

## CROATIAN INTERNATIONAL PUBLICATIONS

**Marton I, Knezevic F, Ramic S, Milosevic M, Tomas D. Immunohistochemical Expression and Prognostic Significance of HIF-1 $\alpha$  and VEGF-C in Neuroendocrine Breast Cancer. *Anticancer Res* 2012; 32(12):5227-32.**

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AIM: To determine the predictive value of HIF-1 $\alpha$  and VEGF-C in primary neuroendocrine breast cancers (NEBC) and their correlation with other clinico-pathological characteristics of NEBC. MATERIALS AND METHODS: HIF-1 $\alpha$  and VEGF-C were determined immunohistochemically in tissue samples from 31 cases of NEBC. RESULTS: The HIF-1 $\alpha$  expression in NEBC was predominantly negative, with only 5 (16.1%) cases showing strong reaction to HIF-1 $\alpha$ . Eighteen (58.0%) NEBC cases showed moderate-to-strong VEGF-C expression. VEGF-C expression negatively correlated with progesterone receptor positivity ( $p=0.014$ ) and duration of follow-up ( $p=0.021$ ). A multivariate Cox proportional hazard regression analysis showed that HIF-1 $\alpha$  ( $p=0.019$ ) was a significant predictor of disease-free survival, whereas VEGF-C ( $p=0.099$ ) showed no such association. CONCLUSION: HIF-1 $\alpha$  overexpression indicated unfavourable prognosis and could serve as an additional prognostic factor in NEBC. Moreover, patients with NEBC exhibiting moderate or strong VEGF-C expression could be candidates for a specific VEGF-C antibody therapy.

**Ajduković D, Pibernik-Okanović M, Sekerija M, Hermanns N. The reach of depression screening preceding treatment: are there patterns of patients' self-selection? *Int J Endocrinol* 2012;2012:148145.**

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This study evaluated the reach of depression screening followed by treatment programs for subsyndromal depression and explored demographic and clinical characteristics of patients who were reached versus those who were not. A two-item Patient Health Questionnaire-Depression was sent to 4196 type 2 diabetic patients. Posi-

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tively screened patients were interviewed to assess the severity of depression, and those with subclinical symptoms were invited to treatment groups. The reach of screening procedure was evaluated by the total response rate, proportion of positive depression screenings, and proportion of eligible patients entering treatment programs. Predictors of responsiveness to screening and of participation in treatment were determined using logistic regression. Of the 34% of patients who returned the questionnaire ( $n = 1442$ ), 40% reported depressive symptoms and a need for professional help ( $n = 581$ ). Age (OR = 1.06, 95% CI = 1.05-1.08), BMI (OR = 1.02, 95% CI = 1.00-1.04), HbA1C (OR = .92, 95% CI = .86-.99), and LDL-cholesterol (OR = .90, 95% CI = .81-1.00) correlated with response to screening. Willingness to accept treatment was predicted by professional status (OR = 3.24, 95% CI = 1.53-6.87), education (OR = 1.21, 95% CI = 1.05-1.38), and BMI (OR = .91, 95% CI = .85-.98). Older patients with better diabetes control were more likely to be reached by postal screening for depressive symptoms. Professionally inactive, better-educated persons and those with lower BMI were more likely to participate in the intervention for subsyndromal depression.

**Boschi V, Pogorelic Z, Gulan G, Vilovic K, Stalekar H, Bilan K, Grandic L. Subbrachial approach to humeral shaft fractures: new surgical technique and retrospective case series study. *Can J Surg*. 2012;55(6):011911-11911.**

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Background: There are few surgical approaches for treating humeral shaft fractures. Here we present our results using a subbrachial approach. Methods: We conducted a retrospective case series involving patients who had surgery for a humeral shaft fracture between January 1994 and January 2008. We divided patients into 4 groups based on the surgical approach (anterior, anterolateral, posterior, subbrachial). In all patients, an AO 4.5 mm dynamic compression plate was used. Results: During our study period, 280 patients aged 30-36 years underwent surgery for a humeral shaft fracture. The average duration of surgery was shortest using the subbrachial approach (40 min). The av-

erage loss of muscle strength was 40% for the anterolateral, 48% for the posterior, 42% for the anterior and 20% for the subbrachial approaches. The average loss of tension in the brachialis muscle after 4 months was 61% for the anterolateral, 48% for the anterior and 11% for the subbrachial approaches. Sixteen patients in the anterolateral and anterior groups and 6 patients in the posterior group experienced intraoperative lesions of the radial nerve. No postoperative complications were observed in the subbrachial group. Conclusion: The subbrachial approach is practical and effective. The average duration of the surgery is shortened by half, loss of the muscle strength is minimal, and patients can resume everyday activities within 4 months. No patients in the subbrachial group experienced injuries to the radial or musculocutaneous nerves.

