ECG Phenotypes Identified in Brugada Syndrome Using Unsupervised Clustering

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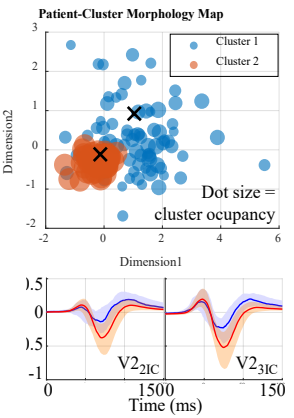
Aim: Brugada syndrome (BrS) is associated with risk of malignant arrhythmias, yet risk stratification remains an unmet clinical need. We aimed to identify ECG phenotypes and assess their link with risk factors. **Methods:** Median QRS complexes were computed every 30 min from high-precordial-lead Holter ECGs of 118 BrS patients. QRS morphology was modelled using four-basis Hermite polynomial fitting, followed by PCA to reduce dimensionality of coefficients and base width across leads; retaining the first two projections. After multicollinearity reduction, PCA projections of QRS morphology were grouped into 5-bpm HR bins, selecting per patient the projections closest to each bin center. One representation per patient was then randomly sampled at each iteration for k-means clustering. Clusters maximizing a score, incorporating inter-cluster separation, compactness, silhouette score, and reproducibility, were selected as reference phenotypes. Stability was assessed per patient after assigning all ECG windows to the reference clusters using the proportion of windows in the dominant cluster (>0.75), the transition rate (<0.15), and the normalized entropy (<0.60). Patients were classified as stable or dynamic using a majority rule across these metrics. **Results:** Two QRS phenotypes were identified. Cluster 1 was less compact and showed slower depolarization, with more positive QRS complexes and J-point elevation compared to Cluster 2, consistent with a transitional conduction phenotype. 89 patients remain stable in Cluster 2 (53[42;65] yr; male 62%; spontaneous type-I 27%; high-risk 29%) whereas others present instability across clusters (54[42;62] yr; male 79%; spontaneous type-I 48%; high-risk 31%). Instability was more frequent in patients with spontaneous type-I pattern, and Cluster 1 may be associated with its manifestation. However, no differences in clinical risk distribution were observed between groups. **Conclusion:** QRS-based clustering alone did not stratify risk, suggesting that integration with T-wave features may better capture phenotypic expression and support subgroup-specific modeling.



Representative clusters and QRS morphologies.