Early repolarization in Wolff–Parkinson–White syndrome: prevalence and clinical significance

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Aims
Idiopathic ventricular fibrillation (IVF) with early repolarization (ER) has recently been reported; however, ER is a common finding in healthy subjects and is also found sporadically in patients with Wolff–Parkinson–White (WPW) syndrome. The present study was designed to evaluate the prevalence and clinical significance of ER in patients with WPW syndrome.

Methods and results
One hundred and eleven patients with WPW syndrome were studied retrospectively. Early repolarization was defined as QRS slurring or notching with J-point elevation ≥ 1 mm. The prevalence of ER was determined before and after successful catheter ablation. Before ablation, ER was found in 35 of 75 patients with a left free wall, 6 of 23 with a right free wall, and 7 of 13 with a septal accessory pathway (48 of 111, 43% as a whole). Early repolarization was always observed in leads with positive deflection of the initial part of the delta wave. After successful ablation of accessory pathways, ER was preserved in 28 (25%), disappeared in 20 (18%), and newly developed in 8 (7%) patients. In the remaining 55 (50%) patients, ER was not observed either before or after ablation. In patients with persistent ER, the amplitude and width of ER were significantly decreased 3–7 days after the ablation (1.7 ± 0.7 vs. 1.4 ± 0.6 mm, \( P < 0.005 \) and 42 ± 11 vs. 34 ± 9 ms, \( P < 0.001 \), respectively).

Conclusion
In patients with WPW syndrome, ER could be partly related to early depolarization through the accessory pathway. However, persistent ER and new ER appearing after the ablation were frequently found. Therefore, in these patients, mechanisms other than early depolarization may be involved in the genesis of ER.

Keywords
WPW syndrome • Delta wave • Accessory pathway • Early repolarization • Ventricular fibrillation • Catheter ablation

Introduction
Recently, several studies have reported that J-point and ST-segment elevation in the inferior or lateral chest leads are associated with arrhythmic sudden death due to ventricular fibrillation (VF) in patients without apparent organic heart diseases, i.e. idiopathic VF (IVF).1–8 An experimental study revealed that the presence of a transient outward current (Ito)-mediated prominent action potential notch in the epicardium, but not in the endocardium, provides a voltage gradient that manifests as J waves.9,10 However, the exact mechanisms responsible for J-wave elevation and the genesis of VF are still under investigation. Moreover, the J-point or ST-segment elevation, i.e. the early repolarization (ER) pattern, in the lateral or inferior leads is usually considered benign because it is often observed in healthy young individuals.1,2,11–13 Although its prevalence has been estimated to be between 1 and 7% in healthy adults,1,2,12,13 there have been no criteria to identify high-risk patients within the broad population of healthy individuals with a similar electrocardiogram (ECG) pattern. Some investigators have reported the coexistence of ER with Wolff–Parkinson–White (WPW) syndrome;11,14,15 however, its clinical characteristics remain unclarified. The
present study was therefore designed to evaluate the prevalence and clinical significance of ER in patients with WPW syndrome.

Methods

Study population
One hundred and thirty-four consecutive patients with manifest WPW syndrome who had undergone successful catheter ablation for the accessory pathway between January 1998 and December 2009 were retrospectively reviewed. Five patients with multiple accessory pathways and 18 patients who exhibited intermittent pre-excitation were excluded from the review. The remaining 111 patients (mean age 40.9 ± 17.7 years) had either episodes of atrioventricular re-entrant tachycardia or paroxysmal atrial fibrillation (AF) and constituted the study group. The present retrospective study protocol was approved by the review board of our institution and carried out in accordance with the Declaration of Helsinki. All patients gave written informed consent before the catheter ablation. In all patients, physical examination, chest x-ray, two-dimensional echocardiography, exercise test, and thallium or 99mTc-tetrofosmin myocardial SPECT failed to disclose apparent evidence of organic heart diseases. None of the patients exhibited Brugada-type ST changes in the V1–V3 leads in either the normal or upper intercostal space.

