Fragmented QRS on twelve-lead electrocardiogram predicts arrhythmic events in patients with ischemic and nonischemic cardiomyopathy

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BACKGROUND Myocardial scar is a substrate for reentrant ventricular arrhythmias and is associated with poor prognosis. Fragmented QRS (fQRS) on 12-lead ECG represents myocardial conduction delays due to myocardial scar in patients with coronary artery disease (CAD).

OBJECTIVE The purpose of this study was to determine whether fQRS is associated with increased ventricular arrhythmic event and mortality in patients with CAD and nonischemic dilated cardiomyopathy (DCM).

METHODS Arrhythmic events and mortality were studied in 361 patients (91% male, age 63.3 ± 11.4 years, mean follow-up 16.6 ± 10.2 months) with CAD and DCM who received an implantable cardioverter-defibrillator for primary or secondary prophylaxis. fQRS included various RSR′ patterns (QRS duration <120 ms), such as ≥1 R prime or notching of the R wave or S wave present on at least two contiguous leads of those representing anterior (V_1–V_5), lateral (I, aVL, V_6), or inferior (II, III, aVF) myocardial segments.

RESULTS fQRS was present in 84 (23%) patients (fQRS group) and absent in 100 (28%) patients (non-fQRS group). Wide QRS (wQRS; QRS duration ≥120 ms) was present in 177 (49%) patients. Kaplan-Meier analysis revealed that event-free survival for an arrhythmic event (implantable cardioverter-defibrillator shock or antitachycardia pacing) was significantly lower in the fQRS group than in the non-fQRS and wQRS groups ($P < .001$ and $P < .019$, respectively). fQRS was an independent predictor of an arrhythmic event but not of death.

CONCLUSION fQRS on 12-lead ECG is a predictor of arrhythmic events in patients with CAD and DCM. fQRS is associated with a significantly decreased time to first arrhythmic event compared with non-fQRS and wQRS.

KEYWORDS Arrhythmic event; Fragmented QRS; Mortality

ABBREVIATIONS **ABCD** = Alternans Before Cardioverter Defibrillator (trial); **CAD** = coronary artery disease; **DCM** = dilated cardiomyopathy; **EF** = ejection fraction; **fQRS** = fragmented QRS; **ICD** = implantable cardioverter-defibrillator; **MASTER** = Microvolt T Wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients (trial); **SCD** = sudden cardiac death; **SCD-HeFT** = Sudden Cardiac Death in Heart Failure Trial; **VF** = ventricular fibrillation; **VT** = ventricular tachycardia; **wQRS** = wide QRS

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Introduction

The implantable cardioverter-defibrillator (ICD) decreases mortality in patients with coronary artery disease (CAD) and nonischemic dilated cardiomyopathy (DCM) by treating an arrhythmic event with an ICD shock or antitachycardia pacing.[1–4] Recurrent arrhythmic events require antiarrhythmic drug therapy and/or ablation of ventricular arrhythmia and is associated with a significantly poorer quality of life.[5,6] Furthermore, an arrhythmic event (ventricular tachycardia [VT] or ventricular fibrillation [VF]) is a predictor of mortality in patients with heart failure who receive an ICD for primary prophylaxis.[7] Few tests predict an arrhythmic event and mortality in these patients. In patients with CAD, poor left ventricular ejection fraction (EF), QRS duration, secondary prevention indication, microvolt T-wave alternans (MTWA), and signal-averaged ECG predict an arrhythmic event.[8–10] In patients with DCM who received an ICD for secondary prevention indication, severely reduced EF with left ventricular end-diastolic diameter ≥7 cm, EF <30% with nonsustained VT, and prolonged HV interval with QRS duration >110 ms predict an arrhythmic event.[11–13] Two major studies of DCM patients report conflicting data on reduced EF, MTWA, and baroreceptor reflex sensitivity.[14,15] Additionally, several tests predicting adverse outcome in ischemic cardiomyopathy, such as programmed electrical stimulation, signal-averaged ECG, and heart rate variability, have limited ability for risk stratification in patients with DCM[14,16] and have a low predictive value for an arrhythmic event or death.[10]

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Segmental myocardial scar present in CAD and areas of patchy myocardial scar present in DCM serve as substrates for reentry of ventricular arrhythmias induced during electrophysiologic study.[17–19] Studies also have shown that the presence of a fragmented QRS (fQRS) on 12-lead ECG signifies myocardial scar in patients with CAD due to resultant myocardial conduction abnormalities.[20–22] fQRS is a sign comparable to the epsilon wave seen in arrhythmogenic right ventricular dysplasia/cardiomyopathy, indicating the presence of myocardial scar.[23] Furthermore, fQRS is a predictor of arrhythmic events in patients with Brugada syndrome.[24] fQRS includes various RSR′ patterns (Figures 1 and 2), such as an additional R prime (R′), notching of the R wave, notching of the S wave, or the presence of multiple (>2) R waves, in the absence of a wide QRS (wQRS).[20,25] The main purpose of this study was to determine the prognostic significance of fQRS for an arrhythmic event in patients with ischemic and nonischemic cardiomyopathy who received an ICD for primary or secondary prevention of sudden cardiac death (SCD). The secondary aim was to determine the prognostic value of fQRS for all-cause mortality in these patients.

