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Original Article

Inducibility of ventricular arrhythmias in early repolarization syndrome and Brugada syndrome: From the J-wave associated with prior cardiac event (J-PREVENT) registry

Yoshihide Takahashi, MD[a,*], Yuki Osaka, MD[b], Akihiko Nogami, MD[c], Mitsuhiro Nishizaki, MD[d], Kaoru Okishige, MD[e], Makoto Suzuki, MD[f], Yasuteru Yamauchi, MD[g], Yuichi Ono, MD[h], Kou Suzuki, MD[i], Kenzo Hirao, MD[j], Mitsuaki Isobe, MD[k]

[a] The Department of Cardiovascular Medicine, National Disaster Medical Center, Midoricho 3256, Tachikawa, Tokyo 190-0014, Japan
[b] Cardiovascular Center, Yokosuka Kyousai Hospital, Yokosuka, Japan
[c] Division of Cardiology, Yokohama Rosai Hospital, Yokohama, Japan
[d] Department of Cardiovascular Medicine, Yokohama Minami Kyousai Hospital, Yokohama, Japan
[e] Department of Cardiovascular Medicine, Yokohama Bayside Red Cross Hospital, Yokohama, Japan
[f] Department of Cardiovascular Medicine, Kameda General Hospital, Kamogawa, Japan
[g] Department of Cardiovascular Medicine, Musashino Red Cross Hospital, Tokyo, Japan
[h] Department of Cardiovascular Medicine, Ome General Hospital, Tokyo, Japan
[i] Department of Cardiology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan
[j] Heart Rhythm Center, Tokyo Medical and Dental University, Tokyo, Japan
[k] Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, Japan

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ABSTRACT

Background: Although electrophysiological study is often performed in Brugada syndrome (BrS) to assess inducibility of ventricular arrhythmias (VA), the utility of electrophysiological study in early repolarization syndrome (ERS) remains unknown. The aim of the present multi-center observational study was to compare inducibility of VA in ERS with BrS, and to investigate any association between inducibility and recurrence of arrhythmic events in these patients.

Methods: The J-PREVENT registry consists of patients with early repolarization or Brugada type 1 ECGs, a history of prior cardiac events, and no structural heart disease. Patients in the registry with implantable cardioverter-defibrillators (ICDs) and who underwent electrophysiological study were enrolled. VA inducibility was assessed by programmed electrical stimulation performed at two different sites in the right ventricle with up to three extrastimuli. The occurrence of VA during follow-up was determined by interrogation of the patients' ICDs.

Results: Of the 79 patients studied (72 males, mean age 44 ± 13 years), 21 patients (27%) had ERS, and 58 had BrS, 20 of whom also had early repolarization in the inferolateral leads. VA was induced in 9 patients (43%) and 45 (78%) with ERS and BrS, respectively ($p=0.006$). During a median follow-up of 1453 days, occurrence rate of VA was similar between ERS and BrS ($p=0.35$). Inducibility was not associated with occurrence of VA in either syndrome.

Conclusions: In patients with ERS with prior history of cardiac events, VA was induced in 43% of patients during electrophysiological study, approximately half that of BrS. Inducibility was not associated with occurrence of VA during follow-up, although this was true of BrS patients as well. Electrophysiological study may play a limited role in risk stratification in ERS.

1. Introduction

Since the recent demonstration of an association between an early repolarization pattern in the inferolateral leads of the ECG and sudden cardiac death [1–3], a distinct clinical entity referred

* Corresponding author. Tel.: +81 42 526 5511; fax: +81 42 526 5535.
E-mail address: yoshihide_takahashi@oboe.ocn.ne.jp (Y. Takahashi).

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to as early repolarization syndrome is now widely recognized. Early repolarization is a relatively common electrocardiographic feature; thus, risk stratification of subjects whose ECGs exhibit this feature is desirable for the prevention of sudden cardiac death.

Brugada syndrome is also associated with life-threatening arrhythmias. Several tests have been vetted for use in risk stratification of Brugada syndrome patients. There have been many reports that ventricular arrhythmias are inducible during electrophysiological study in patients with Brugada syndrome, but whether such study results have predictive value for cardiac events remains controversial [4–8]. Because early repolarization syndrome and Brugada syndrome have similar clinical and electrocardiographic characteristics, some investigators hypothesize that these two syndromes represent points on a continuous spectrum of J-wave abnormalities called the J-wave syndrome [9]. However, unlike Brugada syndrome, inducibility of ventricular arrhythmias in early repolarization syndrome has not received much study.

