JACC: CLINICAL ELECTROPHYSIOLOGY
VOL. 2, NO. 1, 2016

ISSN 2405-500X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacep.2015.09.009

Long-Term Prognostic Role of the Diagnostic Criteria for Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

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ABSTRACT

OBJECTIVES The aim of this study was to evaluate the long-term prognostic role of the 2010 task force criteria (TFC)-based scoring in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D).

BACKGROUND Categories of the 2010 TFC include the risk factors for cardiovascular mortality and sudden cardiac death in patients with ARVC/D.

METHODS Ninety patients with ARVC/D who met the definitive diagnosis of the 2010 TFC were retrospectively studied. ARVC/D risk score was calculated as the sum of major (2 points) and minor (1 point) criteria in all 6 subdivided categories of the TFC and was divided into tertile groups of scores; group A (4 to 6 points), group B (7 to 9 points), and group C (10 to 12 points). The primary endpoints were major adverse cardiovascular events: cardiovascular death, heart failure hospitalization, and sustained ventricular tachycardia or ventricular fibrillation.

RESULTS During the follow-up period of 10.2 ± 7.1 years, 19 patients died because of cardiovascular causes, 28 patients were admitted because of worsened heart failure, and 47 patients experienced sustained ventricular tachycardia or ventricular fibrillation. Patients in groups B and C were at increased risk for major adverse cardiovascular events compared with those in group A (hazard ratio [HR]: 4.80; 95% confidence interval [CI]: 1.87 to 12.33; $p = 0.001$; and HR: 6.15; 95% CI: 2.20 to 17.21; $p = 0.001$, respectively). Patients in groups B and C were at increased risk for sustained ventricular tachycardia or ventricular fibrillation compared with those in group A (HR: 6.64; 95% CI: 2.00 to 22.03; $p = 0.002$; and HR: 9.18; 95% CI: 2.60 to 32.40; $p = 0.001$, respectively).

CONCLUSIONS Our study suggests that risk scoring based on the 2010 TFC is useful to predict major adverse cardiovascular events in patients with ARVC/D. (J Am Coll Cardiol EP 2016;2:107–15) © 2016 by the American College of Cardiology Foundation.

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a cardiomyopathy characterized by ventricular arrhythmias and fibrofatty replacement of the right ventricular (RV) myocardium (1,2). ARVC/D slowly progresses to more diffuse RV and left ventricular (LV) dysfunction (2,3). In the early (concealed) phase, structural change is absent or minor, but patients may be at risk for sudden cardiac death (SCD) caused by sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) in younger patients and athletes (1–5). Life-threatening ventricular arrhythmia and SCD can constitute the initial presentation of ARVC/D (2,3). In the overt (electric) phase, patients have symptomatic ventricular arrhythmia with manifested structural abnormalities of the right and/or left ventricle (2).

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Manuscript received September 1, 2015; accepted September 10, 2015.

ABBREVIATIONS AND ACRONYMS

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia

CI = confidence interval

ECG = electrocardiography

HF = heart failure

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

LV = left ventricular

MACE = major adverse cardiovascular event(s)

RV = right ventricular

SAECG = signal-averaged electrocardiography

SCD = sudden cardiac death

TFC = task force criteria

VF = ventricular fibrillation

VT = ventricular tachycardia

In the later phase, patients experience progressed right or biventricular heart failure (HF) with or without the presence of ventricular arrhythmia (2).

Thus, there is no single diagnostic tool for ARVC/D, and the clinical diagnosis of ARVC/D is often complex and difficult. The 1994 task force criteria (TFC) first provided the clinical diagnosis of ARVC/D on the basis of several categories, such as structure, function, histology, electrocardiography (ECG), arrhythmia, and family history (6). These criteria were modified in 2010 to improve diagnostic sensitivity by advances in the diagnostic modalities and the genetic knowledge of ARVC/D (7).

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Several electrocardiographic and electrophysiological abnormalities and structural features of both ventricles have been reported as clinical markers of a worse prognosis in patients with ARVC/D, but the predictive value of each factor itself is not high (8). The categories of TFC also include risk factors of cardiovascular mortality and SCD in patients with ARVC/D (7,8). We hypothesized that risk scoring on the basis of the 2010 TFC for the diagnosis of ARVC/D has a role in predicting ARVC/D-specific outcomes: cardiovascular death, worsening HF, and sustained VT or VF. The aim of this study was to evaluate the long-term prognostic role of 2010 TFC-based scoring in patients with ARVC/D.

METHODS

SUBJECTS. We retrospectively studied 90 patients with ARVC/D who met the definitive diagnosis of the 2010 TFC. All patients admitted to the Department of Cardiology, Tokyo Women's Medical University Hospital, for evaluation of sustained VT or VF and/or cardiomyopathy between 1974 and 2012 and with available follow-up were included in this study. All patients underwent 12-lead ECG and echocardiography or magnetic resonance imaging or RV angiography. Eighty-one patients also underwent endomyocardial biopsy of the right ventricle. Eighty-five patients underwent signal-averaged ECG (SAECG) (Predictor BSM-32, Arrhythmia Research Technology, Fitchburg, Massachusetts), and 79 patients underwent 24-h Holter ECG.

Antiarrhythmic drugs were prescribed for ventricular and supraventricular arrhythmias. In Japan, amiodarone and sotalol were approved in 1992 and 1998, respectively, and the implantable cardioverter-defibrillator (ICD) was approved in 1996.

Available data were obtained retrospectively from the medical records of our hospital. The patients were followed until December 31, 2013. Information regarding deceased subjects was obtained from medical records, family members, their local hospitals or general practitioners, and the admitting hospital. The patients were followed until the end of the follow-up period (December 31, 2013). The protocol was approved by the Institutional Review Board of Tokyo Women's Medical University.

ARVC/D RISK SCORE. ARVC/D risk score was calculated as the sum of major and minor criteria in all 6 subdivided categories of the 2010 TFC, with major criteria given 2 points and minor criteria given 1 point. The definite diagnosis of ARVC/D according to the 2010 TFC was fulfilled by the presence of 2 major criteria, 1 major plus 2 minor criteria, or 4 minor criteria from different categories. Thus, the minimum score of the ARVC/D risk was 4, and the range of this score was between 4 and 12. The patients were divided into 3 subgroups on the basis of the ARVC/D risk score tertiles: group A (first tertile, 4 to 6 points), group B (second tertile, 7 to 9 points), and group C (third tertile, 10 to 12 points).

OUTCOMES. The primary endpoints were major adverse cardiovascular events (MACEs), a composite of cardiovascular death, hospitalization for worsened HF, and sustained VT or VF. Worsened HF was defined by signs and symptoms, such as dyspnea, rales, and ankle edema, as well as the need for treatment with diuretic agents, vasodilators, positive inotropic drugs, or an intra-aortic balloon pump. Sustained VT was defined as a rate of more than 100 beats/min or more than 30 s in duration (or less if treated by electrocardioversion within 30 s) of VT on ECG, VT that required external defibrillation, intravenous antiarrhythmic agents such as amiodarone, and ICD therapy for termination. The occurrence of these events was validated through a review of medical records by 3 investigators (N.K., D.Y., and A.S.). The details of cardiovascular death were based on the clinical history obtained from medical charts or information from other hospitals. Sudden death was defined as unexpected endogenous death within 24 h after last having been observed alive, unrelated to a specific cause of circulatory failure.

STATISTICAL ANALYSIS. Summary data are presented either as the median and range or the number of patients. Cumulative probabilities of cardiovascular death, first HF hospitalization, and first