Measurements and definition of early repolarization
In study patients, a 12-lead ECG was recorded (with filter band settings of 0.05–150 Hz) after withdrawal of all antiarrhythmic drugs for at least five half-lives both 1–3 days before and 3–7 days after the successful catheter ablation. To blind ECG interpreters to patient characteristics, all ECG tracings were scanned and coded. Segments exhibiting extrasystoles were not used. The scanned ECGs were reviewed in a random order by three investigators. As described in earlier studies,1,2,12 ER was defined as the presence of a QRS-ST junction (J point) that deviated from the baseline by ≥0.1 mV. The J-point elevation was observed either as QRS slurring (a smooth transition from the QRS segment to the ST segment) or notching (a positive J deflection inscribed on the S wave)1,2,12 in any of the leads. The height of the J-point elevation from the baseline was measured using an electronic caliper after the scanned ECGs were enlarged four-fold.2 The width of the J wave, defined as the duration from the QRS-J junction to the intersection between the terminal J wave and the ST segment, was also measured.

Statistical analysis
The values are presented as the mean ± standard deviation. An unpaired t-test was used to compare the mean value between the two groups. Pearson’s χ² test was used to compare the prevalence. Serial changes in the variables of amplitude and duration of the J wave were analysed by analysis of variance for repeated measures. Multiple comparisons were made using the Bonferroni/Dunn test. A P value <0.05 was considered significant.

Results

Prevalence of early repolarization
Among 111 study patients, 73 patients (49 men) had left free wall, 23 patients (12 men) had right free wall, and 15 patients (8 men) had septal accessory pathways. They were categorized into four groups (Figure 1): 28 patients with ER before and after catheter ablation (Group I, Figure 2), 20 patients with ER only before the ablation (Group II, Figure 3), 8 patients with ER only after the ablation (Group III), and 55 patients without ER before and after the ablation (Group IV). Accordingly, the overall prevalence of early repolarization before the ablation (Group I+II) was 43% and that of early repolarization after the ablation (Group I+III) was 32% (A). In each accessory pathway location, the numbers of patients are shown according to the categorization of Groups I–IV (8). LA, left anterior; LL, left lateral; LP, left posterior; LPS, left posteroseptal; MV, mitral valve; RA, right anterior; RL, right lateral; RP, right posterior; RPS, right posteroseptal; TV, tricuspid valve.

Figure 1 Prevalence of early repolarization before and after catheter ablation and accessory pathway location. Study patients were categorized into four groups: early repolarization before and after catheter ablation (Group I), early repolarization only before the ablation (Group II), early repolarization only after the ablation (Group III), and no early repolarization before and after the ablation (Group IV). Accordingly, the overall prevalence of early repolarization before the ablation (Group I+II) was 43% and that of early repolarization after the ablation (Group I+III) was 32% (A). In each accessory pathway location, the numbers of patients are shown according to the categorization of Groups I–IV (8). LA, left anterior; LL, left lateral; LP, left posterior; LPS, left posteroseptal; MV, mitral valve; RA, right anterior; RL, right lateral; RP, right posterior; RPS, right posteroseptal; TV, tricuspid valve.
Clinical characteristics in patients with or without early repolarization

In Table 2, the clinical characteristics are compared between patients with and without ER before the ablation. ER tended to be found frequently in younger and male patients, but the difference did not reach statistical significance. Complication with paroxysmal AF and the minimum RR interval during AF did not differ between ER(+) and ER(−) patients. One patient in each group had resuscitated episode from VF induced by rapid ventricular responses through the accessory pathway conduction during paroxysmal AF. Episodes of syncope during tachyarrhythmias were demonstrated in five patients in group ER(+) and seven

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**Figure 2** Representative changes in electrocardiogram after catheter ablation in a 39-year-old man with a left anterolateral accessory pathway (Group I). J-point notching was demonstrated in V1–5 (arrows) before the ablation (A). Electrocardiogram still showed J-point notching in V2–5 (arrows) 1 week after successful ablation (B). The amplitude of J-point elevation decreased 2 months after the ablation in comparison with 1 week after the ablation (arrows) (C).

