (0.3, 1 and 3 mg/kg) and age-matched control rats by passive avoidance test. Structural changes were assessed by Nissl and Bielschowsky silver staining. Immunohistochemistry and electron microscopy analysis were used to detect amyloid β - ($A\beta$ 1-42) and hyperphosphorylated tau (AT8) accumulation and ultrastructural changes in the brain. Memory decline was time- (≤ 3 months/acute, ≥ 3 months/progressive) and STZ-icv dose-dependent. Morphological changes were manifested as thinning of parietal cortex (≥ 1 month) and corpus callosum (9 months), and were more pronounced in the 3 mg/kg STZ group. Early neurofibrillary changes (AT8) were detected from 1 month onward in the neocortex, and progressed after 3 months to the hippocampus. Intracellular $A\beta$ 1-42 accumulation was found in the neocortex at 3 months following STZ-icv treatment, while diffuse $A\beta$ 1-42-positive plaque-like formations were found after 6 months in the neocortex and hippocampus. Ultrastructural changes revealed enlargement of Golgi apparatus, pyknotic nuclei, and time-dependent increase in lysosome size, number, and density. Our data provide a staging of cognitive, structural/ultrastructural, and neuropathological markers in the STZ-icv rat model that in many aspects seems to be generally comparable to stages seen in human sAD.

Mayer D, Simetin IP, Rodin U, Benjak T, Puntarić E, Puntarić I. The impacts of media messaging and age and sex variance on adolescent smoking habits in Croatia. J Addict Med. 2015;9(2):147-54.

Croatian National Institute of Public Health (DM, IPS, UR, TB), Rockefellerova 7, Zagreb, Croatia; Biology Department (EP), Zagreb University, Zagreb, Croatia; and Zagreb County Institute for Emergency Medicine (IP), Ulica Matice Hrvatske b.b., Velika Gorica, Croatia.

OBJECTIVES: To analyze the effects of age, sex, and media messages that encourage or discourage smoking, in conjunction with having 1 or more parents, close friends, teachers, or family members who smoke, on differences in patterns of adolescent smoking. **METHODS:** This research is based on Croatian responses to the 2011

Global Youth Tobacco Survey. A total of 4245 Croatian youths responded to the Global Youth Tobacco Survey, of which individuals 3551 were aged 13 to 15 years. Of this cross section, 1644 individuals were male; 1856 were female; and 51 were of unknown sex. **RESULTS:** There were significant differences among responses in terms of age. Older adolescents were more likely to smoke ($P < 0.001$) and more likely to experience the following: (1) outdoor exposure to other smokers, including teachers ($P < 0.001$) and fellow students ($P < 0.001$); (2) smoking in the presence of parents or guardians ($P < 0.001$) and best friends ($P < 0.001$). The most prominent predictor of smoking among male adolescents was the existence of a best friend who smokes, with an odds ratio of 6.38 and a corresponding 95% confidence interval of 3.69 to 11.01. Likewise, the most prominent predictor among female adolescents was also the existence of a best friend who smokes, with an odds ratio of 10.21 and a corresponding 95% confidence interval of 4.94 to 21.13. The majority of nonsmokers, 65.5% ($n = 1640$), and smokers, 58.8% ($n = 506$), have never seen advertisements for cigarettes broadcast during televised concerts, and 58.5% of nonsmokers ($n = 1469$) and 58.6% of smokers ($n = 505$) have never seen advertisements for cigarettes while attending concerts. **CONCLUSIONS:** Our study shows that there is no sex difference between the number of nonsmokers and smokers. Older adolescents tend to smoke more, and students who smoke outside reported seeing other adolescents and their teachers smoking almost daily. A majority of youths who reported that they smoke have parents who smoke at home and have close friends who smoke; having a close or best friend who smokes is the highest prediction factor that both male and female youths will begin smoking. The majority of nonsmokers and smokers have never seen prosmoking messages when going to concerts or during other community and social events. This lack of exposure to smoking-related advertising is the result of new legal restrictions imposed in 2008 on tobacco-product producers. There is no statistical significance among smokers' and nonsmokers' perceptions of antismoking media messaging. Peer pressure has been shown to be the second-most influential factor, after having a best friend who smokes, for the likelihood that an individual will become a smoker, among both male and female adolescents.

