

# Early Repolarization, Fragmented QRS and Tpeak-Tend Interval as Electrocardiographic Markers in Patients with Idiopathic Ventricular Arrhythmias: a Brief Review

Javier Pinos<sup>1,\*</sup>, Tiago Luiz Luz Leiria<sup>1</sup>, Clóvis Froemming Jr<sup>1</sup>, Bruno Schaaf Finkler<sup>1</sup>, Danilo Barros Zanotta<sup>1</sup>, Thiago Camargo Moreira<sup>1</sup>, Marcelo Lapa Kruse<sup>1</sup>, Leonardo Martins Pires<sup>1</sup>, Gustavo Glotz De Lima<sup>1</sup>

## ORCID IDs

Pinos J  <https://orcid.org/0000-0001-7237-6136>

Leiria TLL  <https://orcid.org/0000-0002-3905-102X>

Froemming Jr. C  <https://orcid.org/0000-0002-4770-0050>

Finkler BS  <https://orcid.org/0000-0001-6885-3710>

Zanotta DB  <https://orcid.org/0000-0001-5372-0421>

Moreira TC  <https://orcid.org/0000-0001-6907-2895>

Kruse ML  <https://orcid.org/0000-0002-2429-4491>

Pires LM  <https://orcid.org/0000-0001-8003-8081>

Lima GG  <https://orcid.org/0000-0003-0097-5206>

## ABSTRACT

**Introduction:** Idiopathic ventricular tachycardia and ventricular fibrillation, as causes of sudden cardiac death, are entities with mechanisms poorly studied and understood to date. The electrocardiogram (ECG) is a simple tool, but with great diagnostic and prognostic value, which has allowed the identification of certain markers associated with increased risk of development of malignant ventricular arrhythmias and sudden cardiac death. **Methods:** To identify the electrocardiographic markers related to the risk of developing idiopathic malignant ventricular arrhythmias, a review of the literature was performed, looking for the most recent articles with the greatest scientific impact on the topic. **Outcome:** Although the number of studies published to date is scarce, the published evidence has shown three electrocardiographic risk markers that have emerged in recent years and which have been related to the development of idiopathic malignant ventricular arrhythmias: the early repolarization (ER) pattern, QRS fragmentation (QRSF) and the Tpeak-Tend (Tp-Te) interval. The ECG marker that has shown most evidence to date is the pattern of ER, as a cause of changes in both ventricular depolarization and repolarization. The QRSF and the Tp-Te interval have also been related to the development of idiopathic ventricular arrhythmias, although with less evidence in this regard. **Conclusion:** In the last years, three electrocardiographic markers have appeared as variables related to the development of malignant ventricular arrhythmias, as is the case of ER, QRSF and Tp-Te interval. However, evidence is scarce in this specific patient profile and further randomized clinical trials are necessary to demonstrate its true relationship and usefulness.

**KEYWORDS:** Idiopathic ventricular arrhythmias; Ventricular tachycardia; Ventricular fibrillation; Sudden death; Early repolarization; QRS fragmentation; Tpeak-Tend interval.

1. Instituto de Cardiologia do Rio Grande do Sul – Fundação Universitária de Cardiologia – Porto Alegre (RS), Brazil.

\*Corresponding author: [japopv89@hotmail.com](mailto:japopv89@hotmail.com)

Received: May 15, 2020 | Accepted: Jun 12, 2020



## INTRODUCTION

Ventricular arrhythmias, whether ventricular tachycardia (VT) or ventricular fibrillation (VF), are called idiopathic when clinical investigations, including imaging studies, are negative for heart disease in a patient who survives this arrhythmic episode. Some series have shown that in up to 14% of patients who suffered an episode of VF, the cause of the arrhythmic event was not detected<sup>1</sup>. Every patient who survives an episode of idiopathic VF has an indication for implantable cardioverter-defibrillator (ICD) as a secondary prevention<sup>2</sup>. Catheter ablation should be considered in cases where a ventricular extrasystole is identified as a trigger for arrhythmic events<sup>3,4</sup>, probably as an indicator of Purkinje system disease<sup>5</sup>.

The twelve-lead electrocardiogram is a simple tool, but with great diagnostic and prognostic value in patients with idiopathic ventricular arrhythmias. Several electrocardiographic signs compatible with an increased risk of arrhythmic events and sudden death have been described. In addition to the already known risk factors, such as the QT interval and electrical alternation of the T wave, there are other electrocardiographic markers that have been poorly studied.