Methods

This retrospective study included patients with CAD and DCM who received an ICD for primary or secondary prevention of SCD at Indiana University hospitals from January 1, 2002 to December 31, 2005. The study was approved by the Institutional Review Board of Indiana University and Roudebush VA Medical Center, Indianapolis. Patients with CAD had either a history of myocardial infarction or an angiographically significant coronary artery obstruction (>70%) with symptoms related to CAD. The diagnosis of DCM was established by the absence of significant coronary artery narrowing (<50%) on coronary angiogram with EF ≤40%, as well as the absence of a history of myocardial infarction, uncontrolled hypertension, cocaine abuse, or tachycardia-induced cardiomyopathy. In patients in whom coronary angiography had been performed more than 12 months before ICD placement, a symptom-limited exercise stress test was used to screen for newly developed coronary disease.

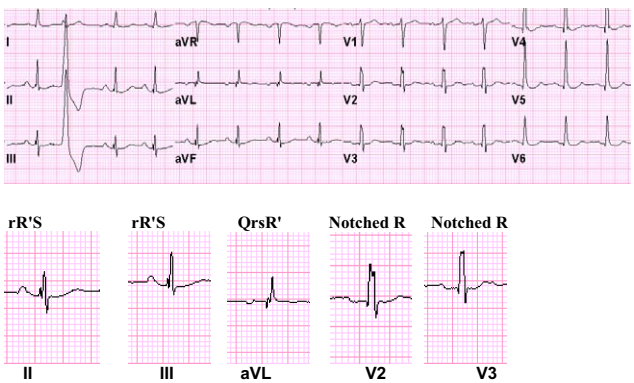

Figure 1 Different morphologies of fragmented QRS (fQRS) on 12-lead ECG in a patient with coronary artery disease. **Top:** Twelve-lead ECG shows fragmented QRS in the inferior leads and one of the lateral leads (aVL) and a notched R wave in leads V_4–V_5. **Bottom:** Enlarged views of various QRS morphologies in different ECG leads consistent with inferior scar (fQRS in leads II and III) and anterior scar (fQRS in lead V_2 and V_3). fQRS is present in only one of the lateral leads (aVL); therefore, it does not meet the criteria for a lateral scar.

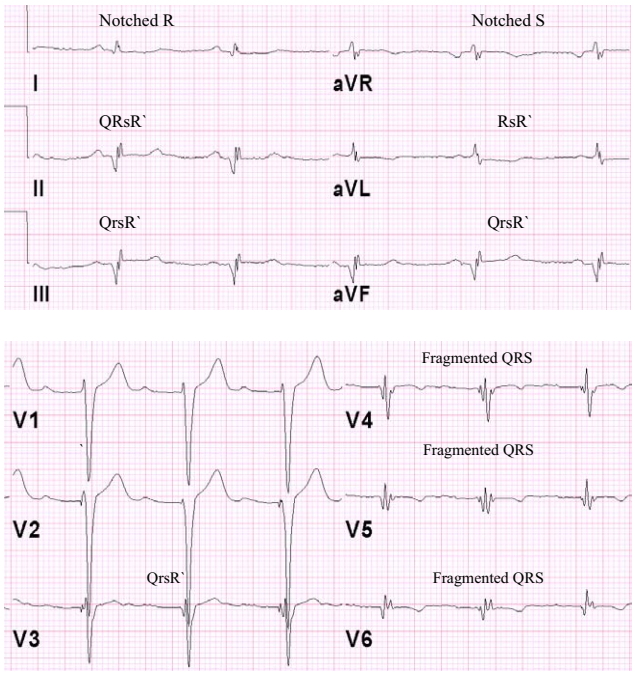

Figure 2 Twelve-lead ECG showing various fragmented QRS (fQRS) patterns in a patient with dilated nonischemic cardiomyopathy. The 12-lead ECG shows fragmented QRS and Q waves in inferior leads (QRsR′ pattern in lead II, QrsR′ pattern in leads III and aVF), lateral leads (notched R wave in lead I, RsR′ in lead aVF, fragmented QRS in lead V_6), and anterior leads (fragmented QRS in leads V_3–V_5) in different ECG leads.

Primary and secondary prevention ICD indications

Primary prevention indications for ICD therapy were (1) CAD, nonsustained VT, EF ≤40%, and inducible sustained VT/VF; (2) history of prior myocardial infarction and EF ≤30%; or (3) CAD or DCM with left ventricular dysfunction (EF ≤35%) and New York Heart Association class II and III congestive heart failure. Secondary prevention indications were (1) VF or cardiac arrest without a transient or reversible cause (2) spontaneous sustained VT (3) spontaneous syncopal VT or syncope of unknown etiology and inducible sustained VT/VF or, (4) unexplained syncope after a thorough evaluation in patients with DCM.

ECG analysis

Baseline 12-lead ECGs (frequency range 0.15–150 Hz, 25 mm/s, 10 mm/mV; GE Marquette, Milwaukee, WI, USA) were obtained prior to ICD placement. fQRS was defined by the presence of various RSR′ patterns (QRS duration <120 ms) with or without Q wave, which include an additional R wave (R prime) or notching of the R wave or notching of the S wave, or the presence of more than two R primes (fragmentation) in two contiguous leads corresponding to a ma-