Poropat G, Giljaca V, Hauser G, Štimac D. Enteral nutrition formulations for acute pancreatitis. Cochrane Database Syst Rev. 2015;3:CD010605.

Department of Gastroenterology, Clinical Hospital Centre Rijeka, Kresimirova 42, Rijeka, Croatia.

BACKGROUND: Acute pancreatitis is a common and potentially lethal disease with increasing incidence. Severe cases are characterised by high mortality, and despite improvements in intensive care management, no specific treatment relevantly improves clinical outcomes of the disease. Meta-analyses suggest that enteral nutrition is more effective than conventional treatment consisting of discontinuation of oral intake with use of total parenteral nutrition. However, no systematic review has compared different enteral nutrition formulations for the treatment of patients with acute pancreatitis. **OBJECTIVES:** To assess the beneficial and harmful effects of different enteral nutrition formulations in patients with acute pancreatitis. **SEARCH METHODS:** We searched the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group Specialised Register of Clinical Trials, the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 7), MEDLINE (from inception to 20 August 2013), EMBASE (from inception to 2013, week 33) and Science Citation Index-Expanded (from 1990 to August 2013); we conducted full-text searches and applied no restrictions by language or publication status. **SELECTION CRITERIA:** We considered randomised clinical trials assessing enteral nutrition in patients with acute pancreatitis. We allowed concomitant interventions if they were received equally by all treatment groups within a trial. **DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed trials for inclusion and extracted data. We performed the analysis using Review Manager 5 (Review Manager 2013) and both fixed-effect and random-effects models. We expressed results as risk ratios (RRs) for dichotomous data, and as mean differences (MDs) for continuous data, both with 95% confidence intervals (CIs). Analysis was based on an intention-to-treat principle. **MAIN RESULTS:** We included 15 trials (1376 participants) in this review. We downgraded the quality of evidence for many of our outcomes on the basis of high risk of bias. Low-quality evidence suggests that immunonutrition decreases all-cause mortality (RR 0.49, 95% CI 0.29 to 0.80). The effect of immunonutrition on other outcomes from a subset of the included trials was uncertain. Subgrouping trials by type of enteral nutrition did not explain any variation in effect. We found mainly very low-quality evidence for the effects of probiotics on the main outcomes. One eligible trial in this comparison reported a higher rate of serious adverse events leading to increased organ failure and mortality due to low numbers of events and low risk of bias. When we excluded this study as a post hoc sensitivity analysis, risks of mortality (RR 0.30, 95% CI 0.10 to 0.84), organ failure (RR 0.74,

95% CI 0.59 to 0.92) and local septic complications (RR 0.40, 95% CI 0.22 to 0.72) were lower with probiotics. In one trial assessing immunonutrition with probiotics and fibres, no deaths occurred, but hospital stay was shorter with immunonutrition (MD -5.20 days, 95% CI -8.73 to -1.67). No deaths were reported following semi-elemental enteral nutrition (EN), and the effect on length of hospital stay was small (MD 0.30 days, 95% CI -0.82 to 1.42). Fibre-enriched formulations reduced the number of other local complications (RR 0.52, 95% CI 0.32 to 0.87) and length of hospital stay (MD -9.28 days, 95% CI -13.21 to -5.35) but did not significantly affect all-cause mortality (RR 0.23, 95% CI 0.03 to 1.84) and other outcomes. Very low-quality evidence from the subgroup of trials comparing EN versus no intervention showed a decrease in all-cause mortality with EN (RR 0.50, 95% CI 0.29 to 0.86). **AUTHORS' CONCLUSIONS:** We found evidence of low or very low quality for the effects of immunonutrition on efficacy and safety outcomes. The role of supplementation of enteral nutrition with potential immunomodulatory agents remains in question, and further research is required in this area. Studies assessing probiotics yielded inconsistent and almost contrary results, especially regarding safety and adverse events, and their findings do not support the routine use of EN enriched with probiotics in routine clinical practice. However, further research should be carried out to try to determine the potential efficacy or harms of probiotics. Lack of trials reporting on other types of EN assessed and lack of firm evidence regarding their effects suggest that additional randomised clinical trials are needed. The quality of evidence for the effects of any kind of EN on mortality was low, and further studies are likely to have an impact on the finding of improved survival with EN versus no nutritional support. Evidence remains insufficient to support the use of a specific EN formulation.

