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Prolonged Ventricular Conduction and Repolarization During Right Ventricular Stimulation Predicts Ventricular Arrhythmias and Death in Patients With Cardiomyopathy

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ABSTRACT

OBJECTIVES The goal of this study was to evaluate whether prolonged ventricular conduction (paced QRS) and repolarization (paced QTc) times observed during ventricular stimulation predict ventricular arrhythmic events and death.

BACKGROUND Abnormal ventricular conduction and repolarization can predispose patients to ventricular arrhythmias.

METHODS Consecutive patients with left ventricular dysfunction (ejection fraction <50%) undergoing electrophysiology studies from January 2002 until May 2014 were identified at Mayo Clinic (Rochester, Minnesota). Patients were followed up until December 2014 for occurrence of ventricular arrhythmias and death.

RESULTS Among the 501 patients included (mean age 65 years; mean left ventricular ejection fraction 33.1%), longer paced ventricular conduction was associated with longer baseline QRS duration, longer QT interval, and lower ejection fraction. On multivariable analysis, longer paced QRS duration was associated with higher risk of ventricular arrhythmia (hazard ratio [HR]: 1.11 per 10-ms increase; 95% confidence interval [CI]: 1.07 to 1.16; $p < 0.001$) and all-cause death or arrhythmia (HR: 1.09; 95% CI: 1.09 to 1.13; $p < 0.001$). A paced QRS duration >190 ms was associated with a 3.6 times higher risk of ventricular arrhythmia (HR: 3.6; 95% CI: 2.35 to 5.53; $p < 0.001$) and a 2.1 times higher risk of death or arrhythmia (HR: 2.12; 95% CI: 1.53 to 2.95; $p < 0.001$), independent of left ventricular function or baseline QRS duration. Longer QTc interval during ventricular pacing was associated with a higher risk of ventricular arrhythmia (HR: 1.03 per 10-ms increase; 95% CI: 1.02 to 1.12; $p < 0.001$) independent of paced QRS duration.

CONCLUSIONS Longer paced QRS duration and paced QTc interval predict ventricular arrhythmias in patients with cardiomyopathy. Ventricular conduction and repolarization prolongation during right ventricular pacing can determine the risk of ventricular arrhythmias. (J Am Coll Cardiol EP 2017;■:■-■) © 2017 by the American College of Cardiology Foundation.

No single clinical parameter can accurately identify patients at risk for ventricular arrhythmic events (1-7); the currently used parameters have, at best, moderate predictive value (6,8,9). The most widely used and accepted criterion for implantation of a defibrillator for primary prevention is severely decreased left ventricular (LV) function (10).

However, many patients who die of sudden cardiac death have moderate or only mildly decreased LV

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ABBREVIATIONS AND ACRONYMS

AUC = area under the receiver-operating characteristic curve

CI = confidence interval

ECG = electrocardiographic

EF = ejection fraction

HR = hazard ratio

LV = left ventricular

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

OR = odds ratio

RV = right ventricular

function, whereas in many others with severely decreased LV function, ventricular arrhythmias do not develop (11,12). Electrocardiographic (ECG) parameters associated with sudden arrhythmic death have poor predictive value and are generally not used clinically (9). Therefore, development of new and better risk markers of ventricular arrhythmic events is needed.

Ventricular conduction and repolarization abnormalities are associated with a higher risk of ventricular arrhythmias (13,14). Most analyses of ventricular conduction and repolarization are conducted in the baseline state, during normal depolarization. However, many abnormalities in these parameters can only be elicited under certain circumstances, such as exercise stress tests (15) or epinephrine administration (16) for long QT syndrome or antiarrhythmic agent infusion (17) for Brugada syndrome. Thus, provoking maneuvers during an apparently normal ventricular depolarization and repolarization assessment may reveal underlying abnormalities that can be associated with a higher risk of ventricular arrhythmias.

The goal of the present study was to evaluate the association of changes in ventricular conduction and repolarization times incited by ventricular stimulation with risk of ventricular arrhythmia and death in patients with LV dysfunction.

METHODS

PATIENTS. Consecutive patients with LV dysfunction undergoing electrophysiological testing from January 2002 through May 2014 at Mayo Clinic (Rochester, Minnesota) were enrolled. The duration changes in ventricular conduction and repolarization times during ventricular stimulation were measured. The study sample was followed up until December 2014 for development of ventricular arrhythmic events and all-cause and cardiovascular death. The study was approved by the Mayo Clinic Institutional Review Board.

ECG ANALYSIS AND DATA ACQUISITION. ECG data were acquired after retrieving and reviewing standard electrophysiology studies using the Prucka MacLab/CardioLab system, version 5.0G (GE Healthcare, Little Chalfont, United Kingdom). All measurements were performed on the electronic system by using incorporated electronic calipers during simultaneous recording of the standard 12-lead electrocardiogram. QRS duration (from the earliest onset of the Q, R, or S wave in any lead to the latest offset of the R or S wave in any lead) and QT interval (from the earliest onset of the QRS complex in any lead to the latest offset of the T wave, the latest indication of ventricular repolarization) were measured. We evaluated baseline QT interval during atrial pacing at a cycle length of 600 ms and the paced QT interval during right ventricular (RV) stimulation at the same cycle length. The QT interval was then corrected for heart rate by using the Bazett formula. Measurements during pacing were considered only from the RV apex, which was confirmed by fluoroscopy and paced QRS morphology analysis.

In total, 501 patients underwent programmed ventricular stimulation for induction of ventricular arrhythmias: 256 (51.1%) as a diagnostic study only, 64 (12.8%) as part of ablation of supraventricular arrhythmias, 9 (1.8%) for ablation of atrial fibrillation, and 172 (34.3%) for ablation of ventricular extrasystoles or tachycardia.

PRIMARY OUTCOMES. Cardiovascular and all-cause deaths that occurred by December 2014 were reviewed. Immediate cause-of-death information was obtained from hospital documents, communication with family members, autopsy reports, and death certificates. Cardiovascular death was defined as non-sudden cardiac death. Sudden cardiac death was defined as death within 1 h after abrupt onset of symptoms or within 24 h after onset of symptoms if autopsy data did not reveal a noncardiac cause or after successful resuscitation from ventricular tachycardia and/or ventricular fibrillation.

Ventricular arrhythmic events were defined as symptomatic episodes of documented ventricular tachycardia or fibrillation requiring intervention (defibrillation shocks or antitachycardia pacing in patients with implantable defibrillators; documented ventricular arrhythmias requiring external shocks or overdrive pacing). In patients with implantable cardiac devices, arrhythmic events were classified after device-retrieved data related to the events were analyzed by 2 cardiac arrhythmia specialists; if findings were discrepant, a third specialist determined the event classification. Other sources of documentation (electrocardiograms, external ambulatory cardiac monitor, or telemetry tracings) were also reviewed. Ventricular arrhythmic events were evaluated blindly to ECG data, starting after the electrophysiology study date.

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD and compared by using the Student *t* test or Mann-Whitney test, as appropriate; categorical variables are expressed as count (%), and