

J point elevation in high precordial leads associated with risk of ventricular fibrillation

Yuki Hasegawa¹, Hiroshi Watanabe¹, Yasuhiro Ikami¹, Sou Otuki¹, Kenichi Iijima², Nobue Yagihara², Daisuke Izumi², and Tohru Minamino²

¹Niigata University Faculty of Medicine Graduate School of Medical and Dental Sciences
Biological Functions and Medical Control

²Niigata University Faculty of Medicine Graduate School of Medical and Dental Sciences
Biological Functions and Medical Control, Cardiovascular Biology and Medicine

July 24, 2020

Abstract

Introduction: The significance of high precordial electrocardiograms in idiopathic ventricular fibrillation (IVF) is unknown. **Method:** This study included 50 consecutive patients (48 men; age, 42±18 years) who had spontaneous ventricular fibrillation not linked to structural heart disease and received implantable cardiac defibrillator therapy. IVF was diagnosed in 35 patients and Brugada syndrome was diagnosed in other 15 patients. Electrocardiograms in high intercostal space were compared between 35 patients with IVF and 105 age- and sex-matched healthy controls (patient: control ratio, 1:3). **Results:** The frequency of J point elevation [?] 0.1mV in the 4th intercostal spaces was similar between patients with IVF (14%) and healthy controls (7%). However, the frequency of J point elevation [?] 0.1mV in the 3rd intercostal space was higher in patients with IVF (40%) than controls (11%) ($P < 0.01$). J point elevation was present only in the 3rd intercostal space but not in the 4th intercostal space in 30% of patients with IVF but only in 6% of controls ($P < 0.01$). During follow up, the recurrence of ventricular fibrillation was higher in patients with IVF who had J point elevation in the 3rd intercostal space (36%) and Brugada syndrome(40%) than those with IVF who did not have J point elevation in the 3rd intercostal space.(11%) ($P < 0.05$ for both). **Conclusion:** J point elevation in the 3rd intercostal space was associated with IVF and recurrences of ventricular fibrillation. Electrocardiogram recordings in the high intercostal space may be useful to identify risk of sudden death.

Key Words; J wave, ventricular fibrillation, early repolarization, Brugada syndrome, Electrocardiogram

Introduction

Ventricular fibrillation (VF) is usually associated with structural heart disease.¹ However, VF also occurs in patients without structural heart disease.^{2, 3} Early repolarization pattern or J point elevation in the inferior and/or lateral leads of the 12-lead electrocardiogram (ECG) is associated with pathogenesis in idiopathic ventricular fibrillation (IVF).⁴⁻⁶ Furthermore, J point elevation in the right precordial leads is also associated with IVF.⁷

Brugada syndrome (BrS) is also characterized by J point elevation in the right precordial leads and is associated with risk of ventricular fibrillation.⁸ The characteristic ECG pattern is often found only in the right precordial leads placed at second and/or third intercostal spaces in BrS.⁹ However, the significance of high precordial ECGs is unknown in IVF. In this study, we compared high right precordial ECGs between patients with idiopathic ventricular fibrillation and healthy controls. We also studied the association of J point elevation in high precordial ECGs with risk of VF recurrences.

Methods

Study population

We enrolled 50 consecutive patients, between 2003 and 2018, who were referred to our institution for resuscitated VF not linked to structural heart disease. IVF was diagnosed in 35 patients and BrS was diagnosed in other 15 patients. During hospitalization, all patients received implantable cardioverter defibrillator (ICD) therapy. Patients with structural heart disease were excluded using 12-lead ECGs, transthoracic echocardiography, cardiac computed tomography, cardiac magnetic resonance imaging, coronary arteriography including spasm induction, and left ventriculography. Patients with long QT syndrome, short QT syndrome, and catecholamine-induced polymorphic ventricular tachycardia were also excluded. Institutional review board approval was obtained.

