PhD THESIS SUMMARY

Study of Cardiac Morphological and Functional Characteristics in Individuals with an Early Repolarization Electrocardiographic Pattern

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Introduction

The early repolarization pattern (ERP) is an electrocardiographic (ECG) abnormality defined by the presence of a distinct J wave or J-point elevation at the end of the QRS complex, appearing as either a notch or a slur, in at least two contiguous leads, with or without ST-segment elevation. Long considered a benign phenomenon, ERP has become an important topic in cardiology over the past two decades, as accumulating evidence has linked it to malignant ventricular arrhythmias and sudden cardiac death. When ERP is associated with ventricular fibrillation or sustained ventricular tachycardia in the absence of structural heart disease, it is defined as early repolarization syndrome (ERS).

The prevalence of ERP in the general population ranges from 1% to 31%, with higher rates among young men and athletes. ERS is classified among the primary electrical diseases of the heart and may share genetic and electrophysiological similarities with other syndromes, such as Brugada syndrome or short QT syndrome.

The current literature describes several ECG characteristics associated with ERP; however, the available data are limited and do not provide a comprehensive understanding of the underlying electrical substrate of ERP. Furthermore, echocardiographic (ECHO) data in individuals with ERP are limited, and the ECG and ECHO responses to exercise have been insufficiently investigated. Based on these gaps, our hypothesis is that ERP-positive individuals may exhibit ECG features and morphological and functional characteristics detectable on ECHO, both at rest and during exercise, with potential clinical relevance for understanding the arrhythmogenic substrate in individuals with ERP.

Objectives

The aim of this research was to characterize ECG and ECHO particularities in individuals with ERP (ERP+ group), compared with those without ERP (ERP− group), at rest, during exercise, and in the early recovery phase, and to identify parameters with potential relevance for evaluating arrhythmic risk associated with ERP. Specifically, we proposed to: (1) analyze resting ECG characteristics associated with ERP; (2) investigate ECG changes in ERP-positive (ERP+) individuals, compared with controls, at rest, at peak exercise, and during the early recovery phase after exercise; (3) assess, by ECHO, cardiac morphological and functional characteristics in ERP+

individuals at rest; and (4) analyze ECHO morphological and functional characteristics at rest and during the early recovery phase after exercise, in order to identify possible exercise-induced morphological and functional changes in ERP+ individuals. By integrating the results of these four studies, this research aims to provide a more comprehensive picture of the electrical and morphological–functional substrate associated with ERP and its potential clinical relevance for arrhythmic risk stratification.

Methods

The research included young, apparently healthy men, investigated according to a protocol consisting of four complementary studies focused on ECG and ECHO assessments performed at rest, during exercise, and in the early recovery phase after exercise. The diagnosis of ERP was established according to the international consensus published by Macfarlane et al. Standard 12-lead ECGs were recorded using a BTL-08 SD3 device, and the exercise test was performed according to the Bruce protocol, with continuous monitoring and analyses at three time points: rest, peak exercise, and early recovery phase. ECHO examinations were performed using a Philips Epiq 7 system (Philips Healthcare) with an S5-1 transducer, employing 2D-ECHO, Doppler and tissue Doppler techniques, as well as myocardial strain analysis by speckle-tracking echocardiography; morphological parameters, systolic and diastolic function, and the cardiac response to exercise were evaluated. Statistical analysis was performed using IBM SPSS 22, using Student's t-test, Mann–Whitney, chi-square and Fisher's exact tests, with a significance threshold of $p < 0.05$. All studies were conducted in accordance with the principles of the Declaration of Helsinki.

Results and discussion

The studies included in this thesis provide an integrated overview of ECG and ECHO features in healthy young men with ERP. Comparative analysis between ERP+ and ERP– individuals allowed characterization of both the electrical substrate and the cardiac morpho-functional profile at rest, during exercise, and in the early recovery phase.

Regarding resting ECG findings (study 1), ERP was associated with slowing of intra- and interatrial conduction and with a higher frequency of atrial premature beats, suggesting a possible predisposition to atrial arrhythmias. Fragmented QRS complexes were more frequent in the ERP+ group, indicating localized delays in depolarization. Repolarization parameters were similar or slightly shorter in ERP+ individuals; in particular, the Tpeak–Tend interval was mildly reduced, in contrast to literature data associating prolongation of this parameter with transmural dispersion of repolarization and with arrhythmogenesis in both Brugada syndrome and ERS.

Exercise-related ECG changes (study 2) highlight findings of arrhythmological relevance: in individuals with ERP, a further increase in P-wave duration is observed

during intense physical exercise, partially persisting during the first minutes of recovery, suggesting stress-related unmasking of an atrial arrhythmogenic substrate. Paradoxically, the QRS complex is shorter on ECGs of individuals with ERP at rest, during exercise, and in the early recovery phase, suggesting that ventricular depolarization does not appear to contribute significantly to ventricular arrhythmogenesis in ERP. In individuals with ERP, the J wave disappears during exercise and reappears during recovery, supporting the hypothesis of a mechanism dependent on autonomic tone, with a potential impact on ventricular arrhythmic vulnerability.

Resting cardiac morpho-functional characteristics (study 3) showed no significant differences: chamber dimensions, ventricular mass, ejection fraction, global longitudinal strain, and diastolic parameters were similar between groups. In the ERP+ group, only a slightly smaller left ventricular end-systolic volume and a higher prevalence of minimal mitral regurgitation were observed, without pathological significance, suggesting physiological features of valvulo-ventricular coupling.

Dynamic ECHO characteristics (study 4) showed that, in the early recovery phase after exercise, the ERP+ group exhibited more pronounced decreases in left ventricular end-diastolic volume and stroke volume, with a similar trend for end-systolic volume, while other morphological and functional parameters remained comparable. This pattern suggests a particular hemodynamic adaptation mediated by the autonomic nervous system, without global myocardial dysfunction.

These results must be interpreted with caution: sample sizes were relatively small, only healthy young men were included, and advanced imaging techniques (e.g. cardiac magnetic resonance, segmental or 3D speckle-tracking echocardiography) were not used systematically. Larger, longitudinal, multimodal studies are needed to validate these markers and refine risk stratification in ERP.

Conclusions

In healthy young men, ERP appears as a predominantly electrical phenotype, in the absence of structural remodeling or global myocardial dysfunction detectable by echocardiography. The electrocardiographic profile of individuals with ERP suggests a possible predisposition to atrial arrhythmias and the presence of local depolarization delays, while J-wave dynamics indicate the influence of autonomic nervous system modulation on the expression of this phenotype. Resting echocardiographic assessment does not reveal significant structural or functional changes, supporting the absence of evident structural cardiac involvement in this population. The left ventricular volumetric response during the early recovery phase after exercise suggests subtle particularities of hemodynamic adaptation, without impairment of global myocardial function in individuals with ERP.