Mihanović M¹, Restek-Petrović B¹, Bogović A², Ivezić E², Bodor D², Požgain I³. Quality of life of patients with schizophrenia treated in foster home care and in outpatient treatment. *Neuropsychiatr Dis Treat.* 2015;11:585-95.

¹Psychiatric Hospital "Sveti Ivan", Zagreb, Croatia; ²Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek; ³Psychiatric Hospital "Sveti Ivan", Zagreb; ³Department of Psychiatry, University Hospital Center Osijek, Croatia.

BACKGROUND: The Sveti Ivan Psychiatric Hospital in Zagreb, Croatia, offers foster home care treatment

that includes pharmacotherapy, group psychodynamic psychotherapy, family therapy, and work and occupational therapy. The aim of this study is to compare the health-related quality of life of patients with schizophrenia treated in foster home care with that of patients in standard outpatient treatment. **METHODS:** The sample consisted of 44 patients with schizophrenia who, upon discharge from the hospital, were included in foster home care treatment and a comparative group of 50 patients who returned to their families and continued receiving outpatient treatment. All patients completed the Short Form 36 Health Survey Questionnaire on the day they completed hospital treatment, 6 months later, and 1 year after they participated in the study. The research also included data on the number of hospitalizations for both groups of patients. **RESULTS:** Though directly upon discharge from the hospital, patients who entered foster home care treatment assessed their health-related quality of life as poorer than patients who returned to their families, their assessments significantly improved over time. After 6 months of treatment, these patients even achieved better results in several dimensions than did patients in the outpatient program, and they also had fewer hospitalizations. These effects remained the same at the follow-up 1 year after the inclusion in the study. **CONCLUSION:** Notwithstanding the limitations of this study, it can be concluded that treatment in foster home care is associated with an improvement in the quality of life of patients with schizophrenia, but the same was not observed for the patients in standard outpatient treatment. We hope that these findings will contribute to an improved understanding of the influence of psychosocial factors on the functioning of patients and the development of more effective therapeutic methods aimed at improving the patients' quality of life.

Abdovic S¹, Pavic AM¹, Milosevic M², Persic M³, Senecic-Cala I⁴, Kolacek S¹. Short Health Scale: A Valid, Reliable, and Responsive Measure of Health-related Quality of Life in Children with Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2015;21(4):818-23.

¹Referral Center for Pediatric Gastroenterology and Nutrition, University Children's Hospital Zagreb, Zagreb Medical School; ²Department of Environmental and Occupational Health, "Andrija Stampar" School of Public Health, University of Zagreb School of Medicine; ³Department for Pediatric Gastroenterology, University Hospital Center Rijeka; ⁴Department for Pediatric Gastroenterology, Hepatology and Nutrition, University Hospital Center Zagreb, Croatia.

BACKGROUND: Inflammatory bowel disease (IBD) presents a growing medical and epidemiological problem. In respect to patients, health-related quality of life (HRQOL) emerged as informative means to evaluate the impact of disease burden on health. The Short Health Scale (SHS), a disease-specific HRQOL instrument with only 4 questions (symptoms, functioning, worry, and general well-being), was demonstrated as valid, reliable, and responsive in adults. Aim of this study was to assess its psychometric properties in children with IBD. **METHODS:** In a multicentric prospective study, HRQOL was assessed in 104 children with IBD by generic (PedsQL) and disease-specific questionnaires (IMPACT-III (HR) and SHS), which were cross-culturally adapted for Croatian. Forty-one patients completed the questionnaires at the second visit 6 to 12 months later. Of them, 27 patients changed from remission to active disease or vice versa and were included in responsiveness to change analysis. **RESULTS:** Patients in remission had significantly better scores for symptoms ($P = 0.022$) and functioning ($P = 0.003$) than those with active disease. Each of the 4 SHS questions was strongly correlated with the corresponding dimensions of PedsQL and IMPACT-III (HR) questionnaires ($r_s = 0.50-0.72$, $P < 0.001$). Reliability was confirmed with Cronbach's $\alpha = 0.74$. Patients who changed from remission to active disease or vice versa showed significant change in following SHS scores: symptoms ($P = 0.032$), functioning ($P = 0.008$), and worry ($P = 0.021$). **CONCLUSIONS:** SHS appears to be valid, reliable, and responsive tool to measure HRQOL in children with IBD. Simplicity of use, compactness, and the possibility of immediate interpretation make SHS well suited for both clinical practice and research studies.