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Early Arrhythmic Events in Idiopathic Dilated Cardiomyopathy

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ABSTRACT

OBJECTIVES The study sought to provide an insight into the prevalence, characterization and possible reliable indicators of early sudden cardiac death/malignant ventricular arrhythmias (SCD/MVAs) in a large cohort of dilated cardiomyopathy (DCM).

BACKGROUND DCM generally affects young individuals and is characterized by an unpredictable prognosis with a non-negligible risk of SCD/MVAs, particularly in early stages of disease.

METHODS From 1988 to 2014, 952 patients with DCM were consecutively included in the Heart Muscle Disease Registry of Trieste.

RESULTS Globally, 20 patients (2.1% of the overall population) experienced SCD/MVAs within the first 6 months after enrollment (primary endpoint). At baseline they showed a worse functional class (New York Heart Association functional class III to IV 42% vs. 22%, $p = 0.038$), a longer QRS complex duration (127 ± 41 ms vs. 108 ± 33 ms; $p = 0.013$) and a larger indexed left ventricular end-systolic volume (LVESVI) (82 ± 49 ml/m^2 vs. 67 ± 34 ml/m^2; $p = 0.049$), as compared to patients without early SCD/MVAs. Beta-blockers were less tolerated (59% vs. 83% in patients with no early SCD/MVAs; $p = 0.008$), mostly due to hemodynamic intolerance. At multivariate analysis, LVESVI (odds ratio [OR]: 1.012; 95% confidence interval [CI]: 1.000 to 1.024; $p = 0.043$) and QRS complex duration (OR: 1.017; 95% CI: 1.003 to 1.030; $p = 0.015$) were independently associated with the primary endpoint, whereas beta-blockers demonstrated a protective effect (OR: 0.169, CI: 0.048 to 0.593; $p = 0.006$).

CONCLUSIONS Patients with DCM present a significant risk of major arrhythmic events in the first phase of the disease. Baseline LVESVI, QRS duration, and intolerance to beta-blocker therapy might be useful tools in the arrhythmic early risk assessment. (J Am Coll Cardiol EP 2016;■:■–■) © 2016 by the American College of Cardiology Foundation.

Dilated cardiomyopathy (DCM) is a heterogeneous myocardial disease with a variable clinical presentation and evolution, generally affecting young individuals (1). After therapy initiation DCM patients frequently recover left ventricular (LV) function with a subsequent favorable outcome (1). Unfortunately some major cardiac events may occur early after diagnosis. Risk stratification of sudden cardiac death (SCD) and malignant ventricular arrhythmias (MVAs) in the early phases of the disease remains challenging in the clinical management of DCM. Primary prevention implantable cardioverter-defibrillator (ICD) implantation indeed is currently recommended only for persisting high-risk patients (New York Heart Association [NYHA] functional class II to III and LV ejection fraction [LVEF] ≤35%) after an adequate period of optimal medical therapy (2), whereas the characterization of DCM patients at risk for early life-threatening arrhythmias during the optimization of

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

DCM = dilated cardiomyopathy

DHF/HTx = heart failure death or urgent heart transplantation

HF = heart failure

ICD = implantable cardioverter-defibrillator

LV = left ventricular

LVEF = left ventricular ejection fraction

LVESVI = indexed left ventricular end-systolic volume

MVA = major ventricular arrhythmia

OR = odds ratio

NYHA = New York Heart Association

SCD = sudden cardiac death

WCD = wearable cardioverter-defibrillator

medical therapy is limited and no large-scale studies examined predictors of early SCD/MVA.

Therefore, we sought to: 1) describe the characteristics and the prevalence of DCM patients with early (i.e., <6 months after enrollment) SCD/MVAs; and 2) identify possible baseline indicators of early major arrhythmic events to improve the arrhythmic risk stratification in the first phase of the disease.

METHODS

STUDY POPULATION. We retrospectively analyzed 952 DCM patients consecutively enrolled in the Heart Muscle Disease Registry of Trieste from 1988 to 2014. The diagnosis of DCM was determined according to the currently accepted criteria (3). Enrolled patients presented LVEF <50% at baseline evaluation in the absence of any possible cause of systolic impairment: significant coronary artery disease (stenosis >50% of a major coronary artery) was ruled out by coronary angiography in each patient; patients with a history of severe systemic hypertension (>160/100 mm Hg), alcohol intake over 100 g/day, severe organic valve diseases, congenital heart diseases, and advanced systemic disease affecting short-term prognosis were excluded. Persistent high-rate supraventricular arrhythmias were considered exclusion criteria if documented in the 6 months before enrollment, but patients with impaired LVEF 6 months after the resolution of the arrhythmia were included (4). Until 1992, all patients underwent endomyocardial biopsy to exclude active myocarditis according to the "Dallas Criteria." Thereafter, biopsy was performed on patients with recent onset heart failure refractory to conventional therapy, severe LV systolic dysfunction, and/or unexplained life-threatening ventricular arrhythmias (5). Patients with biopsy-proven active myocarditis were excluded, whereas patients with previous, healed myocarditis and persistent LV systolic dysfunction 1 year after diagnosis were enrolled in the Registry and included in the analysis. Patients with a history of SCD/MVAs and/or ICD implantation for secondary prevention at the time of the first evaluation at our center have been excluded from the present analysis by protocol.

All patients underwent a complete clinical and laboratory evaluation at baseline and at follow-up, including blood tests, 12-lead electrocardiography, 24-h Holter monitoring, and a complete transthoracic echocardiography. The familial history was strictly investigated and all familial DCM cases fulfilled the published criteria (6).

After enrollment, if not contraindicated, all patients received angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and beta-blocker treatment titrated to the higher tolerated dose. Daily dosages of angiotensin-converting enzyme inhibitors and beta-blockers are reported as equivalents of enalapril and carvedilol, respectively (7), and refer to the end of titration period (generally 1 to 3 months after enrollment).

Decisions regarding ICD implantation for primary prevention were made by the managing cardiovascular specialists in selected patients with DCM considered at high risk for SCD (i.e., persistent LV dysfunction with LVEF ≤35% and NYHA functional class II to III classes on chronic optimal medical treatment) (2). Antitachycardia pacing (at least 2 bursts) followed by multiple shocks (5 to 8) was programmed for the treatment of arrhythmias recognized as ventricular tachycardias ranging between 185 and 220 to 230 beats/min, whereas tachyarrhythmias faster than 220 to 230 beats/min were treated with multiple shocks (on antitachycardia pacing before or during capacitor charging according to device facilities). Arrhythmic events were evaluated during routine or urgent evaluations at the ICD outpatient clinic by an expert electrophysiologist.

The institutional ethical board approved the study and the informed consent was obtained under the institutional review board policies of hospital administration. Information regarding the endpoints was obtained from the patients, their physician or the registers of death of the municipalities of residence.

ECHOCARDIOGRAPHIC ANALYSIS. LV dimensions as well as systolic and diastolic function were assessed according to international guidelines (8). Specifically, LV volumes and LVEF were calculated by Simpson's biplane method, left atrial size was assessed by end-systolic left atrial area. All volumes and areas were indexed according to body surface area.

Functional mitral regurgitation was assessed using a multiparametric approach following current recommendations (9). All measurements were obtained from the mean of 3 beats (patients in sinus rhythm) or 5 beats (atrial fibrillation).

STUDY DESIGN. The primary endpoint was a composite of SCD and MVA (defined as aborted SCD, sustained ventricular tachycardia, appropriate ICD shocks on syncope or >200 beats/min ventricular tachycardia) within the first 6 months after enrollment. SCD was defined as immediate death or death