Artificial intelligence-driven echocardiographic classification identifies Brugada Syndrome patients at higher arrhythmic risk

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Background: Mounting evidence exists to support the hypothesis that patients with Brugada Syndrome (BrS) present morphological and structural anomalies localized to the right ventricle (RV), but this has not been investigated in a large cohort and the association with clinical outcomes are unknown.

Purpose: To investigate the role of echocardiography-derived RV parameters in a large, single-center cohort of patients with BrS.

Methods: We prospectively enrolled n=492 consecutive patients (379 males, 77%; age 46±14 years) with confirmed BrS who underwent an echocardiogram during their last visit at the outpatient clinic for inherited arrhythmogenic disorders. Comprehensive 2D and color Doppler echocardiographic evaluation was performed using the standard clinical protocol. Unsupervised clustering analysis using cluster package sorted body surface area-corrected morphological (RVOT linear dimensions and RV diastolic area) and functional measurements of RV (fractional area shortening [FAC], tricuspid annular plane systolic excursion [TAPSE]), blinded to other variables. We performed clustering with a hierarchical cluster algorithm (h-cluster) and the optimal number of clusters (k=2) was determined using fviz_nbclust-derived plots.

Results: All n=492 patients were classified into 2 stable clusters (l) with the best robustness. The Cluster 1 echocardiograms exhibited normal RV morphological and functional parameters. The Cluster 2 echocardiograms showed a dilatation of the RVOT (PLAX 17.2±2.1 vs. 15.6±2.1, p<0.001; PSAX 18.3±2.2 vs. 16.9±2.2, p<0.001) compared to Cluster 1, while the RV diastolic area was not different (9.9±1.5 vs. 9.9±1.6, p=0.801). Importantly, RV function as assessed by TAPSE was not different between the two groups, but Cluster 2 patients showed a significantly impaired radial contraction (RV FAC 40.1±3.4% vs. 48.6±3.8%, p<0.001). We then investigated the clinical characteristics of patients based on clusters. Patients in Cluster 1 were younger (43.2±12.8 years vs. 47.5±14.0 years, p<0.001) and had significantly less arrhythmic symptoms such as syncope (13% vs. 20%, p=0.046) and life-threatening arrhythmic events (2% vs. 7%, p=0.017). Importantly, no significant differences in terms of gender (77% males in both groups, p=1.000), pattern type (43% with spontaneous type 1 pattern in Cluster 1 vs. 47%, p=0.494) nor genetic status were observed. Multivariate logistic regression confirmed that at parity of age and arrhythmic syncope, Cluster 2 was independently associated with an increased incidence of life-threatening arrhythmic events (odds ratio 3.71, 95% confidence interval 1.31-10.53, p=0.039).

Conclusions: We constructed a novel, echocardiography-guided classification of patients with BrS using unsupervised clustering analysis. Our data suggest that RV structural abnormalities are associated with a higher incidence of life-threatening arrhythmic events in patients with BrS, independently of arrhythmic syncope or age.