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EDITORIAL COMMENT

The pursuit of better arrhythmic risk stratification in coronary artery disease patients: Are we on the right track?

Em busca de uma melhor estratificação de risco arrítmico em doentes com doença coronária: estaremos no caminho certo?

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Although cardiovascular mortality has decreased significantly in the last two decades with the use of more advanced therapies and prevention strategies, there are still 17 million deaths worldwide each year related to cardiac disease. Of these, 25% occur suddenly, and among these arrhythmic death is a major cause. Coronary artery disease (CAD) is the most prevalent factor in these deaths, increasing with age and male gender.[1]

During the acute phase of myocardial ischemia, the main mechanism for ventricular arrhythmias (VA) is abnormal automaticity due to currents of injury (created by increased extracellular potassium) between ischemic and healthy myocardium, while in the late stage after myocardial infarction, reentry is the predominant mechanism, occurring around scars and in areas with low voltage and slow conduction.[2] Modification of ionic currents and the presence of anatomical scar substrates are associated with prolonged ventricular activation and repolarization times, reflected in the surface electrocardiogram (ECG) by prolonged ventricular conduction times with increased QRS and QT duration (QRSd and QTd) and dispersion (DQRS and DQT). It has been reported that these parameters can be used to identify slow conduction zones prone to reentry and the occurrence of VA.[3]

The current issue of the *Journal* sees the publication of an observational study by Chávez-González et al.[4] in a population of 667 ST-elevation myocardial infarction (STEMI) patients treated in the coronary care unit of a single center in Cuba, aiming to determine the ability of electrocardiographic analysis to predict the occurrence of VA (defined by the authors as more than three premature ventricular beats). Left bundle branch block, previous myocardial infarction, atrial fibrillation, and the use of drugs known to prolong QT interval were defined as exclusion criteria in order to remove potential confounders for the ECG analysis. Ninety-two patients (13.8%) had VA, 68 (73.9%) of them within 48 hours of STEMI and 24 (26.1%) more than 48 hours after the index event. This population had a mean age of 68.8 years and was predominantly male (65.2%). There was a history of hypertension in 83.6% and of diabetes in 34.8%, and 51.1% of patients had a known history of coronary artery disease, although overall there were no significant differences between the groups with or without arrhythmias. Only 54.3% of patients underwent coronary revascularization –

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all with the use of recombinant streptokinase – and beta-blockers were only used in 57.6% and 52%, respectively, of patients in the groups with arrhythmic and non-arrhythmic events, without statistically significant differences between the groups. Patients with VA more frequently had anteroapical, large anterior, inferolateral and lateral infarctions and although their initial hemodynamic status was similar, they had lower ejection fraction (42.7% vs. 46.9%) and higher mortality (36.9% vs. 7.5%). The high mortality and rates of arrhythmia reported in this population probably reflect the low rate of revascularization in this STEMI population, as well as the method used (fibrinolysis rather than percutaneous coronary intervention).

It is known that approximately half of patients suffering out-of-hospital cardiac arrest with ventricular fibrillation (VF) as the first identified rhythm have evidence of acute myocardial infarction[2] and in patients with STEMI, 11.6% have VF before revascularization.[5] The occurrence of VA at any time during the course of an acute coronary syndrome is associated with a higher risk of death within 90 days of the event (with a higher risk of death in the setting of late VA occurring after >48 hours).[2] Likewise, it has been demonstrated that QRS and QT duration and dispersion are significantly increased in non-revascularized STEMI patients and when patients treated with fibrinolysis (also more prolonged) are compared with those receiving percutaneous coronary intervention.[6,7] QRS and QT duration and dispersion have also been shown to be significantly increased in lower ejection fraction ranges and can additionally refine assessment of risk of VA when used in conjunction with this parameter.[8,9]

In their study, Chávez-González et al. analyzed 11 ECG variables, performed at admission and every 24 hours during hospital stay, and demonstrated that in patients with VA, there were significant increases in corrected QT duration and dispersion, QRS duration and dispersion, and the presence of ST elevation in more than six leads. The current study also demonstrated that, applying a single cut-point of 45% for left ventricular ejection fraction, QRS dispersion and corrected QT interval were significantly increased in patients with impaired left ventricular function. Further stratifying patients with VA occurring within 48 hours of STEMI or later, the authors demonstrated the independent prognostic significance of QT interval greater than 529 ms, corrected QT dispersion over 66 ms and the presence of ST elevation in more than six leads as the main predictors of VA within 48 hours of admission. More than 48 hours after STEMI, the main predictors of VA were QRS dispersion greater than 50 ms and the presence of ST elevation in more than six leads.

The SCD-HeFT[10] and MADIT[11] trials provided sufficient evidence for the use of implantable cardioverter-defibrillators (ICDs) – especially in patients with CAD – for the prevention of sudden death in a population risk-stratified by ejection fraction (<30% and <35% respectively), with proven mortality reduction in ICD recipients, to make them the cornerstone of current practice.[1,2,10,11] Although ejection fraction is nowadays the primary tool for decision-making, there are gaps where risk assessment needs to be refined. On one hand, only around 20% of ICD recipients have appropriate ICD therapies, and on the other hand, a significant proportion of patients admitted for VT or aborted arrhythmic cardiac death have ejection fraction above 35%.[12] This clearly demonstrates a need to refine patient risk of VA and sudden death and the decision whether to adopt a primary prevention strategy for sudden death in specific subsets. Additionally, there are patients for whom the perceived risk of sudden death is increased after a myocardial infarction, but for whom there is also a gap for decision-making within 40 days of the event, as ejection fraction by itself is insufficient to decide definitively on an early strategy. Although various non-invasive risk markers for sudden cardiac death have been proposed for patients with myocardial ischemia (including heart rate variability, QRS dispersion, microvolt T wave alternans, heart rate turbulence, late potentials and programmed ventricular stimulation), none have become part of standard clinical practice.[1] Similarly, signal-averaged ECG has shown a low predictive value for the identification of high-risk patients, but performs well for low-risk patients, with a high negative predictive value.[13,14] Promising investigations of magnetic resonance imaging or biomarkers such as pro-brain natriuretic peptide may overcome this unmet need.