All patients without spontaneous type 1 Brugada ECGs received sodium channel blocker test. BrS was diagnosed when type 1 ST-segment elevation was observed either spontaneously or during sodium channel blocker test in at least one right precordial lead (V1 and V2), which was placed in a baseline standard or high (second or third) intercostal space.¹⁰

Twelve-lead ECGs recorded in the absence of antiarrhythmic drugs were compared between patients with IVF and control subjects who were matched to patients based on gender and age (patient: control ratio, 1:3). Control subjects without cardiovascular disease or medication use were included. Subjects with bundle branch block, intraventricular conduction disturbances, and/or abnormal QT intervals in ECGs were excluded.

ECG analysis

We evaluated ECGs recorded in the 3rd and 4th ICSs in the absence of antiarrhythmic drugs during sinus rhythm in all study subjects. J point elevation in the right precordial leads was defined as upward/downward notching or downward slurring with an amplitude ≥ 0.1 mV at the end of QRS to early ST segment in any of the right precordial leads (V1 and V2) in the 3rd or 4th ICS (Figure 1). Inferolateral early repolarization (ER) was defined as the presence of a positive J wave, which is a slurring or notch at the QRS terminal that is ≥ 0.1 mV above the isoelectric line in ≥ 2 contiguous leads in any of the inferior leads (II, III, and aVF), the lateral leads (I, aVL, and V4–V6), or both.⁴ All ECGs were manually evaluated separately by two independent cardiologists who were blinded to the patient status (VF patients or healthy controls).

Clinical data

The medical records of all VF patients were investigated for age at VF development, sex, family history of sudden death at ≥ 45 years, patient's activity at the onset of VF, and medications. Activity status at the onset of VF was classified as sleep if VF occurred during sleeping, arousal at rest if VF occurred when the patient was awake without body movement, or physical effort if VF occurred during exertion. Electrophysiologic studies were performed on 27 patients.

After ICD implantation, all patients visited the outpatient clinic every 3–6 months for ICD interrogation. During the follow-up, patients were considered to have VF recurrence if VF was documented by ICD interrogation. An electrical storm was defined as three or more VF events recorded within 24 hours. The beginning of the observation period was the day of ICD implantation. ECGs were recorded in the 3rd and 4th ICSs at clinic visits; however, none of the patients diagnosed with IVF showed type 1 Brugada ECGs during the follow-up.

Data Analysis

The statistical analyses were performed with SPSS version 25 (IBM Inc., Armonk, NY). Data were expressed as the mean \pm SD or number (percentage). Differences in parameters between patients with IVF and control subjects were analyzed using Student's *t*-test for continuous variables and by the Fisher's exact test for categorical variables. Survival curves were constructed by the Kaplan–Meier method and were compared using the log-rank test. A two-sided $P < 0.05$ was considered statistically significant.

Results

Comparisons between patients with IVF and healthy controls

The clinical and ECG characteristics in 35 patients with IVF and 105 age- and sex-matched controls are shown in Table 1. Patients with IVF included 33 men (94%), and the mean age was 42 ± 18 years. The control group included 105 healthy individuals who were matched to patients with IVF based on sex and age (patient:control ratio, 1:3). The frequency of J point elevations ≥ 0.1 mV in the 4th ICS was similar between patients with IVF (14%) and healthy controls (7%) ($P = 0.17$). However, the frequency of J point elevation ≥ 0.1 mV in the 3rd ICS was higher in patients with IVF (40%) than controls (11%) (Odds ratio [OR], 5.2; 95% confidence interval [CI], 2.1–12.8; $P < 0.01$). Furthermore, the frequency of J point elevation ≥ 0.2 mV in the 3rd ICS was higher in patients with IVF (26%) than controls (3%) (OR, 11.7; 95% CI, 3.0–46.6; $P < 0.01$). J point elevation was present only in the 3rd ICS but not in the 4th ICS in 30% of patients with IVF and only in 7% of controls ($P < 0.01$). The frequency of inferolateral early repolarization and the other ECG parameters were not different between the two groups.