### Early repolarization

Patients with aborted cardiac arrest and with no detectable cause have a higher prevalence of the electrocardiographic pattern of early repolarization (ER) in the inferolateral derivations. There is a clear relationship between the number of leads with ER on the electrocardiogram (ECG) and the risk of developing VF<sup>6</sup>. However, the electrocardiographic pattern of ER should be considered a normal variant in young and healthy people, especially men and athletes. Only patients who, in addition to the ER pattern, present syncope or aborted cardiac arrest, should be evaluated<sup>7</sup>.

The diagnostic criteria for the electrocardiographic pattern of the ER are: elevation of the J point greater than or equal to 0.1 mV in at least two leads, terminal part of the QRS with notching or slurring morphology and QRS duration less than 120 ms<sup>8</sup>. Antzelevitch<sup>9</sup> divides the ER pattern into 3 types:

- Type 1: when the ER manifests exclusively in lateral precordials, it is related to low arrhythmic risk and is predominant in male athletes;
- Type 2: when the ER pattern manifests itself in inferior or inferolateral leads, it is related to moderate arrhythmic risk; and
- Type 3: when the ER pattern manifests itself in inferior, lateral and right precordial leads; this type is the one with the highest arrhythmic risk.

Kamakura et al.<sup>10</sup> described that the latter is the type that presents a higher risk of recurrence of VF after a first arrhythmic event, even greater than Brugada syndrome<sup>11</sup>. The main difference between Brugada syndrome and ER syndrome is the affected cardiac region, which in the case of Brugada Sd. is the right ventricle (RV) outflow tract and in the ER Sd. is the lower region of the left ventricle (LV)<sup>9</sup>. Tikkanen et al.<sup>12</sup> described that those patients with ER pattern in whom a horizontal or descending ST segment is observed are at a higher risk of death from arrhythmic causes, unlike those in which the ST segment is ascending, in which long-term mortality does not differ from the population generally. These same findings were corroborated by Nam and Adler et al.<sup>13,14</sup>. An interesting finding is that the J wave tends to increase in amplitude just before of VF appearance<sup>15</sup>. Haisaguerre et al.<sup>16</sup> have observed similar findings, showing that the amplitude of the J wave more than doubles moments before the VF episode. There is an uneven distribution of the *Ito* channel between the epicardium and the endocardium that results in the elevation of the J point. A possible cause of the arrhythmic events could be the *Ito* current which is faster in the epicardium than in the endocardium, producing an electrical gradient, a known mechanism as reentry in phase 2, probable cause of VF<sup>17,18</sup>. However, Haisaguerre et al.<sup>19</sup> have recently shown, through high density electrogram mapping, evidence of a wide spectrum of heterogeneous substrates, which may be a consequence of late depolarization or caused by abnormalities in the ER: the abnormalities of late depolarization are due to

microstructural changes, that due to their small size they are not visible on MRI and are a target for catheter ablation; in the case of ER, the likely mechanism is a voltage gradient across the ventricular wall during the early phase of repolarization, in which case the Purkinje system has an important triggering role, further confirmed by favorable results after ablation.

## QRS fragmentation

Another electrocardiographic marker that has been studied is the QRS fragmentation (QRSF). There is evidence of its usefulness as a predictor of cardiovascular mortality in patients with structural heart disease<sup>20</sup>. QRSF has also been shown to be a risk marker for the development of ventricular arrhythmias in Sd. from Brugada. However, it can also be present in healthy athletes, without a clear relationship with the development of arrhythmic events in this population<sup>21</sup>; for this reason, some authors catalog its presence as a nonspecific finding and claim that its prognostic value should be interpreted only in the presence of relevant clinical evidence<sup>22</sup>. On the other hand, Narayanan et al<sup>23</sup>. observed that in overweight and obese patients, the presence of QRSF is a risk marker for sudden cardiac death, regardless of the ejection fraction. Seong et al<sup>24</sup>. studied patients who received an ICD for idiopathic VF and observed that this population has a higher prevalence of QRSF and ER; in addition, the presence of the two electrocardiographic characteristics together was related to the higher prevalence of clinical cardiac events such as syncope, sudden cardiac arrest and appropriate ICD shocks.

