Adverse Structural Remodeling of the Left Ventricle and Ventricular Arrhythmias in Patients With Depressed Ejection Fraction

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ABSTRACT

Background: The relationship of life-threatening ventricular arrhythmias to specific patterns of adverse LV remodeling has not been reported. We examined the relationship of ventricular tachycardia and/or fibrillation (VT/VF) to the pattern of left ventricular (LV) structural remodeling and to the degree of LV dysfunction in patients with a low ejection fraction (EF).

Methods and Results: Data from 127 patients with a low EF (≤0.45) and an implantable cardioverter-defibrillator (ICD) were examined and VT/VF identified by means of ICD device interrogation. Echocardiographic data were used to define LV structural remodeling (eccentric hypertrophy, concentric remodeling/hypertrophy, and normal geometry). VT/VF occurred in 26% of the 127 patients. VT/VF was more common in the 60 patients with LV hypertrophy versus the 67 with normal LV mass (40% vs 13%; $P = .001$) and in the 61 patients with LV enlargement versus the 66 with a normal chamber size (34% vs 18%; $P = .04$). When LV chamber size, wall mass, and geometry were assessed in a combinatorial fashion, a Kaplan-Meier analysis indicated that the occurrence of VT/VF was highest in the patients with eccentric hypertrophy (43%), intermediate in those with concentric remodeling/hypertrophy (30%), and lowest (12%) in those with normal geometry (all $P < .02$). The EFs were similar (P = ns) in these 3 groups of distinctly different patterns of remodeling.

Conclusions: Life-threatening ventricular arrhythmias in patients with a low EF are related to the pattern of LV remodeling, not the degree of LV dysfunction. Risk stratification of such patients might be improved by a consideration of the pattern of LV remodeling. (*J Cardiac Fail 2015;21:97−102*)

Key Words: Hypertrophy, LV function, LV remodeling, ventricular tachycardia/fibrillation.

The implantable cardioverter-defibrillator (ICD) effectively reduces the incidence of sudden cardiac death (SCD) in patients who are at risk.[1] Such patients are generally said to be those with left ventricular (LV) dysfunction, especially those with clinical evidence of heart failure.[1−3] Therefore, the widely accepted criteria for ICDs include symptoms of heart failure and a low LV ejection fraction (EF).[1] There is evidence, however, that EF alone lacks the predictive accuracy that is necessary to optimally identify the high risk patient. For example, the risk of sudden death in patients with the lowest EF does not always exceed the risk seen in those with a higher EF.[4,5] Indeed, multiple variables in addition to the EF influence mortality particularly in patients with coronary artery disease.[5] For these and other reasons, refinement of the methods for the prediction and prevention of SCD remains an important goal for clinical investigators.[6] Some have reported an association between LV hypertrophy (LVH) and ventricular arrhythmias,[7,8] but there have been no efforts to examine specifically the relationship of serious ventricular arrhythmias and the pattern of adverse structural remodeling of the ventricle in patients with a low EF. Because dilated hearts with the pattern of eccentric hypertrophy generally exhibit important clinical differences from those with concentric hypertrophy,[9] it would seem likely that these different patterns of remodeling might also exhibit a different prevalence of arrhythmia. Accordingly, the primary goal of the present study was to assess the relationship of ventricular

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See page 101 for disclosure information.

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tachycardia and/or fibrillation (VT/VF) to LV structural remodeling in patients with a low EF, and to test the hypothesis that different remodeling patterns are associated with differences in the occurrence of VT/VF. A secondary objective was to assess the risk of VT/VF relative to the degree of LV systolic dysfunction.

Methods

Patients who received an ICD at our institution from 2006 to 2009 were identified and their medical records screened for analysis. We selected those with a single- or dual-chamber device and evidence of LV systolic dysfunction (EF ≤0.45) according to echocardiography performed within 3 months of ICD implantation. All patients in the primary prevention group had an EF ≤0.35; in the secondary prevention group the EF ranged from 0.10−0.45. Patients with a biventricular device (cardiac resynchronization therapy) were not included. One hundred twenty-seven patients (all of whom were followed in our clinic) met these criteria.

