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Ventricular arrhythmia is predicted by sum absolute QRST integral but not by QRS width

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Abstract

Background: There is a controversy regarding the association between QRS width and ventricular arrhythmias (VAs). We hypothesized that predictive value of the QRS width could be improved if QRS width were considered in the context of the sum magnitude of the absolute QRST integral in 3 orthogonal leads sum absolute QRST integral (SAI QRST). We explored correlations between QRS width, SAI QRST, and VA in primary prevention implantable cardioverter-defibrillator (ICD) patients with structural heart disease.

Methods: Baseline orthogonal electrocardiograms were recorded at rest in 355 patients with implanted primary prevention ICDs (mean age, 59.5 ± 12.4 years; 279 male [79%]). Patients were observed prospectively at least 6 months; appropriate ICD therapies because of sustained VA served as end points. The sum magnitude of the absolute QRST integral in 3 orthogonal leads (SAI QRST) was calculated.

Results: During a mean follow-up of 18 months, 48 patients had sustained VA and received appropriate ICD therapies. There was no difference in baseline QRS width between patients with and those without arrhythmia (114.9 ± 32.8 vs 108.9 ± 24.7 milliseconds; $P = .230$). SAI QRST was significantly lower in patients with VA at follow-up than in patients without VA (102.6 ± 27.6 vs 112.0 ± 31.9 mV·ms; $P = 0.034$). Patients with SAI QRST (≤145 mV·ms) had a 3-fold higher risk of ventricular tachycardia (VT)/ventricular fibrillation (VF) (hazard ratio [HR], 3.25; 95% confidence interval [CI], 1.59-6.75; $P = .001$). In the univariate analysis, QRS width did not predict VT/VF. In the bivariate Cox regression model, every 1 millisecond of incremental QRS widening with a simultaneous 1 mV·ms SAI QRST decrease raised the risk of VT/VF by 2% (HR, 1.02; 95% CI, 1.01-1.03; $P = .005$).

Conclusion: QRS widening is associated with ventricular tachyarrhythmia only if accompanied by low SAI QRST.

Keywords: Ventricular tachyarrhythmia; QRS; Risk stratification; Implantable cardioverter-defibrillator

Background

Controversy remains regarding the association between QRS width and sudden cardiac death (SCD). In the early analysis of the Multicenter Automatic Defibrillator Implantation Trial II Multicenter Automatic Defibrillator Implantation Trial (MADIT) II study, a wide QRS of greater than 150 milliseconds was associated with a more substantial benefit from implantable cardioverter-defibrillator (ICD)[1] than was a narrow QRS of less than 120 milliseconds. Subsequent studies did not confirm the relation between QRS width and ventricular arrhythmia (VA) occurrence in primary and secondary prevention ICD patients with structural heart disease.[2,3] However, QRS width predicted SCD in medically treated MADIT II heart failure patients.[3]

We proposed a novel marker of susceptibility to VA, namely sum absolute QRST integral (SAI QRST), measured as the sum magnitude of the absolute QRST integral on 3 orthogonal electrocardiogram (ECG) leads. To study the predictive value of SAI QRST and to further elucidate

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associations between SAI QRST, QRS width, and VA, we undertook analysis of prospective observational cohort study Prospective Observational Study of the ICD in Sudden Cardiac Death Prevention (PROSE-ICD) patients with structural heart disease and routine indications for primary prevention single-chamber or dual-chamber ICD.

Methods

All patients gave written informed consent before entering the study. The study protocol was approved by the Johns Hopkins University Institutional Review Board (Baltimore, MD).

Study population

PROSE-ICD (NCT00733590) is an ongoing prospective observational multicenter cohort study of patients with either ischemic or nonischemic cardiomyopathy, who have routine indications for ICD as primary prevention of SCD. Patients were eligible for the study if the left ventricular ejection fraction (EF) was 35% or less, myocardial infarction was at least 4 weeks old, or nonischemic cardiomyopathy was present for at least 9 months. Patients were excluded if the ICD was indicated for secondary prevention of SCD, if the patient had a permanent pacemaker or a class I indication for pacing, if the patient had New York Heart Association (NYHA) class IV, or if the patient was pregnant. Consecutive patients with indications for single-chamber or dual-chamber ICD, but not Cardiac Resynchronization Therapy Defibrillator (CRT-D), and followed up for at least 6 months were included in this report.