## Tpeak-tend Interval

Another ECG marker that has been shown to be related to the risk of fatal ventricular arrhythmias is the Tpeak-Tend interval (Tp-Te). The peak of the T wave coincides with epicardial repolarization and the end of the T wave with myocardial repolarization, so that the Tp-Te interval provides a measure of transmural dispersion of repolarization<sup>25</sup>. The prolongation of the Tp-Te interval is associated with sudden cardiac death, with particular utility when the QTc interval is normal<sup>26</sup>. In a meta-analysis published by Tse G et al<sup>27</sup>., it was observed that in the general population, a prolonged Tp-Te interval (with an average duration of  $103.3 \pm 17.4$  ms) was also predictive of arrhythmic events and total mortality, and not only in patients with arrhythmogenic syndromes. The Tp-Te/QT ratio is an index that, unlike Tp-Te, remains constant, regardless of variations in heart rate and therefore, an arrhythmogenesis index more sensitive than Tp-Te<sup>25</sup>. It seems that the V6 lead of the electrocardiogram is the most suitable to measure the Tp-Te/QT interval<sup>28</sup>. Although there is clear evidence about the usefulness of the Tp-Te intervals and the Tp-Te/QT ratio as markers of ventricular repolarization dispersion and arrhythmic markers, there is debate about whether the dispersion occurs at the transmural, global level or is a combination of the two. However, it seems less likely that dispersion of interventricular repolarization will lead to an increased gradient and therefore less likely to be associated with arrhythmic risk, unlike transmural dispersion<sup>29</sup>.

## CONCLUSION

Over the years, electrocardiographic risk markers related to the development of idiopathic ventricular arrhythmias and sudden death have been investigated. However, in the last few years, three electrocardiographic markers appeared as variables related to the development of malignant ventricular arrhythmias, as is the case with the ER pattern, QRSF and Tp-Te interval (Fig. 1). Nevertheless, evidence is scarce in this specific patient profile and further randomized clinical studies are needed to demonstrate its true relationship and usefulness.

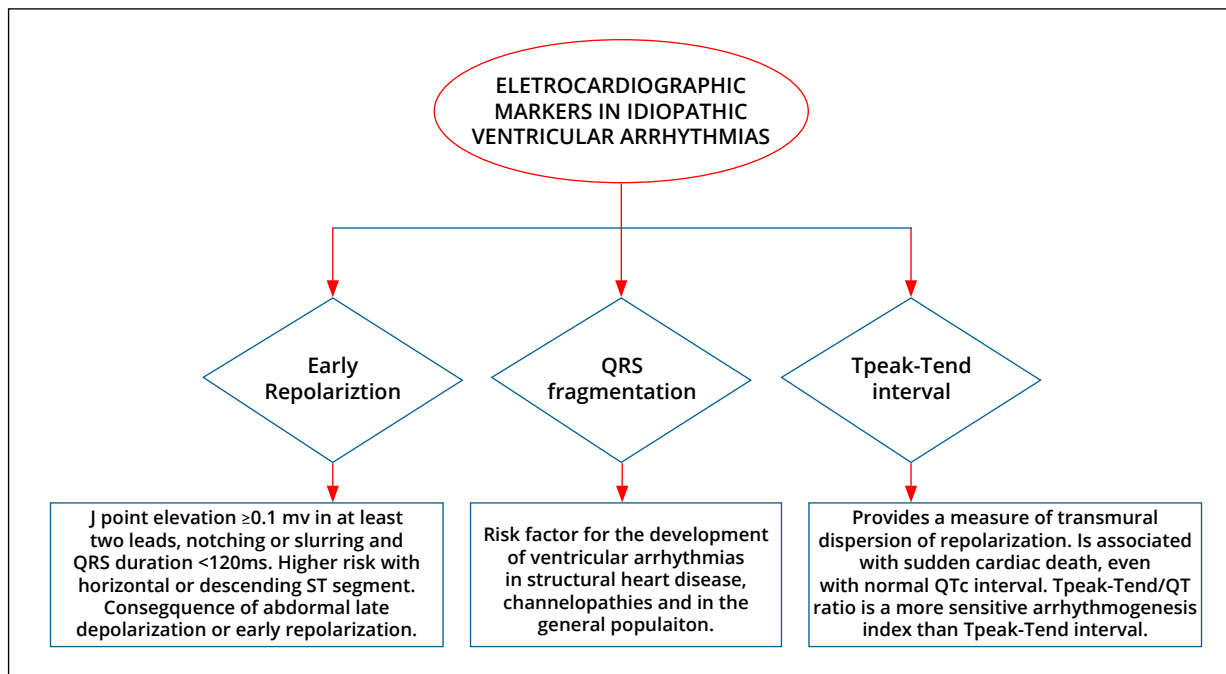


Figure 1. Electrocardiographic markers in idiopathic ventricular arrhythmias.

