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Early repolarization of surface ECG predicts fatal ventricular arrhythmias in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy and symptomatic ventricular arrhythmias

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ABSTRACT

Background: The clinical characteristics and prognostic value of early repolarization (ER) in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) and symptomatic ventricular arrhythmias remain unclear. We investigated the prevalence, clinical features, and cardiovascular outcomes of patients with symptomatic ARVD/C and ER.

Methods: A total of 59 consecutive ARVD/C patients hospitalized for catheter ablation, presenting with and without J-point elevations of ≥0.1 mV in at least 2 inferior leads or lateral leads were enrolled. Clinical characteristics, electrophysiological study, substrate mapping, catheter ablation, and future clinical outcomes in a prospective patient registry were investigated.

Results: ER was observed in 38 patients (64.4%). Among these patients, ER was found in the inferior leads in 18 patients (47.4%), in the lateral leads in 2 patients (5.3%), and in both inferior and lateral leads in 18 patients (47.4%). Patients exhibiting ER were commonly men, had lower right ventricular ejection fraction, had higher incidence of clinical ventricular fibrillation or aborted sudden cardiac death, had more defibrillator implantations, had higher the need of epicardial ablation, and had more major criteria according to the task force criteria. Significant higher incidence of induced ventricular fibrillation and shorter tachycardia cycle length of induced ventricular tachycardia were found during procedure. The recurrence rate of ventricular arrhythmias did not differ between patients with and without ER after catheter ablation.

Conclusions: A high prevalence of electrocardiographic ER was found among symptomatic ARVD/C patients undergoing catheter ablation. ER in 12-lead ECG is associated with an increased risk of clinical fatal ventricular arrhythmias.

1. Introduction

Early repolarization (ER), which is characterized by an elevation of the QRS–ST junction in leads other than V_1 through V_3 on 12-lead electrocardiography (ECG), has been generally considered as a benign finding [1]. However, prior investigators have linked ER to idiopathic ventricular fibrillation (VF) in patients without structural heart disease [2,3]. In addition, recent studies have evaluated the association between ER and structural heart disease. The high prevalence of ER is found in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) [4]. ER may be associated with the VF occurrence in patients with chronic coronary artery disease and acute myocardial infarction [5–7]. ARVD/C is an inherited cardiomyopathy characterized by fibrofatty infiltration of the right ventricle resulting in ventricular arrhythmias (VAs) and right ventricular dysfunction [8,9]. Up to 23% of patients present with sudden cardiac death (SCD) [10].

The clinical characteristics and prognostic value of ER in patients with ARVD/C and symptomatic VAs remain unclear. Therefore, our study was designed to investigate the prevalence, clinical characteristics, and the long-term cardiovascular outcomes of ER in a prospective registry of patients with ARVD/C and symptomatic VAs. These patients were referred for electrophysiological (EP) study, substrate mapping,

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catheter ablation, and potential implantable cardioverter defibrillator (ICD) implantation in a tertiary care arrhythmia center.

2. Methods

2.1. Patient population

Between April 2008 and March 2014, a total of 59 consecutive ARVD/C patients admitted for catheter ablation due to symptomatic VAs were included. The study population consisted of 51 patients with documented ventricular tachycardia (VT) and ventricular fibrillation (VF), 8 patients with symptomatic premature ventricular complexes (PVCs). Among these patients, 25 patients were admitted for consideration of ICD implantation. All of the patients were diagnosed with ARVD/C based on the modified criteria for diagnosis of ARVD/C proposed by an international working group [11]. All of these patients underwent 12-lead rest ECG, chest X-ray, 24-hour Holter monitoring, transthoracic echocardiography, left and right ventriculography, coronary artery angiography (CAG) and EP study. Structural heart diseases were assessed by echocardiography, cardiac magnetic resonance imaging, cardiac ventriculography, and CAG before the EP study. Among these 59 patients, 38 patients (64.4%) underwent signal averaged electrocardiogram (SAECG), and myocardial biopsy was performed in 19 patients (32.2%). The density of VAs was measured. The clinical manifestations of VAs were further categorized into symptomatic PVCs, nonsustained VT (<30 s), sustained VT (regular tachycardia with a mean cycle length of >240 msec) and VF (mean tachycardia cycle length ≤240 msec). The protocol was approved by the institution's human research committee.

2.2. Definition and measurements of early repolarization

Digitalized ECGs were analyzed independently by 2 electrophysiologists before the patients were included in the study. ER in the 12-lead ECG was defined as an elevation of the QRS–ST junction (J point) ≥0.1 mV that was either notched (a positive J-deflection inscribed on the S-wave) or slurred (a smooth transition from the QRS to ST segment) in at least 2 inferior leads (II, III, and aVF), or lateral leads (I, aVL, and $V_{4–6}$). The anterior precordial leads ($V_{1–3}$) were not included for the analysis of ER to avoid the inclusion of epsilon wave. Epsilon wave was defined as reproducible low-amplitude signals between the end of QRS complex and the onset of the T wave in the right precordial leads ($V_{1–3}$). The Kappa value of two electrophysiologists for consistency of determination of ER was 0.85 ($P < 0.01$).