**Figure 3** Representative changes in electrocardiogram after catheter ablation in a 57-year-old man with a posteroseptal accessory pathway (Group II). J-point notching was demonstrated in V2–4 (arrows) before the ablation (A) but disappeared after successful ablation (B).
patients in group ER(−), and the prevalence was not different between the two groups (Table 2). The mean RR interval during sinus rhythm, and the pre-cordial QRS voltage (SV1 + RV5), did not differ between the two groups. None of the electrophysiological parameters, including effective refractory period of the antegrade and retrograde accessory pathway, the right atrium, and the right ventricle, were significantly different between ER(+) and ER(−) patients.

In Table 3, the clinical characteristics were also compared between patients with and without ER after the ablation. The mean age was not significantly different between the two groups; however, the ER(+) group included more male patients than the ER(−) group. Moreover, the pre-cordial QRS voltage (SV1 + RV5) was significantly higher in ER(+) patients than in ER(−) patients. The mean RR interval during sinus rhythm and effective refractory period of the right atrium and the right ventricle did not differ between the two groups.

Changes in early repolarization after catheter ablation

Three to seven days after successful catheter ablation, the amplitude and width of ER were significantly decreased (1.7 ± 0.7 vs. 1.4 ± 0.6 mm, P < 0.005 and 42 ± 11 vs. 34 ± 9 ms, P < 0.001, respectively) among the patients in Group I. The mean RR intervals did not change significantly 3–7 days after the ablation in comparison with the pre-ablation values. Among 23 of 28 patients in Group I, ECG was repeatedly recorded 27 ± 46 (1–141) months after the ablation and ER was disappeared in 4 patients during the follow-up periods. In the remaining 19 patients with persistent ER, the amplitude and width of ER did not differ during the follow-up periods in comparison with those obtained 3–7 days after the ablation. In five of eight patients in Group III, who had newly developed ER after the ablation, follow-up ECGs were obtained and the amplitude and width of ER did not change during 29 ± 57 (2–131) months of follow-up periods.

Discussion

Major findings

This is the first report showing the prevalence and clinical characteristics of ER in patients with WPW syndrome. The major findings of the present study are as follows: (i) Before the successful ablation, ER was found in 48 of 111 (43%) patients and was always demonstrated in the leads with positive deflection of the initial part of the delta wave. (ii) After the ablation of the accessory pathway, ER was preserved in 28 (25%), disappeared in 20 (18%), and newly developed in 8 (7%) patients. In the remaining 55 (50%) patients, ER was not found either before or after the ablation.
ablation. (iii) In patients with persistent ER, the amplitude and width of ER were significantly decreased 3–7 days after the ablation.

**Early repolarization in Wolff–Parkinson–White syndrome**

Recently, it has been shown that ER in 12-lead ECG is associated with IVF and atypical Brugada syndrome. Rosso et al. reported that J-point elevation was more common among 45 patients with IVF than among 124 matched control subjects (42 vs. 13%, P = 0.001). These results are similar to those reported by Haisaguerre et al., who found J-point and/or ST-segment elevation in 31% of 216 IVF patients and 5% of 412 control subjects. However, ER is a common ECG finding that affects 1–7% of healthy subjects; the condition is usually considered benign. ER is more common in young men, especially athletes, and is also associated with other conditions such as left ventricular hypertrophy and WPW syndrome. Moreover, the prevalence and clinical characteristics of ER in patients with WPW syndrome have not yet been described. In the present study, ER was found in 43% of patients with manifest WPW syndrome and the prevalence was higher in comparison with healthy subjects. The prevalence of ER in patients with WPW syndrome was slightly higher than that in patients with IVF.