## REFERENCES

1. Dalos D, Fiedler L, Radojevic J, Sponder M, Dichtl W, Schukro C. Prevalence of early repolarization syndrome and long-term clinical outcome in patients with the diagnosis of idiopathic ventricular fibrillation. *Heart Vessels*. 2019;34(4):625-31. <https://doi.org/10.1161/01.cir.95.1.265>
2. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. Guía ESC 2015 sobre el tratamiento de pacientes con arritmias ventriculares y prevención de la muerte súbita cardiaca. *Rev Esp Cardiol*. 2016;69(2):176.e1-e77. <https://doi.org/10.1016/j.recesp.2016.01.001>
3. Knecht S, Sacher F, Wright M, Hocini M, Nogami A, Arentz T, et al. Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study. *J Am Coll Cardiol*. 2009;54(6):522-8. <https://doi.org/10.1016/j.jacc.2009.03.065>
4. Haissaguerre M, Shoda M, Jaïs P, Nogami A, Shah DC, Kautzner J, et al. Mapping and ablation of idiopathic ventricular fibrillation. *Circulation*. 2002;106(8):962-7. <https://doi.org/10.1161/01.CIR.0000027564.55739.B1>
5. Haissaguerre M, Cheniti G, Escande W, Zhao A, Hocini M, Bernus O. Idiopathic ventricular fibrillation associated with repetitive activity inducible within the distal Purkinje system. *Heart Rhythm*. 2019;16(8):1268-72. <https://doi.org/10.1016/j.hrthm.2019.04.012>
6. 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. <https://doi.org/10.1016/j.jacc.2011.04.022>
7. Kukla P, Jastrzębski M, Pérez-Riera AR. Some Controversies about Early Repolarization: The Haissaguerre Syndrome. *Ann Noninvasive Electrocardiol*. 2015;20(5):409-19. <https://doi.org/10.1016/j.jacc.2017.10.053>
8. Macfarlane PW, Antzelevitch C, Haissaguerre M, Huikuri HV, Potse M, Rosso R, et al. The Early Repolarization Pattern: A Consensus Paper. *J Am Coll Cardiol*. 2015;66(4):470-7. <https://doi.org/10.1016/j.jacc.2015.05.033>
9. Antzelevitch C. J wave syndromes: molecular and cellular mechanisms. *J Electrocardiol*. 2013;46(6):510-8. <https://doi.org/10.1016/j.jelectrocard.2013.08.006>
10. Kamakura T, Kawata H, Nakajima I, Yamada Y, Miyamoto K, Okamura H, et al. Significance of non-type 1 anterior early repolarization in patients with inferolateral early repolarization syndrome. *J Am Coll Cardiol*. 2013;62(17):1610-8. <https://doi.org/10.1016/j.jacc.2013.05.081>

