EARLY REPOLARIZATION PATTERN: CLINICAL CORRELATES OF SPECIFIC ELECTROCARDIOGRAPHIC SUBTYPES AND GENOME WIDE ASSOCIATION STUDY OF A SARDINIAN POPULATION

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Background: Early repolarization pattern (ERP) on electrocardiogram (ECG) is common in the general population. ERP, especially in the inferior distribution, has been associated with sudden cardiac death. The aim of this study was to assess clinical correlates and conduct a preliminary genome wide association study (GWAS) of ERP.

Methods: ERP, defined as J-point elevation ≥ 0.1 mV in ≥2 leads of any of the following distributions: lateral leads (I, aVL, V4-6), inferior leads (II, III, aVF), or global (both lateral and inferior), was determined in 3,231 participants from the SardiNIA study, an initiative sponsored by the National Institute on Aging. The same individuals were assessed for a range of ECG and serum parameters and for 2,500,000 HapMap single-nucleotide polymorphisms (SNPs).

Results: ERP was present in 285 (8.8%) of 3,231 participants. Lateral, inferior, and global ERP was present in 135 (4.1%), 102 (3.1%), and 48 (1.5%) participants, respectively. Male gender and younger age were strongly associated with ERP. After adjustment for these parameters, lower heart rate and higher Sokolow-Lyon (S-L) index remained independently associated with the presence of ERP, driven by the lateral ERP group. Participants with lateral ERP were more often male and exhibited lower heart rates and higher S-L indexes compared to participants with inferior ERP. Serum markers showed no association with ERP. GWAS of all ERP yielded near genome wide significance (p<5 x 10^-7) of two SNPs localized to KCNMA1, a K+ channel gene, and FANK1, a fibronectin gene.

Conclusions: ERP has a robust association with specific clinical characteristics, including lower heart rate and higher S-L index, driven almost exclusively by lateral ERP. Differences between lateral and inferior ERP suggest mechanistic distinction, and may help reconcile possible differences in arrhythmogenicity noted in current literature. GWAS of ERP in this Sardinian population suggests the possible involvement of the KCNMA1 gene, a large conductance Ca2+ activated K+ channel, previously not reported. Efforts to substantiate this finding and investigate potential genetic differences between lateral and inferior ERP by replication are in progress.