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Heart Rhythm Disorders

Electrical Storm in Idiopathic Ventricular Fibrillation Is Associated With Early Repolarization

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Objectives This study sought to characterize patients with idiopathic ventricular fibrillation (IVF) who develop electrical storms.

Background Some IVF patients develop ventricular fibrillation (VF) storms, but the characteristics of these patients are poorly known.

Methods Ninety-one IVF patients (86% male) were selected after the exclusion of structural heart diseases, primary electrical diseases, and coronary spasm. Electrocardiogram features were compared between the patients with and without electrical storms. A VF storm was defined as VF occurring ≥3 times in 24 h and J waves >0.1 mV above the isoelectric line in contiguous leads.

Results Fourteen (15.4%) patients had VF storms occurring out-of-hospital at night or in the early morning. J waves were more closely associated with VF storms compared to patients without VF storms: 92.9% versus 36.4% ($p < 0.0001$). VF storms were controlled by intravenous isoproterenol, which attenuated the J-wave amplitude. After the subsidence of VF storms, the J waves decreased to the nondiagnostic level during the entire follow-up period. Implantable cardioverter-defibrillator therapy was administered to all patients during follow-up. Quinidine therapy was limited, but the patients on disopyramide (n = 3), bepridil (n = 1), or isoprenaline (n = 1) were free from VF recurrence, while VF recurred in 5 of the 9 patients who were not given antiarrhythmic drugs.

Conclusions The VF storms in the IVF patients were highly associated with J waves that showed augmentation prior to the VF onset. Isoproterenol was effective in controlling VF and attenuated the J waves, which diminished to below the diagnostic level during follow-up. VF recurred in patients followed up without antiarrhythmic agents. (J Am Coll Cardiol 2013;62:1015–9) © 2013 by the American College of Cardiology Foundation

Ventricular fibrillation (VF) may occur in patients without structural heart disease or primary electrical disease; this form of VF is known as idiopathic ventricular fibrillation (IVF) (1). J waves, a component of the early repolarization, have been shown to be associated with IVF in case studies (2–5) and in epidemiological studies (6), but the characteristics of IVF patients who develop VF storms are unknown.

As an extension of our IVF study (7,8), we attempted to characterize IVF patients who develop VF, with a special concentration on J waves.

Methods

Patients. This case study consisted of IVF patients who met the following inclusion criteria for IVF: 1) documented VF at the time of cardiac arrest; 2) absence of structural heart disease and normal cardiac function; 3) negative serology for inflammatory diseases and absence of electrolyte imbalances; and 4) absence of coronary artery disease and a negative provocative test for coronary spasms.

Patients with other electrical diseases including Brugada syndrome and coronary spasm were excluded based on

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Abbreviations and Acronyms

ECG = electrocardiogram

IVF = idiopathic ventricular fibrillation

VF = ventricular fibrillation

appropriate provocation tests (8). The patients were divided into subgroups according to the presence of VF storms or J waves.

Management of VF. Prior to 1998, conventional antiarrhythmic drugs were used to control VF storms; in the studies after 1998, isoproterenol was used as the first drug of choice. Quinidine was given if it was available and tolerated. For long-term follow-up, quinidine or another drug was prescribed, depending on the patient's tolerance and the decision of the attending physicians.

Electrocardiogram analysis. Electrocardiogram (ECG) recordings were analyzed for the usual parameters and J waves, which were defined as reported elsewhere (3,8). When available, ECGs recorded prior to the VF storm and those recorded during the follow-up were analyzed for J waves.

The ECGs were interpreted by 2 cardiologists. When there was disagreement regarding J waves, the cardiologists discussed the results to reach an agreement.

Data analysis. The prevalence of VF storms and their relation to J waves were determined among the IVF patients (8). A VF storm was defined as that occurring ≥3 times per 24 h.

The clinical and ECG features were compared between the IVF patients with and without VF storms, and between the patients showing J waves, with and without VF storms. The effects of the therapeutic interventions on the J-wave amplitudes and their time course were analyzed with respect to VF storms.

Statistical analyses. Numerical values are presented as mean ± SD, and categorical variables are expressed as absolute numbers or percentages. The differences between the groups were analyzed by analysis of variance for continuous variables and with Pearson's chi-square test for categorical variables. The serial changes of J-wave amplitude before and after isoproterenol were compared by paired *t* test.