2.3. Electrophysiological study and programmed ventricular stimulation

As described in our previous studies [12], after written informed consent was obtained, EP study was performed in the fasting and nonsedated status. Before the study, all antiarrhythmic drugs were discontinued for at least 5 half-lives. All patients underwent 3-dimensional electroanatomical mapping using either the NavX Velocity Navigation & Visualization Technology (St. Jude Medical, St. Paul, MN) or the Carto system (Biosense Webster, Diamond Bar, CA). The programmed ventricular stimulation protocol provided up to 3 extrastimuli delivered during sinus rhythm at 2 ventricular paced cycle lengths. First the right ventricular apex, then the right ventricular outflow tract was stimulated if no sustained VA was induced from the right ventricular apex. Isoproterenol (1–4 μg/min) was administered intravenously to facilitate induction of VA if no tachycardia was induced during baseline programmed ventricular stimulation. The positive endpoint of programmed ventricular stimulation was induction of a sustained VT or VF. Non-sustained VT was defined as 3 or more consecutive beats with duration of less than 30 s. Monomorphic VT was defined as a VT with a uniform beat-to-beat surface QRS morphology. Polymorphic VT had a variable surface QRS morphology with a cycle length of more than 240 msec, and VF was defined as a rapid, disorganized rhythm without consistently identifiable complexes or polymorphic VT with a cycle length of less than 240 msec.

2.4. Mapping and catheter ablation

First, electroanatomical mapping was performed in the right ventricle (RV) during VT or PVCs and an activation map was constructed in all cases. When VT or PVCs were infrequent, electroanatomical mapping of the RV was performed during sinus rhythm to create a geometry of the RV. The mapping procedure used to detect an appropriate site for ablation included pace mapping during sinus rhythm, activation mapping, identification of diastolic potentials and entrainment mapping during VT. The exit site of VT was considered if the paced QRS configuration was identically matched to the clinical VT in a 12-lead ECG recording. Entrainment mapping was performed to identify the critical component of the VT reentrant circuit and to guide selective ablation. Activation mapping was performed to record the earliest activation and diastolic potentials during VT.

In patients with non-inducible or unstable VAs, substrate-based catheter ablation in sinus rhythm was applied. RV voltage mapping in sinus rhythm, with voltage settings of ≤0.5 mV as scar, ≥1.5 mV as normal myocardium, delineated the scar, the possible channels of surviving myocardium and the culprit substrate for VT. The substrate-based catheter ablation during sinus rhythm was accomplished by creating linear ablation lesions based on the location of the best pace map, the location of valvular anatomical boundaries, and the substrate defined by the voltage mapping. The strategy of substrate-based catheter ablation included creating the linear lesions by sequential point by point RF delivery to (1) partially encircle the VT exit sites at the scar borders; (2) connect the scar to an anatomic barrier such as the tricuspid valve; and (3) interconnect 2 or more areas of dense scars thus intercepting the channels between the dense scars, which were potentially involved in the reentrant circuits.

Radiofrequency (RF) energy was delivered in a temperature-controlled mode at 50–60 °C with pulse duration of 60 s; maximal power was 50 W for non-irrigated catheter and 30–35 W for irrigated catheter targeting for an impedance drop of 10 Ω. If VA was suppressed within 30 s, RF energy would be maintained for a total of 60 s, and additional energy would be applied up to a maximum of 5 burns. For substrate ablation, we aimed at terminating the hemodynamically tolerated VT or eliminating of all recorded abnormal electrocardiograms from detailed mapping. The procedural success was defined as VA was not induced under infusion of isoproterenol following the same induction protocol for 30 min to exclude acute recurrence. If procedural success was not achieved, a second procedure was conducted.

2.5. Implantable cardioverter defibrillator

The patients in this study underwent ICD implantation with trans-venous devices between April 2008 and March 2014. Indications for ICD implantation were to prevent SCD; these include previous episode of resuscitated cardiac arrest, unexplained syncope with inducible VT/VF or inducible VT/VF according to the regulation policy of the national health insurance in Taiwan based on secondary prevention. Most of the devices were third- and fourth-generation ICDs able to provide antitachycardia and antibradycardia pacing. The ICD device was equipped with diagnostic memory and the ability to record and store electrographic data, including intracardiac electrocardiograms for subsequent review. Decisions regarding programming of these devices were made by the patients' attending physicians. Stored data were reviewed with ICD interrogations performed routinely every 3–6 months.