Analysis of dispersion of ventricular repolarization on the ECG for risk stratification of arrhythmic risk has been the subject of interest and several publications in recent years, but findings are mixed and standardization is complex, precluding its translation into clinical practice. While an association with increased likelihood of arrhythmic death has been documented in some works,[15–17] others have failed to consistently show the role of QRS duration and QT interval dispersion as predictors of events.[18,19] On the other hand, using risk markers in conjunction seems to be better for refinement of risk assessment and may be the way to direct patient management.[9,12,14] The study by Chávez-González et al. is in line with previous research by demonstrating the utility of the ECG for stratification of arrhythmic risk, particularly in a STEMI population, and giving insights on markers of VA in the acute and subacute phase of the disease. This emphasizes the need for additional intensive surveillance and care during hospital stay and for early reassessment and decision-making in later stages of the disease. In an area where there is clearly an unmet need, larger studies to validate this strategy would be of great value. These results demonstrate that we are probably on the right track for redefining risk of VA and sudden death, by using markers other than just ejection fraction, and that a stepwise approach using additive markers in conjunction may be the way to overcome this problem.

Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Priori S, Blomstrom-Lundqvist C, Mazzantini A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2015;36:2793–867.
2. Al-Khatib S, Stevenson W, Ackerman M, et al. 2017 AHA/ACC/HRS guideline for the management of patients with

ventricular arrhythmias and the prevention of sudden cardiac death. Circulation. 2018;138:e272–391.
3. Haugaa K, Edvardsen T, Amlie J, et al. Prediction of life-threatening arrhythmias: still an unresolved problem. Cardiology. 2011;118:129–37.
4. Chávez-González E, Rodríguez-Jiménez AE, Ferrer-Rodríguez CF, et al. Ventricular arrhythmias are associated with increased QT interval and QRS dispersion in patients with STEMI. Rev Port Cardiol. 2022;41:395–404.
5. Jabari R, Engstrom T, Glinge C, et al. Incidence and risk factors of ventricular fibrillation before primary angioplasty in patients with first ST-elevation myocardial infarction: a nationwide study in Denmark. J Am Heart Assoc. 2015;4:e001399.
6. Valizadeh A, Soltanabadi S, Koushafar S, et al. Comparison of QT dispersion in patients with ST elevation acute myocardial infarction (STEMI) before and after treatment by streptokinase versus primary percutaneous coronary intervention (PCI). BMC Cardiovasc Disord. 2020;20:493–501.
7. Papandonakis E, Tsoukas A, Christakos S. QT dispersion as a non-invasive arrhythmogenic marker in acute myocardial infarction. Ann Noninvas Electrocardiol. 1999;4:35–8.
8. Brembilla-Perrot B, Houriez P, Claudon O, et al. Evolution of QRS duration after myocardial infarction: clinical consequences. PACE. 2006;22:1466–75.
9. Donoiu I, Tartea G, Chávez-Gonzalez E, et al. Is there a utility for QRS dispersion in clinical practice? J Mind Med Sci. 2017;4:132–41.
10. Hardy G, Lee K, Mark D, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Eng J Med. 2005;352:225–37.
11. Moss A, Zareba W, Hall W, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Eng J Med. 2002;346:877–83.
12. Bhar-Amato, Davies W, Agarwal S, et al. ventricular arrhythmia after acute myocardial infraction: ''the perfect storm''. Arrhyth Electrophysiol Rev. 2017;6:134–9.
13. Tse G, Yan B, et al. Traditional and novel electrocardiographic conduction and repolarization markers of sudden cardiac death. Europace. 2017;19:712–21.
14. Bailey J, Hodges M, Church T, et al. Decision to implant a cardioverter defibrillator after myocardial infraction: the role of ejection fraction V. Other risk factor markers. Med Decis Making. 2007;27:151–60.
15. Zareba W, Moss A, Cessie S, et al. Dispersion of ventricular repolarization and arrhythmic cardiac death in coronary artery disease. Am J Cardiol. 1994;74:550–3.
16. Zaidi M, Robert A, Fesler R, et al. Dispersion of ventricular repolarization: a marker of ventricular arrhythmias in patients with previous myocardial infarction. Heart. 1997;78:371–5.
17. Ostovan M, Khosropanah S, Hooshmand S, et al. Adjacent QT dispersion: a good predictor of ventricular arrhythmias after myocardial infarction. Centr Eur J Med. 2008;3:179–82.
18. Kirchhof P, Eckardt L, Arslan O, et al. Prolonged QRS duration increases QT dispersion but does not relate to arrhythmias in survivors of acute myocardial infarction. PACE. 2003;24:789–95.
19. Pedretti R, Catalano O, Ballardini L, et al. Prognosis in myocardial infarction survivors with left ventricular dysfunction is predicted by electrocardiographic RR interval but not QT dispersion. Int J Cardiol. 1999;68:83–93.