The statistical analyses were performed with SPSS version 12.0 (SPSS Inc., Chicago, Illinois). A 2-sided $p < 0.05$ was considered statistically significant. This study was approved by the ethics committee of Niigata University School of Medicine and the institutional review board of the Tachikawa Medical Center.

Results

Patients with VF storms. Among the 91 IVF patients, 14 (15.4%) had VF storms (Table 1). The first VF episodes occurred out-of-hospital between 8:00 p.m. and 9:00 a.m. and were managed by an emergency team. VF recurred after admission 2 to 50 times in a 24-h period.

Patients with and without VF storms and J waves. J waves were present in 92.9% and 36.4% of patients with and without VF storms, respectively ($p < 0.0001$) (Table 2). In 2 patients, J waves were not present on ECGs recorded 6 or 12 months prior (Fig. 1A). Otherwise, there were no differences in the ECG parameters except for the PR and QT intervals between the 2 groups. The presence of J waves had a sensitivity and specificity for VF storms of 92.9% and 63.6%, respectively. The positive and negative predictive values were 31.7% and 98.0%, respectively.

The J-wave amplitudes and the PR intervals were different between the patients with and without VF storms (Table 3). The J waves were similarly distributed in the 2 groups.

VF storms and interventions. VF developed in 10 patients following a short-long-short sequence; in 9 patients, this was due to premature ventricular beats (Fig. 1B) and in 1 due to a Wenckebach-type atrioventricular block. Two patients had VF following a short-long-short sequence and during regular rhythm, and 2 developed VF during regular rhythm.

Table 1 Clinical Characteristics of the Patients With VF Storms

Patient #	Age (yrs)/Sex	Time of the First VF	Mode of VF Onset	Control of VF	Drugs Tried	FU	Follow-Up Duration, yrs	ICD/VF Rec
1	49/M	00:00	SLS/Reg	ISP	Q, BB, N	D	2.5	+/–
2	45/M	07:00	Reg	ISP	A, N, L, BB	D	3.5	+/–
3	42/M	22:00	SLS	—	V	—	18.0	+/–
4	42/M	04:00	Reg	ISP	—	—	1.5	+/–
5	58/M	07:00	SLS/Reg	ISP	L, N, Mg	—	1.5	+/–
6	49/M	02:50	SLS	ISP	—	Bep	1.1	–/–
7	24/M	22:00	SLS	ISP	At, BB,	D	1.6	+/–
8	27/M	09:00	SLS	ISP	Mex, V, D	I	3.3	+/–
9	48/F	08:00	SLS	—	A	—	5.3	+/–
10	13/M	20:00	SLS	ISP	Mex, PA, AL	—	5.0	+/+*
11	50/M	21:35	Unknown	Adr	Dof	—	4.8	+/+*
12	37/M	05:24	Unknown	Adr	L	—	1.5	+/+*
13	37/M	04:00	SLS	—	—	—	2.8	+/+
14	34/F	09:00	SLS	ISP	—	—	1.8	+/+

A = amiodarone; Adr = adrenaline; At = atropine; BB = beta-blockers; Bep = bepridil; D = disopyramide; Dof = dofetilide; FU = antiarrhythmic agents during follow-up; I = isoprenaline; ICD = implantable cardioverter-defibrillator; ISP = isoproterenol L = lidocaine; Mex = mexiletine; Mg = magnesium; N = nifekalant; PA = procainamide; Q = quinidine; Reg = regular rhythm; SLS = short-long-short sequence; V = verapamil; VF = ventricular fibrillation; +* = recurrence of VF in a storm.

Table 2 The ECG Characteristics of the IVF Patients With and Without VF Storms

	With Storms (n = 14)	Without Storms (n = 77)	p Value
Male, %	85.7	85.7	1.000
Age, yrs	40 ± 12	43 ± 16	0.3789
RR, ms	820 ± 42	886 ± 23	0.1757
PR interval, ms	192 ± 8	164 ± 6	0.0078
QRS interval width, ms	103 ± 5	94 ± 4	0.2684
QT interval, ms	396 ± 6	382 ± 3	0.0449
QTc interval, $ms^{1/2}$	415 ± 10	396 ± 8	0.0620
J wave, %	92.9	36.4	<0.0001

Values are % or mean ± SD.
ECG = electrocardiogram; IVF = idiopathic ventricular fibrillation; VF = ventricular fibrillation.

