

## Does Early Repolarization Affect the Risk of Death and Ventricular Arrhythmias?

Guilherme Fenelon<sup>1</sup>

Hospital Israelita Albert Einstein,<sup>1</sup> São Paulo, SP – Brazil

*Short Editorial related to the article: Mortality and Ventricular Arrhythmia in Patients with Early Ventricular Repolarization*

Early repolarization (ER) pattern, defined as J-point elevation of  $\geq 1$  mm in  $\geq 2$  contiguous inferior and/or lateral electrocardiography (ECG) leads, is a common finding, with a prevalence of approximately 6% in the adult population.<sup>1,2</sup> ER has long been considered a benign phenomenon, as most affected individuals — typically young males and athletes — have a very low incidence of sudden cardiac death.<sup>1,2</sup>

However, a pivotal study by Haïssaguerre et al.<sup>3</sup> demonstrated a significantly higher occurrence of ER (31%) in patients with idiopathic ventricular fibrillation (VF) compared to controls (5%). Subsequent studies confirmed an association between ER and malignant ventricular arrhythmias (VA) in patients without structural heart disease.<sup>4,5</sup> Additionally, ER has been linked to adverse outcomes in patients with primary electrical disorders such as long QT syndrome and Brugada syndrome.<sup>2,6</sup>

Unlike these disorders, which are diagnosed based on specific ECG abnormalities, ER syndrome is identified in patients resuscitated from polymorphic ventricular tachycardia or VF who exhibit ER patterns.<sup>1,2</sup> Most individuals with ER are asymptomatic, making the identification of markers for risk stratification crucial. Proposed high-risk features include J-waves  $\geq 2$  mm, dynamic changes in J-point elevation ( $>0.1$  mV), and J-waves associated with a horizontal or descending ST segment.<sup>1,2</sup> However, the predictive value of these markers remains uncertain, and transient ER — present on baseline ECG but absent on subsequent recordings — appears to be benign.<sup>7</sup>

The mechanisms of ER are poorly understood. Animal studies suggest that an increased transient outward potassium current ( $I_{to}$ ) during phase 2 of the action potential plays a central role by promoting premature myocardial repolarization and variable loss of the action potential dome.<sup>1,2,8</sup> This phenomenon is more prominent in the epicardium, leading to repolarization heterogeneity, which subsequently promotes phase 2 reentry. ER appears to

exhibit some degree of heritability, being overrepresented in families of unexplained cardiac arrest survivors.<sup>1,2</sup> Nevertheless, current genetic testing for ER provides limited diagnostic value.<sup>2,8</sup>

Patients diagnosed with ER syndrome — those resuscitated from VF — require an implantable cardioverter-defibrillator (ICD) for secondary prevention.<sup>1,2</sup> Recurrent VA episodes occur in approximately 40% of cases, sometimes presenting as electrical storms that necessitate multiple ICD discharges. Isoproterenol infusion is effective for acute management, while quinidine (an  $I_{to}$  blocker) may reduce recurrences.<sup>1,2,9</sup> In selected cases, catheter ablation targeting VF triggers at the right ventricular outflow tract or the Purkinje system may be attempted.<sup>10</sup>

Managing patients with ER patterns is challenging, as reliable risk markers for malignant VA are lacking and the overall prognosis in this population is very favorable. In asymptomatic individuals, reassurance alone is recommended.<sup>2,9</sup> An implantable loop recorder may be considered in patients with ER and unexplained syncope.<sup>2</sup>

The prevalence of ER is influenced by factors such as age, sex, and ethnicity, with a higher occurrence observed in African Americans.<sup>1,9</sup> Consequently, its frequency may vary across different countries. The study by Baldisserotto et al.<sup>11</sup> provides valuable insights into the prognostic significance of ER in the Brazilian population.

This retrospective, single-center cohort study analyzed 478 patients with ER, stratifying them by ER type (lateral, inferior, and inferolateral). Outcomes included sustained VA and all-cause mortality over a 10-year follow-up period. Survival probability and cumulative risk functions were assessed using Kaplan-Meier analysis, and Cox regression models were used to adjust for confounders such as age and sex.

The study population was predominantly male (74%), with a mean age of 45.6 years. Among the cohort, 2.7% (13 patients) experienced VA, and 2.3% (11 patients) died from all causes. Significant differences in age, sex, and the prevalence of heart failure with reduced ejection fraction were observed among ER subgroups. Nevertheless, Kaplan-Meier analysis showed no statistically significant differences in survival or VA rates across ER types ( $p=0.7$  and  $p=0.5$ , respectively). However, cumulative risk estimates varied, with the inferolateral ER group demonstrating the highest mortality risk.

Adjusted Cox regression models indicated no significant hazard ratios for VA or mortality across ER types, with age emerging as the only significant predictor for both outcomes. The study concluded that ER does not impact the risk of VA or overall mortality in this cohort.