Comparisons between patients with IVF and those with BrS

The clinical and ECG characteristics of 35 patients with IVF and 15 patients with BrS are shown in Table 2. Among patients with IVF, J point elevation ≥ 0.1 mV in the 3rd ICS was present in 14 patients. VF developed during physical efforts more often in IVF patients without J point elevation in the 3rd ICS than BrS patients ($P < 0.05$). There was no difference in activity status at the onset of VF between IVF patients with and without J point elevation in the 3rd ICS. There was no difference in other clinical characteristics and ECG findings among three groups. The frequency of inferolateral ER was similar in three groups. There was no difference in ECG findings except for Brugada ECG in three groups.

Clinical outcome

The follow-up period after ICD implantation in the IVF group with J point elevations in the 3rd ICS, the IVF group without, and the BrS group was 118 ± 80 months, 109 ± 61 months, and 105 ± 70 months, respectively. Two patients in BrS group were treated with bepridil. None of patients with IVF received antiarrhythmic drugs.

During a follow up of 110 ± 69 months, the recurrence of VF was observed in 5 of 14 IVF patients with J point elevation in the 3rd ICS (36%), 2 of 21 IVF patients without J point elevation in the 3rd ICS (10%), and 6 of 15 BrS patients (40%). The frequency of VF recurrences was higher in IVF patients with J point elevation in the 3rd ICS and Brugada syndrome than IVF patients without J point elevation in the 3rd ICS ($P < 0.05$ for both). Electrical storm was observed in one of IVF patient (7%) with J point elevation in the 3rd ICS, none of IVF patient without J point elevation in the 3rd ICS, and one of BrS patient (7%). None of the patients died during the follow-up.

Discussion

We directly compared ECG findings in the high ICS in IVF patients and generally healthy individuals. The frequency of J point elevation in high precordial leads was higher in patients with IVF than healthy controls, although the frequency of J point elevation in standard precordial leads was similar between two groups. Furthermore, J point elevation in high precordial leads was associated with risk of VF recurrences in patients with IVF.

Frequency of J point elevation in high intercostal spaces

There have been several reports on ECGs in high right precordial leads in healthy individuals. In a study from South Korea including 225 healthy men, J point elevation > 0.2 mV was observed in the 4th ICS in 0% of subjects, and was observed in the 3rd ICS in 1.3%.¹¹ In a report from Turkey including 504 healthy men, J point elevation ≥ 0.2 mV were observed in the 4th ICS in 3% of subjects, whereas the prevalence increased to 5% in the 3rd ICS¹². In a report from Japan including 206 men, the prevalence of J point elevation ≥ 0.2 mV increased from 1.5% in the 4th ICS to 5.8% in the 3rd ICS¹³. In this study, the prevalence of J point

elevation [?] 0.2 mV in healthy control group (1.9% of in the 4th ICS and 2.9% in the 3rd ICS) was similar to those in the previous studies.

The frequency of J point elevation in the 3rd ICS [?] 0.1 mV was higher in patients with IVF than healthy controls, and the difference became more pronounced when limited to J point elevation [?] 0.2mV. There have been few previous studies investigating ECGs in the high intercostal space in IVF patients. In a study by Kamakura *et al.*¹⁴ including 32 patients with early repolarization syndrome, J point elevation [?] 0.1mV was observed in the 4th ICS in 8 patients (25%) and was observed in the high ICS in 13 patients (41%). The frequency of J point elevation in right precordial leads seems similar between the previous study and this study, although there was only 17% of patients with early repolarization syndrome in this study.

Characteristics of IVF patients with J point elevation in the 3rd intercostal space

There is a strong male dominance in IVF, early repolarization syndrome, and BrS.^{15, 16} Similar to these diseases characterized by risk of VF unassociated with structural heart diseases, majority of patients with J point elevation in the 3rd ICS were men (93%). In this study, VF occurred less frequently during exercise in IVF patients with J point elevation in the 3rd ICS than those without J point elevation in right ICS, suggesting that increased vagal tone is associated with risk of VF in patients with J point elevation in the 3rd ICS. In BrS, VF is associated increased vagal tone and often develops at rest and during sleep.^{17, 18} The characteristic J point and ST-segment elevation is often pronounced in the 3rd and 2nd ICS in BrS. Although Type I Brugada ECG was not observed in patients with J point elevation in the 3rd ICS at rest and during sodium channel blocker test, IVF with J point elevation in the 3rd ICS and BrS share clinical and electrophysiological characteristics, suggesting the presence of common arrhythmogenic substrate between two disorders.