**Bursac S, Brdovcak MC, Pfannkuchen M, Orsolic I, Golomb L, Zhu Y, Katz C, Daftuar L, Grabusic K, Vukelic I, Filic V, Oren M, Prives C, Volarevic S. Mutual protection of ribosomal proteins L5 and L11 from degradation is essential for p53 activation upon ribosomal biogenesis stress. Proc Natl Acad Sci U S A. 2012;109(50):20467-72.**

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Impairment of ribosomal biogenesis can activate the p53 protein independently of DNA damage. The ability of ribosomal proteins L5, L11, L23, L26, or S7 to bind Mdm2 and inhibit its ubiquitin ligase activity has been suggested as a critical step in p53 activation under these conditions. Here, we report that L5 and L11 are particularly important for this response. Whereas several other newly synthesized ribosomal proteins are degraded by proteasomes upon inhibition of Pol I activity by actinomycin D, L5 and L11 accumulate in the ribosome-free fraction where they bind to Mdm2. This selective accumulation of free L5 and L11 is due to their mutual protection from proteasomal degradation. Furthermore, the endogenous, newly synthesized L5 and L11 continue to be imported into nucleoli even after nucleolar disruption and colocalize with Mdm2, p53, and promyelocytic leukemia protein. This suggests that the disrupted nucleoli may provide a platform for L5- and L11-dependent p53 activation, implying a role for the nucleolus in p53 activation by ribosomal biogenesis stress. These findings may have important implications with respect to understanding the pathogenesis of diseases caused by impaired ribosome biogenesis.

**Cavka M, Petaros A, Boscic D, Kavur L, Jankovic I, Despot R, Trajkovic J, Brkljacic B. Scenes from the Past: CT-**

**guided Endoscopic Recovery of a Foreign Object from the Cranial Cavity of an Ancient Egyptian Mummy. Radiographics. 2012;32(7):2151-7.**

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The aim of this study was to test the value of computed tomography (CT)-guided endoscopy in the scientific study of mummified remains and the recovery of unidentified objects from ancient mummified remains. CT-guided endoscopy was performed on an Egyptian mummy from the Late Period to help retrieve an unidentified object from its skull. The combined use of CT and endoscopy facilitated the recovery of the object, minimizing further damage to the remains and to the object itself. The successful recovery of the brittle object allowed detailed analysis of the item to be performed in an attempt to determine the nature of its presence in the cranial cavity. It was confirmed that the object was a monocotyledon stem fragment. Relying on the existing literature on mummification and excerebration methods in ancient Egypt, we concluded that the stick was probably used for transnasal removal of the brain. The results of this study demonstrate the great potential of CT-guided endoscopy for minimally invasive recovery of small unidentified items from mummies that could yield important information about mummification procedures and the materials used to preserve bodies.

**Fiolic Z, Bosnjak Z, Snajdar I, Crkvenac Gregorek A, Kalenic S, Budimir A. The Screening of Methicillin-Resistant Staphylococcus aureus in Vascular Surgery Patients: A Comparison of Molecular Testing and Broth-Enriched Culture. Chemotherapy. 2012;58(4):330-6.**

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major global health care-associated pathogen. This study sought to examine the prevalence of MRSA in patients who were admitted to a vascular surgery ward during a 3-month period. Methods: MRSA screening was accomplished through the acquisition of nasal, throat and perineal swabs. These swabs were placed in tryptic soy broth that had been supplemented with 6.5%

