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Relative Wall Thickness and the Risk for Ventricular Tachyarrhythmias in Patients With Left Ventricular Dysfunction

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ABSTRACT

BACKGROUND Relative wall thickness (RWT), defined as 2 times posterior wall thickness divided by the left ventricular (LV) diastolic diameter, is a measure of LV geometry and may be a marker for adverse events in patients with LV dysfunction.

OBJECTIVES The aim of this study was to investigate the relationship between RWT and the risk for ventricular tachyarrhythmia (VA) in patients enrolled in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) study.

METHODS The study population comprised 1,260 patients with mild heart failure and left bundle branch block.

RESULTS In a multivariable model, RWT was the most powerful echocardiographic measure for estimating the risk of VAs compared with commonly used echocardiographic variables. Patients with low RWT (<0.24) had 83% ($p < 0.001$) increased risk for VA and 68% ($p < 0.001$) increase in VA risk or death (VA/death) compared with patients with higher RWT values. Each 0.01-unit decrease in RWT was associated with 12% ($p < 0.001$) and 10% ($p < 0.001$) increases in the risk of VA and VA/death, respectively. Treatment with cardiac resynchronization therapy with defibrillator (CRT-D; CRT with implantable cardioverter-defibrillator) was associated with a greater increase in RWT compared with implantable cardioverter-defibrillator at 12 months ($4.6 \pm 6.8\%$ vs. $1.5 \pm 2.7\%$; $p < 0.001$), and every 10% increase in RWT in CRT-D patients was associated with 34% ($p = 0.027$) and 36% ($p = 0.009$) reductions in the risk of subsequent VA and VA/death, respectively.

CONCLUSIONS In patients with mild heart failure and left bundle branch block, decreased RWT was associated with an increase in the risk of VA and VA/death. CRT-D therapy was associated with a favorable increase in RWT and reduction in risk of VA and VA/death. (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy [MADIT-CRT]; NCT00180271) (J Am Coll Cardiol 2016;67:303–12)

Reduced left ventricular ejection fraction (LVEF) and the presence of myocardial scar are associated with higher risk of ventricular arrhythmia (VA) and sudden cardiac death (1). The implantable cardioverter-defibrillator (ICD) is an established therapy for reducing mortality associated with VA (1,2). Cardiac resynchronization therapy with defibrillator (CRT-D) compared with ICD was shown

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ABBREVIATIONS AND ACRONYMS

CRT-D = cardiac resynchronization therapy with defibrillator

HF = heart failure

ICD = implantable cardioverter-defibrillator

LBBB = left bundle branch block

LVEDD = left ventricular end-diastolic diameter

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

PWT = posterior wall thickness

RWT = relative wall thickness

SWT = septal wall thickness

VA = ventricular tachyarrhythmia

VF = ventricular fibrillation

VT = ventricular tachycardia

to reduce VA incidence, most likely through a mechanism of reverse remodeling in patients with prolonged QRS duration and left bundle branch block (LBBB) morphology (3-6).

Remodeling patterns of the LV can be assessed by echocardiographic measurement of relative wall thickness (RWT) and broadly categorized as normal or adverse remodeling, either eccentric or concentric. Previous studies have shown that concentric remodeling (high RWT) is associated with increased morbidity and mortality in hypertensive patients with hypertrophic cardiomyopathy (7-9). However, data regarding the relation between the magnitude of eccentric hypertrophy (low RWT) and the risk of VA in patients with dilated cardiomyopathy are scarce.

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The present study was carried out in 1,260 patients with mild heart failure (HF) and LBBB enrolled in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) study. We aimed to investigate: 1) the predictive value of RWT for the risk of VA compared with other commonly used echocardiographic variables; 2) the relationship between LV morphology and the risk of VA by measuring RWT; and 3) the remodeling effect of CRT-D on RWT.

METHODS

The study population comprised 1,260 patients enrolled in the MADIT-CRT trial with LBBB at baseline electrocardiogram (70% of the original 1,820 patients). The design and results of the MADIT-CRT study have been reported previously (3,10). Briefly, patients who had ischemic cardiomyopathy (New York Heart Association [NYHA] functional class I or II) or nonischemic cardiomyopathy (NYHA functional class II), LVEF ≤30%, normal sinus rhythm, and QRS duration ≥130 ms, were randomized to receive CRT-D or ICD therapy in a 3:2 ratio.

Device interrogation and programming were performed as previously reported (10). All devices were programmed to monitor and deliver therapy, antitachycardia pacing, and/or shock therapy. All devices were interrogated 1 month after enrollment and thereafter every 3 months; arrhythmia episodes were adjudicated by an independent core laboratory for pre-defined categories of appropriate or inappropriate therapy. A VA episode was defined when device-rendered therapy including antitachycardia pacing or shock was appropriately delivered. Ventricular tachycardia (VT) was defined as an episode with ventricular rates between 180 and 250 beats/min; ventricular fibrillation (VF) was defined as an episode with ventricular rates >250 beats/min. Fast VT was defined as an episode with ventricular rates ≥200 beats/min or VF.

Echocardiograms were obtained according to a study-specific protocol at baseline, which was before device implantation, and at 1 year. Echocardiography recordings were analyzed offline by a single technician in an independent core laboratory. Echocardiography investigators analyzing the images were blinded to treatment assignment and clinical outcome. Reproducibility of the primary measures was assessed by the primary observer reanalyzing 101 random studies.

LV volumes were measured with the Simpson disk method in the apical 4- and 2-chamber views, and LVEF was calculated according to the established

TABLE 1 Patient Characteristics

	Low RWT (<0.24) (n = 414)	High RWT (≥0.24) (n = 846)
Age at enrollment, yrs	61.2 ± 11.0	65.7 ± 10.5*
Female	22	35*
CRT-D assigned therapy	58	61
Ischemic cardiomyopathy	43	45
Diabetes	30	30
Hypertension	57	66*
Smoking	14	9*
Prior atrial arrhythmia	10	12
Prior ventricular arrhythmia	9	5*
Prior HF hospitalization	40	38
Prior CABG	23	22
Antiarrhythmic treatment	8	6
ACE inhibitor or ARB	97	96
Aspirin	58	63
Beta-blocker	95	93
Diuretic	71	67
Statin	61	65
QRS duration, ms	168.0 ± 21.3	160.6 ± 17.7*
Heart rate, beats/min	69.1 ± 11.0	67.9 ± 10.9*
BMI, kg/m^2	29.0 ± 5.2	28.3 ± 5.1*
Creatinine, mg/dl	1.15 ± 0.31	1.13 ± 0.32
BNP, pg/ml	147.5 ± 185.2	100.9 ± 128.4*
SBP, mm Hg	118.5 ± 16.6	124.8 ± 17.0*
LVEF, %	26.8 ± 3.4	29.7 ± 3.1*
LVEDV indexed by BSA, ml/m^2	147.3 ± 35.3	115.6 ± 20.1*
LVESV indexed by BSA, ml/m^2	108.3 ± 28.8	81.5 ± 15.7*
LAV indexed by BSA, ml/m^2	52.4 ± 10.8	44.5 ± 8.6*

Values are mean ± SD or %. *p < 0.05.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; BNP = B-type natriuretic peptide; BSA = body surface area; CABG = coronary artery bypass graft; CRT-D = cardiac resynchronization therapy with defibrillator; HF = heart failure; LAV = left atrial volume; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; RWT = relative wall thickness; SBP = systolic blood pressure.