Kamakura *et al.*¹⁶ reported that the frequency of VF recurrences is higher in ERS patients with J point elevation in standard and/or high right ICS (58%) than those without J point elevation in right ICS (11%). In this study, the frequency of VF recurrences was also higher in IVF patients with J point elevation in high right ICS (36%) than those without J point elevation in right ICS (11%). Taken together, J point elevation in 3rd ICS may be an electrographic risk factor for VF recurrence in patients with VF unassociated with structural heart diseases.

Study Limitations

This study had some limitations. This was a retrospective analysis at a single center. The small number of IVF patients may have influenced our interpretation of the results, despite the number being comparable to other previous studies.^{14, 16} There is a need for a large prospective study.

Conclusion

Our study found that the prevalence of J point elevation in the 3rd ICS was high in patients with IVF. J point elevation in the 3rd ICS may be a risk factor for VF recurrence in patients with IVF. Electrocardiogram recordings in high ICS may be useful to identify risk of sudden death.

References

1. Huikuri HV, Castellanos A and Myerburg RJ. Sudden death due to cardiac arrhythmias. *The New England journal of medicine* . 2001;345:1473-82.
2. Conte G, Caputo ML, Regoli F, Marcon S, Klersy C, Adjibodou B, Del Bufalo A, Moccetti T and Auricchio A. True idiopathic ventricular fibrillation in out-of-hospital cardiac arrest survivors in the Swiss Canton Ticino: prevalence, clinical features, and long-term follow-up. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology* . 2017;19:259-266.
3. Waldmann V, Bougouin W, Karam N, Dumas F, Sharifzadehgan A, Gandjbakhch E, Algalarrondo V, Narayanan K, Zhao A, Amet D, Jost D, Geri G, Lamhaut L, Beganton F, Ludes B, Bruneval P, Plu I, Hidden-

- Lucet F, Albuissou J, Lavergne T, Piot O, Alonso C, Leenhardt A, Lellouche N, Extramiana F, Cariou A, Jouven X and Marijon E. Characteristics and clinical assessment of unexplained sudden cardiac arrest in the real-world setting: focus on idiopathic ventricular fibrillation. *European heart journal* . 2018;39:1981-1987.
4. Haissaguerre M, Derval N, Sacher F, Jesel L, Deisenhofer I, de Roy L, Pasquie JL, Nogami A, Babuty D, Yli-Mayry S, De Chillou C, Scanu P, Mabo P, Matsuo S, Probst V, Le Scouarnec S, Defaye P, Schlaepfer J, Rostock T, Lacroix D, Lamaison D, Lavergne T, Aizawa Y, Englund A, Anselme F, O'Neill M, Hocini M, Lim KT, Knecht S, Veenhuyzen GD, Bordachar P, Chauvin M, Jais P, Coureau G, Chene G, Klein GJ and Clementy J. Sudden cardiac arrest associated with early repolarization. *The New England journal of medicine* . 2008;358:2016-23.
 5. Rosso R, Kogan E, Belhassen B, Rozovski U, Scheinman MM, Zeltser D, Halkin A, Steinvil A, Heller K, Glikson M, Katz A and Viskin S. J-point elevation in survivors of primary ventricular fibrillation and matched control subjects: incidence and clinical significance. *Journal of the American College of Cardiology* . 2008;52:1231-8.
 6. Tikkanen JT, Anttonen O, Junttila MJ, Aro AL, Kerola T, Rissanen HA, Reunanen A and Huikuri HV. Long-term outcome associated with early repolarization on electrocardiography. *The New England journal of medicine* . 2009;361:2529-37.
 7. Antzelevitch C and Yan GX. J wave syndromes. *Heart rhythm* . 2010;7:549-58.
 8. Brugada P and Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. *Journal of the American College of Cardiology* . 1992;20:1391-6.
 9. Savastano S, Rordorf R, Vicentini A, Petracci B, Taravelli E, Castelletti S, D'Errico A, Torchio M, Dossena C, Novara P, Dagradi F, Landolina M, Spazzolini C, Crotti L and Schwartz PJ. A comprehensive electrocardiographic, molecular, and echocardiographic study of Brugada syndrome: validation of the 2013 diagnostic criteria. *Heart rhythm* . 2014;11:1176-83.
 10. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekval TM, Spaulding C and Van Veldhuisen DJ. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *European heart journal* . 2015;36:2793-2867.
 11. Shin SC, Ryu HM, Lee JH, Chang BJ, Shin JK, Kim HS, Heo JH, Yang DH, Park HS, Cho Y, Chae SC, Jun JE and Park WH. Prevalence of the Brugada-type ECG recorded from higher intercostal spaces in healthy Korean males. *Circ J* . 2005;69:1064-7.
 12. Hunuk B, Kepez A and Erdogan O. Prevalence of Brugada-type electrocardiogram pattern by recording right precordial leads at higher intercostal spaces. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology* . 2013;15:590-4.
 13. Hisamatsu K, Morita H, Fukushima Kusano K, Takenaka S, Nagase S, Nakamura K, Emori T and Ohe T. Evaluation of the usefulness of recording the ECG in the 3rd intercostal space and prevalence of Brugada-type ECG in accordance with recently established electrocardiographic criteria. *Circ J* . 2004;68:135-8.
 14. Kamakura T, Wada M, Nakajima I, Ishibashi K, Miyamoto K, Okamura H, Noda T, Aiba T, Takaki H, Yasuda S, Ogawa H, Shimizu W, Makiyama T, Kimura T, Kamakura S and Kusano K. Significance of electrocardiogram recording in high intercostal spaces in patients with early repolarization syndrome. *European heart journal* . 2016;37:630-7.