NaCl and incubated for 24 h. The resulting isolates were subcultured on agar plates containing 5% sheep blood. The BD GeneOhm MRSA assay for screening swabs was performed in accordance with the manufacturer's instructions. Results: A total of 58 patients were included in the study and swabs from 232 sites were obtained during the sampling period. MRSA was detected in 33 samples of 12 patients during the study period; thus, there was a 20.6% prevalence of patients who were recognized as MRSA carriers. There were discrepancies between the results of classical bacteriological screening and molecular MRSA detection methods in 8 of the patients. Conclusions: Nasal, throat and perineal MRSA screening can detect the carriage of this pathogen and allow for the timely use of appropriate infection control measures. The choice of screening techniques poses a challenge; it has been demonstrated that molecular detection methods should be performed with great sensitivity, specificity and, most importantly, speed. The cost of the PCR screening method is the only disadvantage of this approach.

**Persec J, Persec Z, Kopljar M, Sojic N, Husedzinovic I. Effect of bispectral index monitoring on extubation time and analgesic consumption in abdominal surgery: a randomised clinical trial. Swiss Med Wkly. 2012 Oct 9;142:0.**

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**PRINCIPLES:** The aim of this study was to investigate the effect of bispectral index (BIS) monitoring on intra-operative anaesthesia consumption and extubation time. **Design:** Randomised controlled study. **METHODS:** The study included 45 patients undergoing major abdominal surgery under general anaesthesia in a six month period (February - July 2011), aged 18 years or older, and classified as ASA (American Society of Anaesthesiologists) physical status II or III. Patients were randomly assigned to receive BIS-guided anaesthesia or routine anaesthesia care as a non BIS-guided group. At the induction of anaesthesia, and during the operation the following parameters were continuously recorded: BIS level, heart rate (HR), systolic blood pressure (sBP), end-tidal CO<sub>2</sub> (etCO<sub>2</sub>). Operation time and time to extubation were also recorded. On the first post-operative day all patients were visited and interviewed about intra-operative recall. **RESULTS:** BIS levels in the non BIS-guided group were significantly lower from 30 minutes further to the end of the operation, compared to the BIS-

guided group ( $p < 0.05$ ). Time to extubation was significantly shorter in the BIS-guided group (17.5 min vs. 75 min,  $p < 0.001$ ). There were no statistically significant differences in the required amounts of anaesthetics. In the post-operative interview, none of the patients reported an episode of intra-operative awareness. **CONCLUSION:** Guiding anaesthesia according to BIS level will result in significantly faster recovery after anaesthesia.

**Kruljac I, Cerina V, Pećina HI, Pažanin L, Matić T, Božikov V, Vrkljan M. Pituitary Metastasis Presenting as Ischemic Pituitary Apoplexy Following Heparin-induced Thrombocytopenia. Endocr Pathol. 2012;23(4):264-7.**

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Pituitary apoplexy (PA) typically results from infarction or hemorrhage in a pituitary adenoma, while PA in nonadenomatous pituitary gland is uncommon. Prothrombotic states have never been recognized as precipitating factors for PA. The authors report a case of an elderly female who received prophylactic fractionated heparin therapy due to sepsis, consequent rhabdomyolysis, and overt disseminated intravascular coagulation. On the seventh day of heparin therapy, she reported sudden vision loss, ptosis, diplopia, and severe headache. Severe thrombocytopenia and positive antibodies to the complex of platelet factor 4 and heparin confirmed heparin-induced thrombocytopenia type 2 (HIT). Magnetic resonance imaging disclosed a homogenous pituitary tumor mass with pronounced sphenoid sinus mucosa thickening and two hypointense zones within the tumor mass on contrast-enhanced images consistent with focal ischemic necrosis. The tumor was confirmed to be squamous cell carcinoma with no signs of necrosis. Ischemic necrosis was found within marginal pituitary tissue. This is the first reported case of ischemic PA associated with pituitary metastasis and the first case in which HIT triggered PA. Our case demonstrates that prothrombotic states such as HIT can precipitate ischemic PA. Pituitary metastasis can present with ischemic PA, but radiological features differ from those described in pituitary adenomas. Segregated low-signal intensity zones within the tumor mass on postcontrast images indicate partial infarction of the tumor, which could be a special feature of ischemic PA in pituitary metastasis and has never been described in pituitary adenomas. These are all novel findings and might enlighten the pathogenesis of PA.