11. Viskin S. Is There Anyone Left With a Normal Electrocardiogram? *J Am Coll Cardiol.* 2013;62(17):1619-20. <https://doi.org/10.1016/j.jacc.2013.06.037>
12. Tikkanen JT, Junttila MJ, Anttonen O, Aro AL, Luttinen S, Kerola T, et al. Early repolarization: electrocardiographic phenotypes associated with favorable long-term outcome. *Circulation.* 2011 Jun 14;123(23):2666-73. <https://doi.org/10.1161/circulationaha.110.014068>
13. Nam GB. Idiopathic ventricular fibrillation, early repolarization and other J wave-related ventricular fibrillation syndromes: from an electrocardiographic enigma to an electrophysiologic dogma. *Circ J.* 2012;76(12):2723-31. <https://doi.org/10.1253/circj.cj-12-1306>
14. Adler A, Rosso R, Viskin D, Halkin A, Viskin S. What do we know about the “malignant form” of early repolarization? *J Am Coll Cardiol.* 2013;62(10):863-8. <https://doi.org/10.1016/j.jacc.2013.05.054>
15. Aizawa Y, Chinushi M, Hasegawa K, Naiki N, Horie M, Kaneko Y, et al. Electrical storm in idiopathic ventricular fibrillation is associated with early repolarization. *J Am Coll Cardiol.* 2013;62(11):1015-9. <https://doi.org/10.1016/j.jacc.2013.05.030>
16. 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. <https://doi.org/10.1056/NEJMoa071968>
17. Sinner MF, Reinhard W, Müller M, Beckmann BM, Martens E, Perz S, et al. Association of early repolarization pattern on ECG with risk of cardiac and all-cause mortality: a population-based prospective cohort study (MONICA/KORA). *PLoS Med.* 2010;7(7):e1000314. <https://doi.org/10.1371/journal.pmed.1000314>
18. Sethi KK, Sethi K, Chutani SK. Early repolarisation and J wave syndromes. *Indian Heart J.* 2014;66(4):443-52. <https://doi.org/10.1016/j.ihj.2014.06.002>
19. Haïssaguerre M, Nademanee W, Hocini M, Duchateau J, André C, Lavergne T, et al. The Spectrum of Idiopathic Ventricular Fibrillation and J-Wave Syndromes: Novel Mapping Insights. *Card Electrophysiol Clin.* 2019;11(4):699-709. <https://doi.org/10.1016/j.ccep.2019.08.011>
20. Rosengarten JA, Scott PA, Morgan JM. Fragmented QRS for the prediction of sudden cardiac death: a meta-analysis. *EP Europace.* 2015;17(6):969-77. <https://doi.org/10.1093/eurospace/euu279>
21. Mozos I, Caraba A. Electrocardiographic Predictors of Cardiovascular Mortality. *Dis Markers.* 2015;2015:727401. <https://doi.org/10.1155/2015/727401>
22. Jain R, Singh R, Yamini S, Das MK. Fragmented ECG as a risk marker in cardiovascular diseases. *Curr Cardiol Rev.* 2014;10(3):277-86. <https://doi.org/10.2174/1573403X10666140514103451>
23. Narayanan K, Zhang L, Kim C, Uy-Evanado A, Teodorescu C, Reinier K, et al. QRS fragmentation and sudden cardiac death in the obese and overweight. *J Am Heart Assoc.* 2015;4(3):e001654. <https://doi.org/10.1161/JAHA.114.001654>
24. Seong CS, Gwang HB, Hwang JK, Park SJ, Park K-M, Kim JS, et al. Clinical significance of fragmented QRS complexes or J waves in patients with idiopathic ventricular arrhythmias. *PLoS ONE* 2018;13(4):e0194363. <https://doi.org/10.1371/journal.pone.0194363>
25. Talib AK, Sato N, Sakamoto N, Tanabe Y, Takeuchi T, Saijo Y, et al. Enhanced transmural dispersion of repolarization in patients with J wave syndromes. *J Cardiovasc Electrophysiol.* 2012;23(10):1109-14. <https://doi.org/10.1111/j.1540-8167.2012.02363.x>
26. Panikkath R, Reinier K, Uy-Evanado A, Teodorescu C, Hattenhauer J, Mariani R, et al. Prolonged  $T_{peak}$ -to- $t_{end}$  interval on the resting ECG is associated with increased risk of sudden cardiac death. *Circ Arrhythm Electrophysiol.* 2011;4(4):441-7. <https://doi.org/10.1161/CIRCEP.110.960658>
27. Tse G, Gong M, Wong WT, Georgopoulos S, Letsas KP, Vassiliou VS, et al. The  $T_{peak} - T_{end}$  interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: A systematic review and meta-analysis. *Heart Rhythm.* 2017;14(8):1131-7. <https://doi.org/10.1016/j.hrthm.2017.05.031>
28. Lambiase PD.  $T_{peak}$ - $T_{end}$  interval and  $T_{peak}$ - $T_{end}$ /QT ratio as markers of ventricular tachycardia inducibility in subjects with Brugada ECG phenotype. *EP Europace.* 2010;12(2):158-9. <https://doi.org/10.1093/europace/eup424>
29. Antzelevitch C, Di Diego JM.  $T_{peak}$ - $T_{end}$  interval as a marker of arrhythmic risk. *Heart Rhythm.* 2019;16(6):954-5. <https://doi.org/10.1016/j.hrthm.2019.01.017>