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## Heart rate variability in Eisenmenger syndrome and its correlation with echocardiographic parameters and plasma BNP, high sensitivity troponin-I level

To the Editor,

Eisenmenger syndrome (ES) is the latest stage of congenital heart disease associated pulmonary arterial hypertension (PAH) and is more common in our daily practice lately. Despite all improvements, there are several limitations to determining prognosis of these patients (1). Therefore, different parameters with high prognostic values are needed. Heart rate variability (HRV) and autonomic dysfunction can be early prognostic markers in patients with ES.

Twenty patients with ES (12 female, 8 male) and 20 healthy matched volunteers were enrolled in the study. Plasma brain natriuretic peptide (BNP) and troponin-I levels were measured. HRV parameters were calculated from 24-hour Holter electrocardiogram recordings. HRV parameters were compared with those of 20 healthy subjects. Bivariate analysis was performed to evaluate correlation between echocardiographic parameters and plasma BNP, high sensitivity (hs)-troponin-I levels. Mean age was  $29.25 \pm 12.53$  years and patients were clinically stable. All patients were receiving specific pulmonary hypertension treatment. Eight patients (40%) were receiving combination therapy, while 12 patients (60%) were receiving single agent.

There were significantly lower time-domain HRV parameters [SD of all RR intervals (SDNN):  $125.8 \pm 36.96$  vs.  $173.30 \pm 34.47$  ( $p < 0.0001$ ); mean of SD of all RR intervals for all 5-minute segments over the entire recording (SDNNi):  $48.30 \pm 14.65$  vs.  $71.65 \pm 19.74$  ( $p < 0.0001$ ); SD of averaged normal RR intervals calculated for all 5-minute periods (SDANN):  $116.15 \pm 37.22$  vs.  $157.00 \pm 31.18$  ( $p < 0.0001$ );  $32.25 \pm 14.32$  vs.  $39.05 \pm 14.98$  ( $p = 0.151$ ); triangular index (TI):  $40.31 \pm 20.05$  vs.  $48.45 \pm 14.16$  ( $p = 0.150$ )] in ES patients compared to healthy controls. Root-mean-square of successive normal sinus RR interval difference (RMSSD) and TI were lower in ES patients, but without statistical significance ( $p = 0.151$ ).

There was no statistically significant correlation between HRV parameters and 6-minute walking test, functional capacity, right ventricular systolic function, BNP and hs-troponin-I levels.

Most common cause of death in these patients is arrhythmia, and autonomic dysfunction may be triggering factor (2). HRV parameters are now being used for prognostic evaluation in PAH patients. There are also studies suggesting HRV reduction may be associated with mortality and need for transplant in children and poor prognosis in adults with idiopathic PAH (3). Considering the fact that our patients were clinically stable and were also under appropriate treatment, guideline-recommended prognostic markers were not severely affected, despite significantly reduced HRV parameters. As a result, HRV parameters may be an early marker of prognosis even before deterioration of currently suggested markers. These data suggest that HRV parameters can be utilized as an early marker of poor prognosis in ES patients, but additional prospective studies are needed.

The limited number of patients and lack of long-term follow up are the major limitations of this study. Frequency-domain parameters would also provide additional benefit.

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