Risk stratification in hypertrophic cardiomyopathy based on QRS and T wave morphological biomarkers identifies three phenotypic subgroups

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Abstract:

Introduction: Hypertrophic cardiomyopathy (HCM) is a common genetic disease in which most patients remain asymptomatic. Yet it is the leading cause of sudden cardiac death in the under 30's.

Purpose: Identifying high-risk patients remains a challenge and therefore our goal is to identify different subpopulations in HCM to stratify risk based on the ECG.

Methods: Computational analysis of 12-lead Holter ECG recordings from 65 HCM patients and 32 healthy volunteers were used to extract QRS and T wave morphological markers. Clustering techniques were applied to blindly extract groups of HCM patients based solely on QRS morphologies. Traditional clinical risk factors, left ventricular structure and function by cardiovascular magnetic resonance imaging and the proposed T wave based biomarkers were then compared for each subgroup.

Results: Three HCM subgroups were identified based on the QRS morphology. Group 1 (n=31) displayed normal QRS morphology but inverted T waves in precordial leads (Fig A) and prolonged JTc intervals compared to controls (359±90 vs 305±48 ms, $p<0.01$). There was a significantly higher risk of syncope in group 1 compared to group 2 and 3. ($p<0.02$, Fig D). Group 2 (n=22) showed moderate QRS abnormalities with rS pattern in septal leads with no difference in clinical risk factors. Group 3 (n=12) exhibited severely abnormal and fragmented QRS complexes mainly in lateral leads (Fig C), with increased S wave depth, but no abnormal T wave morphological features with respect to control. Group 3 had significantly higher left ventricular wall thickness (24±5mm, $p<0.04$) and higher ejection fraction (80%, $p<0.03$) (Fig EF).

Conclusion: Morphological QRS and T wave biomarkers detect three phenotypic subgroups in HCM. Patients exhibiting T wave abnormalities and normal QRS may be associated with an increased risk of syncope. Other patients present severely abnormal QRS in lateral leads, distal to the site of hypertrophy. This novel computational ECG analysis achieves characterisation of HCM beyond standard ECG and left ventricular hypertrophy measures.

Figure: Three phenotypic subgroups in HCM