### Keywords

Cardiac Arrhythmias; Cardiac Sudden Death; Electrocardiography

**Mailing Address:** Guilherme Fenelon •

Hospital Israelita Albert Einstein – Centro de Arritmia – Av. Albert Einstein, 627 Pavilhão Vicky e Joseph Safrá, Sala 416. Postal Code 05652-900, São Paulo, SP – Brazil

E-mail: guilhermefenelon@uol.com.br

Manuscript received April 14, 2025, revised manuscript April 22, 2025, accepted April 22, 2025

**DOI:** <https://doi.org/10.36660/abc.20250275i>

While the study provides valuable epidemiological insights, its retrospective design introduces potential biases. Only a single ECG was analyzed, preventing assessment of temporal changes in the ER pattern. The relatively small number of outcomes (VA and mortality) limits the statistical power to detect differences among ER types. Nevertheless, the findings are consistent with previous reports,<sup>12</sup> suggesting that the role of ER as a predictor of cardiovascular death

remains uncertain after adjusting for confounding factors such as age, sex, and heart disease.

In summary, for most individuals, ER is a benign finding that does not require intervention beyond reassurance.<sup>2,9</sup> Patients with ER who present with unexplained syncope, a strong family history of sudden cardiac death, or high-risk ECG features require careful evaluation.<sup>2</sup> Further research is needed to improve risk stratification in asymptomatic individuals who may be at increased arrhythmic risk.

## References

1. Antzelevitch C, Yan GX, Ackerman MJ, Borggreffe M, Corrado D, Guo J, et al. J-Wave Syndromes Expert Consensus Conference Report: Emerging Concepts and Gaps in Knowledge. *Europace*. 2017;19(4):665-94. doi: 10.1093/europace/euw235.
2. Zeppenfeld K, Tfelt-Hansen J, Riva M, Winkel BG, Behr ER, Blom NA, et al. 2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. *Eur Heart J*. 2022;43(40):3997-4126. doi: 10.1093/eurheartj/ehac262.
3. Haïssaguerre M, Derval N, Sacher F, Jesel L, Deisenhofer I, Roy L, et al. Sudden Cardiac Arrest Associated with Early Repolarization. *N Engl J Med*. 2008;358(19):2016-23. doi: 10.1056/NEJMoa071968.
4. Rosso R, Kogan E, Belhassen B, Rozovski U, Scheinman MM, Zeltser D, et al. J-Point Elevation in Survivors of Primary Ventricular Fibrillation and Matched Control Subjects: Incidence and Clinical Significance. *J Am Coll Cardiol*. 2008;52(15):1231-8. doi: 10.1016/j.jacc.2008.07.010.
5. Derval N, Simpson CS, Birnie DH, Healey JS, Chauhan V, Champagne J, et al. Prevalence and Characteristics of Early Repolarization in the CASPER Registry: Cardiac Arrest Survivors with Preserved Ejection Fraction Registry. *J Am Coll Cardiol*. 2011;58(7):722-8. doi: 10.1016/j.jacc.2011.04.022.
6. Laksman ZW, Gula LJ, Saklani P, Cassagneau R, Steinberg C, Conacher S, et al. Early Repolarization is Associated with Symptoms in Patients with Type 1 and Type 2 Long QT Syndrome. *Heart Rhythm*. 2014;11(9):1632-8. doi: 10.1016/j.hrthm.2014.05.027.
7. Liu LJ, Tang N, Bi WT, Zhang M, Deng XQ, Cheng YJ. Association between Temporal Changes in Early Repolarization Pattern with Long-Term Cardiovascular Outcome: A Population-Based Cohort Study. *J Am Heart Assoc*. 2022;11(6):e022848. doi: 10.1161/JAHA.121.022848.
8. Wilde AAM, Semsarian C, Márquez MF, Shamloo AS, Ackerman MJ, Ashley EA, et al. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the State of Genetic Testing for Cardiac Diseases. *Europace*. 2022;24(8):1307-67. doi: 10.1093/europace/euac030.
9. Krahn AD, Tfelt-Hansen J, Tadros R, Steinberg C, Semsarian C, Han HC. Latent Causes of Sudden Cardiac Arrest. *JACC Clin Electrophysiol*. 2022;8(6):806-21. doi: 10.1016/j.jacep.2021.12.014.
10. Nademanee K, Haïssaguerre M, Hocini M, Nogami A, Cheniti G, Duchateau J, et al. Mapping and Ablation of Ventricular Fibrillation Associated with Early Repolarization Syndrome. *Circulation*. 2019;140(18):1477-90. doi: 10.1161/CIRCULATIONAHA.118.039022.
11. Baldisserotto H, Lima BA, Saffi MA, Silveira AD, Baldisserotto ML, Leiria TLL. Mortality and Ventricular Arrhythmia in Patients with Early Ventricular Repolarization. *Arq Bras Cardiol*. 2025; 122(4):e20240516. DOI: https://doi.org/10.36660/abc.20240516.
12. Ilkhanoff L, Soliman EZ, Prineas RJ, Walsh JA 3rd, Ning H, Liu K, et al. Clinical Characteristics and Outcomes Associated with the Natural History of Early Repolarization in a Young, Biracial Cohort Followed to Middle Age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Circ Arrhythm Electrophysiol*. 2014;7(3):392-9. doi: 10.1161/CIRCEP.113.000874.



This is an open-access article distributed under the terms of the Creative Commons Attribution License