In 2 other patients, the onset pattern of VF was not recorded (Table 1).

Initially, rapid pacing was effectively attempted, but it was replaced by isoproterenol infusion, which was administered in 10 patients for 10.9 ± 17.3 days (range: 1 to 17 days; median: 4.5 days). The VF storms were suppressed soon after the administration of isoproterenol. Adrenaline was administered to 2 patients in the emergency room for 1 to 2 days and was effective in suppressing the VF. Two other patients were followed who were not treated with a specific drug, but the VF storms subsided within 4 h.

The J-wave amplitude significantly increased from 0.335 ± 0.172 mV to 0.493 ± 0.198 mV prior to VF recurrence (p = 0.0040, n = 10), the largest amplitude just prior to VF onset. J waves were attenuated by isoproterenol to 0.091 ± 0.101 mV (p < 0.0001) (Figs. 2 and 3).

Procainamide (n = 1), lidocaine (n = 4), verapamil (n = 2) amiodarone (n = 3), nifekalant (n = 3), dofetilide (n = 1), beta-blocker (n = 3), and magnesium sulfate (n = 2) failed in suppressing the VF. Quinidine suppressed the VF and attenuated the J waves, but it was attempted in only 3 patients.

Outcomes. When the VF storms were considered to have subsided, all of the patients underwent implantation of an implantable cardioverter-defibrillator. J waves were absent or

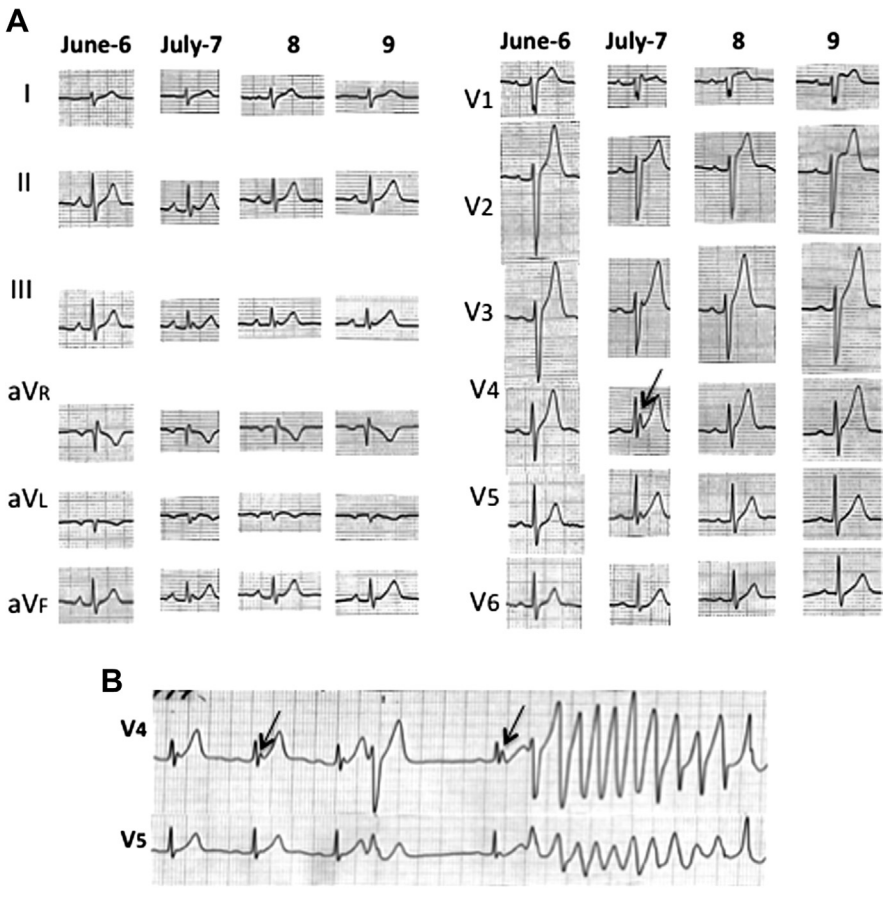

Figure 1 Transient Appearance of J Waves

A 48-year-old man was admitted with syncope. His electrocardiogram, recorded a month before, was normal (**A**, June-6). However, upon admission, J waves were observed in the inferior and left precordial leads (**A**, July-7, **arrow**). Ventricular fibrillation occurred repeatedly overnight **(B, arrows)** but subsided on the next day, with a diminution of the J waves (**A**, July-8). Two days later, the J waves became invisible (**A**, July-9).

