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EDITORIAL

High-Resolution ECG for Predicting Ventricular Arrhythmia in Hypertrophic Cardiomyopathy: Another Tool in the Toolbox

Anil K. Gehi, MD

Hypertrophic cardiomyopathy (HCM) is a not uncommon cause of tragic sudden death events, particularly in young people. However, with the proper use of implantable defibrillators, prevention of sudden cardiac death can extend the life expectancy of patients with HCM on par with the general population.[1,2] The substrate underpinning the risk for ventricular arrhythmia in HCM is the disorganized myocyte architecture, hypertrophy with associated microvascular dysfunction, and replacement fibrosis.[3] The development of myocardial scar is arrhythmogenic by enabling reentrant ventricular circuits potentially triggered by enhanced automaticity as, for example, with vigorous exercise. The development of left ventricular (LV) aneurysm has been recently identified to increase the risk for arrhythmia by providing a discrete source for reentrant ventricular tachycardia.[4]

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Several risk markers have been demonstrated to identify patients at high risk for sudden death. Established markers include cardiac syncope, nonsustained ventricular tachycardia episodes on ambulatory monitoring, massive LV hypertrophy (≥30 mm), sudden death in first-degree relatives, end-stage heart failure, extensive late gadolinium enhancement (LGE) by cardiac magnetic resonance imaging (CMR), and LV aneurysm. Less established markers include coronary artery disease and marked LV outflow gradient.[2]

There have been varied approaches for risk stratification of sudden death in patients with HCM. Initially, patients were considered at high risk and potentially warranting implantable cardioverter-defibrillator (ICD) implantation when carrying ≥2 traditional risk factors for sudden death.[5] The European Society of Cardiology moved to a risk score in their 2014 guidelines.[6] The American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines recommend an approach for establishing a patient as high risk based on the presence of any single traditional risk factor (syncope, massive LV hypertrophy, or family history of sudden cardiac death).[7] If only nonsustained ventricular tachycardia is the risk factor, then "risk modifiers" should be considered, which include age <30 years, LGE on CMR, LV outflow tract obstruction, or LV aneurysm. The most reliable approach has not been established.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Suszko and colleagues present a study considering the use of QRS peak (QRSp)

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Correspondence to: Anil K. Gehi, MD, University of North Carolina Medical Center, Cardiac Electrophysiology, CB 7075, 160 Dental Circle, 6025 Burnett-Womack Bldg., Chapel Hill, NC 27599-7075. Email: anilgehi@med.unc.edu

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quantification on high-resolution ECGs for the prediction of ventricular arrhythmias in patients with HCM.[8] Because arrhythmogenesis in HCM is likely related to heterogeneity of conduction in the presence of myocardial fibrosis, QRSp, a marker of alterations in conduction, may be useful in identifying patients at high risk for arrhythmia. Current recommendations for risk stratification in HCM do not consider QRS metrics, which may provide valuable information. Moreover, the authors have previously demonstrated the use of this novel risk marker in patients with ischemic or nonischemic cardiomyopathy.[9]

For their study, the authors enrolled all patients at their institution with HCM implanted with a prophylactic ICD according to American Heart Association/American College of Cardiology practice guidelines between 2009 and 2017. Patients had at least 1 risk marker for sudden cardiac death. Secondary prevention patients were excluded from the study. Following ICD implantation, high-resolution, signal-averaged ECG was performed for >3 minutes. A method for quantifying the number of QRS peaks was developed using automated software. QRSp represents the total number of QRS deflections deviating from a smoothed QRS template. Both QRSp maximum and mean were calculated. The authors collected information on traditional risk markers and measured the European Society of Cardiolog (ESC) HCM risk score to compare the predictability of QRSp. In addition, they measured other ECG markers such as QRS duration and QRS fragmentation. The outcome of interest was appropriate ICD therapy (shock or antitachycardia pacing).

Overall, 134 patients, 21 of whom had ventricular arrythmia events, were included in the analysis. There was no correlation of QRSp with LV wall thickness and a weak correlation with LV ejection fraction. Patients with ventricular arrhythmias had higher mean and maximum QRSp but ventricular arrhythmias did not correlate with QRS duration or QRS fragmentation. Area under the curve for ventricular arrhythmia events with ≥4 QRS peaks was 0.76 with 91% sensitivity and 39% specificity. Patients with high QRSp had lower ejection fractions, more often had LV aneurysm, had larger left atrial, had more risk factors for sudden cardiac death, and had higher ESC risk scores. There was no collinearity of QRSp with other risk markers.

The authors conclude that QRSp may be a useful risk marker to identify patients at high risk for ventricular arrhythmia and helpful in determining which patients may warrant prophylactic ICD implantation. QRS peaks ≥4 dichotomized patients into those with 4.4% and 1% annual risks for ventricular arrhythmia. In patients aged <50 years, QRS peaks ≥4 dichotomized patients between those with 6.9% and 0% annual risk for ventricular arrhythmia.

Although the novel QRSp tool presented in this study shows promise for use in the risk stratification of patients with HCM, there are several potential limitations that should be considered. First, the authors state that CMR was only performed in 63% of patients in this study, so LGE by CMR was excluded in analysis. Given that the mechanism for development of QRSp is the presence of myocardial fibrosis, the absence of CMR LGE in the analysis is particularly problematic. We do not know whether QRSp provides information of value beyond that of CMR. There may be benefit of having an alternative measure for quantifying myocardial fibrosis as CMR may not be available in many institutions. However, the value of LGE by CMR in risk stratification is well established. Second, it would be helpful to see whether there was a gradient effect of the number of maximum QRS peaks and risk for arrhythmia. This would help substantiate the relationship between QRSp and ventricular arrhythmia. Third, ventricular arrhythmia is an intermediate but pragmatic outcome to use for analysis. However, not all ventricular arrhythmia would lead to sudden death. Whether QRSp would provide discriminatory value for an end point of sudden death is unclear. Finally, like all risk markers for HCM, these values are dynamic. It is unclear how often to repeat a QRSp assessment.

In conclusion, the authors should be commended for developing and studying a novel risk marker for sudden death and demonstrating its utility in a variety of pathogenic substrates. Although QRSp shows promise as another tool for risk stratification in HCM, it would likely need to be used in combination with other well-established risk markers. We look forward to a larger study of QRSp in patients with HCM potentially including those without an ICD in place.

ARTICLE INFORMATION

Affiliation

Division of Cardiology, Department of Medicine, University of North Carolina Medical Center, Chapel Hill, NC

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