Surface ECG recording

Digital orthogonal ECG was recorded before ICD implantation during 5 minutes at rest, using the modified Frank orthogonal XYZ leads by PC ECG machine (Norav Medical Ltd, Thornhill, Ontario, Canada), with a 1000-Hz sampling frequency, high-pass filter 0.05 Hz and low-pass filter 350 Hz. QRS width on the clinical 12-lead ECG was measured automatically by the built-in algorithm (Marquette ECG 12SL & MUSE system, GE Healthcare Clinical Systems, Wauwatosa, WI, USA).

QRST integral measurement

All ECGs were analyzed by customized software in a robust automated fashion. QRS onset and end of T wave were identified by the user (LGT). The first 15 beats were used by the algorithm to construct templates. The user viewed templates of all 3 orthogonal leads, selected the best quality lead (default lead X), and manually defined the onset of the QRS and end of T wave fiducial points. Then, the algorithm measured absolute QRST integral of each beat and calculated the average value for the time epoch. Absolute QRST integral was measured as the arithmetic sum of areas under the QRST curve (absolute area under the QRST curve above baseline was added to the area below baseline), averaged during a 5-minute epoch. The sum magnitude of 3 orthogonal leads absolute QRST integral (SAI QRST) was calculated.

End points

Appropriate ICD therapies (either shock or antitachycardia pacing) for VA served as the primary end points for analysis. Programming of the ICD was based on the attending electrophysiologist's clinical evaluation. The ICD device was interrogated during follow-up visits every 6 months. All ICD interrogation data were reviewed by an independent end points adjudication committee, blinded to the results of SAI QRST analysis.

Statistical analysis

Study participants were categorized according to their baseline SAI QRST value, with SAI QRST of 69 mV·ms or less labeled low, SAI QRST of 70 to 145 mV·ms labeled intermediate, and SAI QRST of greater than 145 mV·ms labeled high. Linear regression analysis was used to study the correlation between SAI QRST and QRS width. Adjusted by QRS width, Kaplan-Meier survival curves were constructed for subjects with low, intermediate, or high SAI QRST. The log-rank (Mantel-Cox) and Tarone-Ware statistics were computed to test the equality of survival distributions. Univariate, bivariate, and multivariate Cox proportional hazards regression analyses were performed. An interaction between SAI QRST and QRS duration was tested in the Cox model. STATA 10 software (StataCorp LP, College Station, TX) was used for calculations.

Results

Patient population

Baseline clinical characteristics of patients are presented in Table 1. Study participants (n = 355) were predominantly males with ischemic cardiomyopathy, heart failure NYHA classes II to III, and narrow QRS about 110 milliseconds at baseline. There were no statistically significant differences between baseline clinical and ECG characteristics of patients with low, intermediate, and high SAI QRST, with the exception of QRS duration. QRS was incrementally wider in

Table 1
Clinical and baseline ECG characteristics of patients

Characteristic	n = 355
Age ± SD, y	59.5 ± 12.4
Male sex, n (%)	279 (78.6)
Whites, n (%)	238 (67.0)
Ischemic cardiomyopathy, n (%)	220 (62.0)
Baseline left ventricular EF ± SD, %	22.96 ± 9.19
QRS, ms	109.79 ± 26.04
Left ventricular diastolic diameter ± SD, cm	5.87 ± 0.93
Body mass index ± SD	28.67 ± 6.00
Beta blockers, n (%)	336 (94.6)
NYHA class I, n (%)	78 (22.0)
NYHA class II, n (%)	110 (31.0)
NYHA class III, n (%)	167 (47.0)
Inducible VT, n (%)	92 (25.9)
Heart rate ± SD, beats per minute	72.6 ± 14.3