Table 3 The ECG Parameters of the Patients With and Without VF Storms Among the Patients With J Waves

	With Storms (n = 13)	Without Storms (n = 28)	p Value
Male, %	85.7	88.6	0.7856
Age, yrs	39 ± 12	42 ± 15	0.5023
RR, ms	820 ± 42	858 ± 30	0.4601
PR interval, ms	192 ± 8	152 ± 10	0.0065
QRS interval	103 ± 5	92 ± 6	0.1778
QT interval	396 ± 6	384 ± 4	0.1160
QTc interval	415 ± 10	399 ± 8	0.2113
J-wave amplitude, mV	0.427 ± 0.017	0.218 ± 0.016	<0.0001
Location of J waves (%)			0.3563
Inferior	9 (69.2)	16(57.1)	—
Left precordial	8 (61.5)	12(42.9)	—
Right precordial	1 (7.6)	6 (21.6)	—
High lateral	3 (23.1)	1 (3.6)	—
>1 site	10 (76.9)	14 (50.0)	—

Values are %, mean ± SD, or n (%).
RR = relative risk; other abbreviations as in Table 2.

at a nondiagnostic level at the time of the last observation at 4.0 ± 4.6 years (range: 1 to 18 years; median: 2.7 years).

Due to quinidine intolerance, disopyramide (n = 3), bepridil (n = 1), or isoprenaline (n = 1) was administered to 5 patients, while nothing was given to the other 9 patients. VF recurred between midnight and 9:00 a.m. at 13.2 ± 19.6 months after the first VF storm in 5 of the 9 patients who were followed without antiarrhythmic drugs, and 3 had VF storms. The difference in the VF recurrence rate was significant (p = 0.0376).

Discussion

VF storms (≥3 per 24 h) have been noted in IVF patients with early repolarization: 16 of 122 IVF patients (13.1%) (7), and 5 of 11 IVF patients (45.5%) (9). In the present study, VF storms were highly associated with J waves (92.9%), and the absence of J waves had a strong negative predictive value (98.0%).

Isoproterenol has been shown to be effective in suppressing VF in IVF patients, and quinidine has been another drug of choice for effective suppression of VF, as reported earlier (7,10–12). The latter can be administered orally and can be used for the long-term prophylaxis of VF (11,12). The efficacy of isoproterenol in suppressing VF was confirmed in the present study, but because of the intolerance to quinidine or its unavailability in some hospitals, we were unable to fully confirm the efficacy of quinidine. However, drugs such as disopyramide, bepridil, and isoprenaline were suggested to be effective for VF prophylaxis in IVF patients.

There were patients in which J waves appeared concurrently with VF storms and disappeared within days (Fig. 1). After hospitalization, the J-wave amplitude reached its peak just prior to VF onset (3,5). Most of the VF developed following the short-long-short sequence (9,13), and the augmentation of the J-wave amplitude may be partly due to the pause-dependent nature of the J wave, which is characteristic of IVF patients (8). Although isoproterenol attenuated the J waves dramatically, the J waves remained attenuated even after cessation of the drug and remained as such during the follow-up. Therefore, the waxing and

