

**Clinical, neurohormonal and psychological characteristics predict on a long term basis, adverse cardiac events in patients with congenital heart defects**

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**INTRODUCTION:** The growing cohort of adult patients with congenital heart disease (CHD) has an increased risk of mortality and morbidity, due to its medical condition per se, but also due to psychological issues. Aim of this study is to identify the clinical, psychological and neurohormonal predictors of survival shared by this group of patients.

**METHODS:** 60 consecutive clinical stable patients with various forms of CHD were recruited from a tertiary center. Patients' neurohormonal and psychological status, exercise capacity and cardiac function were assessed through plasma B-type brain natriuretic peptide (BNP) and interleukin 6 (IL-6) measurements, Beck depression inventory and Zung depression scale questionnaires, cardiopulmonary exercise test (CPET) and transthoracic echocardiography respectively. Patients were followed for major adverse cardiovascular events (MACE), including death or hospitalization for  $5.1 \pm 1.1$  years.

**RESULTS:** Most patients were symptomatic (48.3% with NYHA II and 36.7% with NYHA III). Mean plasma concentrations of BNP and IL-6 were  $106.6 \pm 98.6$  pg/ml and  $2.4 \pm 2.6$  pg/ml respectively. 17 patients (28.3%) were characterized as depressed. Patients with depression had higher plasma BNP levels ( $p=0.030$ ), limited exercise capacity, as expressed with peak  $VO_2$  ( $p=0.019$ ) and higher probability of experiencing a MACE compared to non-depressed patients (95% CI: 1.630 to 3.616,  $p<0.05$ ). 22 patients (36.6%) experienced a MACE, among them 8 patients (13.3%) died. BNP, IL-6, peak  $VO_2$ ,  $VE/VCO_2$  were proved to be strong predictors of survival; BNP value  $> 241$  pg/ml predicted MACE with a sensitivity of 65.38% and a specificity of 73.53% (AUC = 0.693,  $p< 0.0001$ ), IL-6 value  $> 1.54$  pg/ml predicted MACE with a sensitivity of 61.53% and a specificity of 73.53% (AUC = 0.627,  $p< 0.0001$ ),  $VE/VCO_2$  value  $> 38$  predicted MACE with a sensitivity of 73.08% and a specificity of 76.47% (AUC = 0.808,  $p< 0.0001$ ) and peak  $VO_2$  value  $\leq 21.4$  ml/Kg/min predicted MACE with a sensitivity of 76.92% and a specificity of 70.59% (AUC = 0.794,  $p< 0.0001$ ) respectively.

**CONCLUSIONS:** BNP, IL-6 levels, CPET parameters as well as depressive symptoms, predicted MACE and could be used as simple clinical markers for routine risk stratification and therapeutic manipulation of this population.