The diagnosis of VT/VF was established by means of device interrogation and review of the medical records. An event was confirmed when the ICD interrogation revealed an episode of VT/VF requiring appropriate therapy (ICD shock and/or antitachycardia pacing). Inappropriate shocks were not included in the analysis. Our analysis related the occurrence of the 1st VT/VF event to LV structure and function. We also collected data on total mortality. Other data, including duration of ICD monitoring and clinical characteristics of the patients, were collected. The Institutional Review Board of the Lahey Hospital and Medical Center approved the study.

Echocardiography

We used commercially available equipment and standard techniques that we have applied in our previous echocardiographic studies.[10] All measurements were made according to the recommendations of the American Society of Echocardiography,[11] and the LV EF was determined with the use of the Teichholz method supplemented by visual inspection.[10,12] All measurements were taken directly from the echocardiographic reports in the medical record. LV mass was calculated with the use of the autopsy-validated method of Devereux et al.[13] LV enlargement was defined as a sex-dependant end-diastolic dimension >59 mm in men and >53 mm in women.[11] LVH was defined as LV mass >115 g/m^2 in men and >95 g/m^2 in women.[11] LV relative wall thickness (RWT) was determined as the ratio of end-diastolic wall thickness (sum of septal and posterior wall thickness) to the end-diastolic dimension (minor-axis diameter). The normal range for RWT is 0.32−0.42.[9]

Remodeling Definitions

Our definitions of the various patterns of LV remodeling were based on the presence or absence of LV enlargement, with further classification based on LV mass and RWT.[9] First, a nondilated ventricle with increased mass was classified as concentric hypertrophy and a nondilated ventricle with normal mass but high RWT was classified as concentric remodeling. Concentric remodeling appears to represent an early phase of concentric hypertrophy.[9] Accordingly, we combined these 2 patterns of concentric geometry and refer to this group as concentric remodeling/hypertrophy. Second, enlarged ventricles are described as exhibiting eccentric geometry. If the LV chamber was enlarged and LV mass was increased, the ventricle was classified as eccentric hypertrophy; those without an increase in LV mass were classified as eccentric geometry without hypertrophy. Third, normal geometry was defined as normal LV chamber size, wall mass, and RWT.

Initially, we assessed the association of VT/VF and adverse LV remodeling in patients with and without LV enlargement and in patients with and without hypertrophy. We then studied the occurrence of VT/VF in 3 specific structural patterns that combine LV size, mass, and geometry (concentric remodeling/hypertrophy, eccentric hypertrophy, and normal geometry). Finally, we assessed the relationship of VT/VF to the degree of LV dysfunction.

Data Analysis

Summary statistics for continuous data are presented as mean ± standard deviation. We used a Pearson chi-square test (Sigmastat 3.5; Sysstat Software, Point Richmond, California) to examine differences in selected categoric factors between our primary comparison groups of those with and without VT/VF over the course of follow-up. Unpaired *t* tests were used when comparing continuous variables. Time-to-event rates were assessed with the use of the Kaplan-Meier method. For all comparisons, *P* values of <.05 were considered to be statistically significant.

Results

Clinical characteristics of patients who did and did not develop VT/VF are presented in Table 1. These 2 groups were very similar regarding age, sex, comorbidities, functional classification, medications, and LV EF. Twenty-six percent (33/127) developed VT/VF during the follow-up period. In this group, the mean time to the first VT/VF event was 1.4 ± 1.1 years; the median was 1.4 years. In contrast, those without VT/VF had been monitored for an average of 3.5 ± 1.2 years.

LV Size, Mass, and EF

LV chamber size was significantly larger and myocardial mass significantly greater in the patients with than in those without VT/VF (Table 1). LV enlargement was present in 64% of those with VT/VF and in 43% of those without VT/VF (P = .037). LVH was present in 73% of those with VT/VF and in 38% of those without VT/VF (P = .0007). As shown in Figure 1, there was more VT/VF in the 61 patients with LV enlargement than in the 66 with a normal chamber size (34% vs 18%; P = .04). Similarly, VT/VF was more often seen in the 60 patients with LV hypertrophy than in the 67 patients with a normal LV mass (40% vs 13%; P = .001). This latter group included 19 patients with eccentric geometry without LV hypertrophy. The occurrence of VT/VF in these patients was similar to that seen in those with normal geometry (16% vs 12%; P = .2). The median EF for the entire group of 127 was 0.30 and the prevalence of VT/VF was the same (26%) in those with an EF above or below this value. We also examined a possible association between VT/VF and the degree of LV systolic dysfunction (ie, EF <0.20 vs