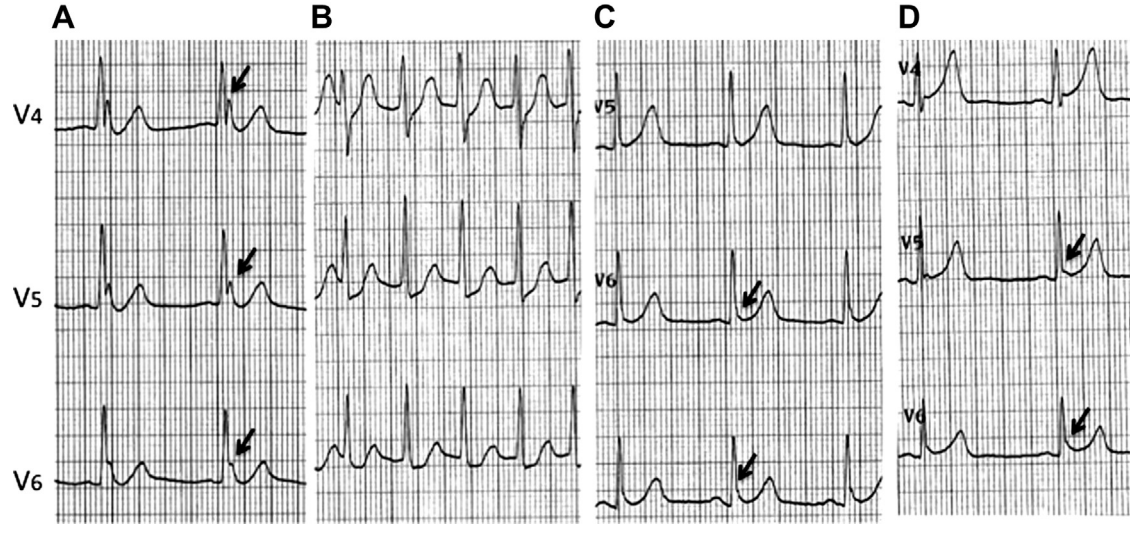

Figure 2 J Waves During VF Therapy With Isoproterenol

The patient was a 34-year-old man. J waves were found in the inferior and left precordial leads **(A)**. Ventricular fibrillation (VF) occurred out-of-hospital, and VF recurred 5 times after admission. Intravenous isoproterenol was started at 12 μg/h, which suppressed the premature ventricular beat and VF **(B)**. The drug dosage was reduced to 4 μg/h **(C)**, and on the fourth day after admission, the drug was terminated **(D)**. No VF occurred during isoproterenol or even after its cessation. The J waves were diminished by isoproterenol **(B and C)**, and small J waves appeared when the drug was terminated.

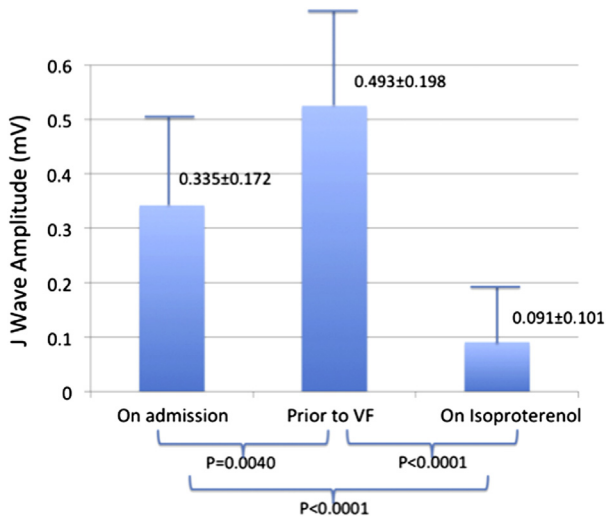

Figure 3 The Response of the J Waves to Isoproterenol

The J waves were evident on admission and were augmented during the VF storms. After isoproterenol administration (n = 10), the J waves became smaller. When the VF storm was considered to be controlled, the J waves were <0.1 mV in all patients.

waning nature of J waves might not necessarily be related to isoproterenol or other drugs, and thus, its mechanism needs to be clarified.

Study limitations. This was a small case study, but our findings are consistent with those previously reported (7,9). Because of the evolving nature of VF storm management, we could not present the efficacy of each drug in a systematic way. The attenuation or abolishment of J waves seemed a maker of drug efficacy, but we were unable to provide definite evidence. A genetic screening of the IVF patients would be of great importance (14).

Conclusions

The VF storms in the IVF patients were highly associated with J waves that showed augmentation prior to VF onset. Isoproterenol was effective in controlling VF and attenuated the J waves. The J waves further diminished below the diagnostic level during follow-up. VF recurred in patients who were not followed up with antiarrhythmic agents.

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Key Words: early repolarization ▪ electrical storm ▪ idiopathic ventricular fibrillation ▪ isoproterenol.