15. Benito B, Sarkozy A, Mont L, Henkens S, Berruezo A, Tamborero D, Arzamendi D, Berne P, Brugada R, Brugada P and Brugada J. Gender differences in clinical manifestations of Brugada syndrome. *Journal of the American College of Cardiology* . 2008;52:1567-73.
16. Kamakura T, Kawata H, Nakajima I, Yamada Y, Miyamoto K, Okamura H, Noda T, Satomi K, Aiba T, Takaki H, Aihara N, Kamakura S, Kimura T and Shimizu W. Significance of non-type 1 anterior early repolarization in patients with inferolateral early repolarization syndrome. *Journal of the American College of Cardiology* . 2013;62:1610-8.
17. Matsuo K, Kurita T, Inagaki M, Kakishita M, Aihara N, Shimizu W, Taguchi A, Suyama K, Kamakura S and Shimomura K. The circadian pattern of the development of ventricular fibrillation in patients with Brugada syndrome. *European heart journal* . 1999;20:465-70.
18. Mizumaki K, Fujiki A, Tsuneda T, Sakabe M, Nishida K, Sugao M and Inoue H. Vagal activity modulates spontaneous augmentation of ST elevation in the daily life of patients with Brugada syndrome. *Journal of cardiovascular electrophysiology* . 2004;15:667-73.

Figure legends

Figure 1

J point elevation in the right precordial lead was defined as upward/downward notching or downward slurring with an amplitude [?] 0.1 mV at the end of QRS to early ST segment in any of the right precordial leads (V1 and V2) in the 4th or 3rd ICS. Arrows indicate J point elevation in the 3rd intercostal space in patients with IVF.

Figure 2

Kaplan-Meier analysis of freedom from recurrent VF during follow-up. The IVF group with J point elevation in the 3rd ICS and the BrS group both had significantly higher recurrences of VF compared with the IVF group without J point elevation in the 3rd ICS.

Hosted file

J point elevation JCE figure.docx available at <https://authorea.com/users/345878/articles/471968-j-point-elevation-in-high-precordial-leads-associated-with-risk-of-ventricular-fibrillation>

Hosted file

J point elevation JCE table.docx available at <https://authorea.com/users/345878/articles/471968-j-point-elevation-in-high-precordial-leads-associated-with-risk-of-ventricular-fibrillation>