**Mechanism of early repolarization in Wolff–Parkinson–White syndrome**

A more prominent transient outward current (Ito)-mediated spike and dome action potential morphology in the ventricular epicardium than in the endocardium is likely to be the electrophysiological basis of the J wave. The different location of the heterogeneous distribution of Ito may contribute to different syndromes presenting with J waves in different ECG leads. Commonly, the J wave presents in the right pre-cordial leads in Brugada syndrome, whereas it presents in the left pre-cordial and inferior leads in ER syndrome and IVF. As these clinical syndromes have the same electrophysiological basis, they have similar responses to drugs, heart rate, and neural regulation.

Although the electrophysiological mechanism of the J wave has been proposed, the exact difference in the mechanism between benign and malignant J-wave elevation remains to be clarified. Rosso et al. reported that J-point elevation was more common among patients with IVF than among matched control subjects in both the inferior leads and the I and aVL leads. Merchant et al. observed that left precordial terminal QRS notching is more prevalent in malignant variants of ER than in benign cases. The difference in the ECG leads location where ER was evident between IVF patients and healthy control subjects may shed light on the mechanisms of IVF. In the present study, there was no evident localization of ECG leads in which ER was found in patients with WPW syndrome. Because ER was always demonstrated in the leads with positive deflection of the initial part of the delta wave in the study patients, ER in patients with WPW syndrome may be related to the early depolarization through accessory pathways.

The effects of the successful ablation of the accessory pathway on ER differed among patients (Figure 1). Therefore, mechanisms other than early depolarization may be related to ER in WPW syndrome. Based on the health examination data, the prevalence of ER was higher in young men and higher QRS voltage (SV1 + RV5 ≥ 35 mm) was more common in subjects with ER. In the present study, ER tended to be found in younger and male patients but the difference did not reach statistical significance. The QRS voltage (SV1 + RV5) did not differ between patients with and without ER. In contrast, after successful ablation, the frequency of male patients and the pre-cordial QRS voltage were significantly higher in patients with ER than in those without ER. Therefore, in some male patients and patients with higher QRS voltage after the ablation, ER might be affected by early depolarization before the ablation. In some study patients, the amplitude of ER after the ablation gradually decreased over time (Figure 2) and ER was disappeared in four patients in Group I during a follow-up period of 27 ± 46 months. Therefore, the cardiac memory of the repolarization might be in part associated with the preserved ER after the ablation. Many other factors could be involved in the genesis of ER in WPW syndrome, and further studies are needed to clarify the mechanism of ER in WPW syndrome.

**Clinical significance of early repolarization in Wolff–Parkinson–White syndrome**

Complications with paroxysmal AF and the minimum RR interval during AF did not differ between ER(+) and ER(−) patients, and only one patient in each group had been resuscitated from VF. None of the electrophysiological parameters differed significantly between ER(+) and ER(−) patients. Therefore, ER might not be associated with fatal or nonfatal arrhythmias in patients with WPW syndrome. Although the combination of WPW syndrome and Brugada-type ST elevation has been reported, the relationship of these two syndromes remains to be clarified. Moreover, larger studies are required to establish the clinical significance of ER in patients with WPW syndrome.

**Methodological considerations and study limitations**

The present study had several limitations. First, all subjects underwent ECG at least twice before and after the ablation; however, the day-to-day variability of ECG patterns should have been evaluated using more frequent ECG recordings. Additionally, slightly different positions of electrode patches for follow-up ECGs might have affected the results. Second, in patients with IVF, circadian variation of J wave and effects of both autonomic blockades and antiarrhythmic agents on J wave have been reported. The effects of both the autonomic nervous system and antiarrhythmic agents, especially class Ic drugs, on ER should also have been evaluated.

**Conclusions**

In patients with WPW syndrome, ER was frequently present and could be partly related to the early depolarization through the
Conflict of interest: none declared.

References