The aim of the present multi-center observational study was to compare inducibility of ventricular arrhythmias in early repolarization syndrome with Brugada syndrome, and to investigate any association between inducibility and recurrence of arrhythmic events in these patients.

2. Methods

2.1. Study population

The J-PREVENT registry consists of patients who meet the following criteria: (i) prior history of aborted sudden cardiac arrest, ventricular fibrillation, ventricular tachycardia, or syncope, (ii) no structural heart disease as verified by echocardiography and coronary angiography, (iii) Brugada type 1 ECG [10] in the presence or absence of sodium channel-blocking agent, or early repolarization (J-point elevation by at least 0.1 mV above the baseline level) ECG in at least 2 contiguous leads in the inferior (II, III, and aVF) or lateral leads (I, aVL and V4-6) (1,2). Exclusion criteria were the following: (i) a resting corrected QT interval (QTc) >460 ms for men or a QTc >480 ms for women, or short QT interval (QTc ≤ 340 ms), (ii) a reversible cause of cardiac arrest such as marked hypokalemia or drug intoxicity. In patients with syncope, brain CT scanning, electroencephalogram, head-up tilt test or coronary angiogram was performed. Patients were not enrolled in the present study, if non-cardiac etiologies of syncope were identified. No patients were taking antiarrhythmic drugs at the time of enrollment in this study. For the purposes of the present study, a subset of patients enrolled in the J-PREVENT registry was selected, namely, patients who received electrophysiological study and who had an implantable cardioverter-defibrillator (ICD).

All patients gave written informed consent for the study protocol, which was approved by the Institutional Review Board at each center.

2.2. Electrophysiological study

The protocol of programmed electrical stimulation differed at each center, and consisted of one drive cycle of 500 or 600 ms, or two drive cycles of 600 and 400 ms with up to 3 extrastimuli (S2–S4) delivered from the apex and outflow tract of the right ventricle. The coupling interval of extrastimuli was reduced in decrements of 10 ms until 200 ms was reached for S1–S2 or S2–S3. For S3–S4, the coupling interval of extrastimuli was until 180 ms or 200 ms at the discretion of each center. If VF or sustained polymorphic VT (>30 s of duration) was induced by programed electrical stimulation, the patient was categorized as inducible. Once VT or VF which required electrical cardioversion was induced, electrophysiological study was terminated regardless of completion of the stimulation protocol.

2.3. Follow-up

All patients studied had an ICD, this was an inclusion criterion. ICDs were programmed at the discretion of each institution. The study endpoint was occurrence of arrhythmic events defined as sudden death or appropriate ICD therapy for VT/VF. During the follow-up period, the ICD was interrogated at least every 6 months to assess arrhythmic events. If ICD therapy had been delivered, electrograms stored in the ICD were examined at each center by electrophysiologists and appropriateness of the ICD therapy was determined. For patients who had multiple episodes of appropriate ICD therapy, antiarrhythmic drugs were administered at the discretion of each center.

2.4. Statistical analysis

The data are presented as the mean $\pm$ standard deviation for normally distributed variables and median and interquartile range for non-normally distributed variables. Continuous variables were compared using one-way analysis of variance (ANOVA). Comparison of proportions was performed by Fisher's exact test. Freedom from arrhythmic events was analyzed using the Kaplan–Meier method. A log-rank test was used to compare estimates of the arrhythmic event-free rate across groups. A p value less than 0.05

Table 1
Clinical characteristics and electrocardiographic type.

	Early repolarization syndrome ($n=21$)	Brugada syndrome without early repolarization ($n=38$)	Brugada syndrome with early repolarization ($n=20$)	Value
Mean age at the first event	41 ± 15	47 ± 13	43 ± 12	0.17
Male, n (%)	17 (81%)	35 (92%)	20 (100%)	0.09
First event				0.0002
Aborted sudden cardiac death	1 (5%)	4 (10.5%)	0 (0%)	
Ventricular tachycardia/ventricular fibrillation	19 (90%)	11 (29%)	10 (50%)	
Syncope	1 (5%)	23 (60.5%)	10 (50%)	
Family history	2 (10%)	6 (18%)	2 (10%)	0.7
Heart rate (bpm)	68 ± 12	69 ± 13	74 ± 13	0.26
PR interval (ms)	168 ± 27	172 ± 21	186 ± 34	0.09
QRS width (ms)	97 ± 15	104 ± 26	118 ± 23	0.015
QTc interval (ms)	428 ± 36	426 ± 30	432 ± 57	0.9
Atrial tachyarrhythmias	3 (14%)	6 (16%)	5 (25%)	0.69