The Role of the Ratio of J-Point Elevation Magnitude and R-Wave Amplitude on the Same ECG Lead in the Risk Stratification of Subjects With Early Repolarization Pattern

Xu-Miao Chen MD | Cheng-Cheng Ji MD | Yun-Jiu Cheng MD | Li-juan Liu MD, PhD | Wei-Qi Zhu MD | Ying Huang MD | Wei-Ying Chen MD | Su-Hua Wu MD, PhD

Department of Cardiology, the First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Corresponding Author: Su-Hua Wu, MD, Department of Cardiology, The First Affiliated Hospital, Sun Yat-Sen University, No. 58 Zhongshan Rd II, Guangzhou 510080, China (wusuhua@hotmail.com)

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Background: Just as high-risk populations for cardiac arrest exist in patients with Brugada syndrome or long QT syndrome, high-risk and low-risk populations for cardiac arrest also exist in patients with early repolarization pattern (ERP).

Hypothesis: Electrocardiographic (ECG) characteristics can aid the risk stratification of patients with ERP.

Methods: Electrocardiographic parameters such as magnitude of J-point elevation and J/R ratio were measured. The magnitude of J-point elevation, leads with J points elevated, J/R ratio, morphology of the ST segment, and QT/QTc interval were used in comparative analysis in 2 groups: 57 patients with ERP and cardiac arrest (cardiac arrest group) and 100 patients with ERP but without cardiac arrest (control group).

Results: There was no statistical difference in clinical characteristics of the 2 groups. The J/R ratio in the cardiac arrest group was significantly higher than in the control group ($26.8\% \pm 18.1\%$ vs $16.3\% \pm 10.3\%$, respectively; $P < 0.001$) and the proportion of horizontal/descending ST segments (70.2%) was significantly higher than in the control group (29.0%), but the proportion of ascending/upsloping ST segments (29.8%) was significantly lower than in the control group (71.0%; $P < 0.001$). Multivariate logistic regression revealed that higher J/R ratio and horizontal/descending ST segment were independently associated with increased risk of cardiac arrest in patients with ERP.

Conclusions: In patients with ERP and cardiac arrest, J/R ratios were relatively higher and mostly with horizontal/descending ST segments, suggesting that J/R ratio and ST-segment morphology may be used as indicators for risk stratification in patients with ERP.

KEYWORDS

Arrhythmia/all, sudden death, Electrocardiography ambulatory ECG

1 | INTRODUCTION

The early repolarization pattern (ERP) is characterized by an elevation of ≥ 0.1 mV of the QRS-ST junction (J point) in 2 adjacent electrocardiographic (ECG) leads with either slurring or notching morphology. In the past, ERP was considered a normal ECG variation, but recent studies have shown that ERP increases the risk of arrhythmic death.¹⁻⁴

Clinical observational studies showed that incidence of ERP in the normal population was 2.3% to 13.1%;^{2,3,5,6} however, the incidence in patients with ERP and primary cardiac arrest was 31% to 42%, much higher than that of an age- and sex-matched population.^{7,8} Our previous study showed that the risk of arrhythmic death in patients with ERP was increased (risk ratio: 1.7, 95% confidence interval [CI]: 1.19-2.42) after adjusting for confounding factors.⁹ Although the risk of arrhythmic death in patients with ERP is increased, the absolute risk is not too high. Therefore, the identification of the actual high-risk population and appropriate risk stratification for ERP are very important.

Xu-Miao Chen, MD, and Cheng-Cheng Ji, MD, contributed equally to this work.

Just as there are subpopulations at high risk for cardiac arrest in patients with Brugada syndrome or long QT syndrome, populations at low and high risk for cardiac arrest also exist in ERP. A surface 12-lead ECG plays an important role in risk stratification of patients with Brugada syndrome and long QT syndrome;^{10–16} therefore, we speculate that ECG can also be used in the risk stratification of patients with ERP. The purpose of the present study is to investigate the role of the ratio of J-point elevation magnitude and R-wave amplitude on the same ECG lead (J/R ratio) and the morphology of the ST segment in risk stratification of patients with ERP.

2 | METHODS

2.1 | Participants

We screened 1045 consecutive patients with cardiac arrest from January 2003 to February 2014, of which 127 cases exhibited a typical ERP. After carefully reviewing clinical data, such as ECG, echocardiography, coronary computed tomography, and coronary angiography, the following patients were excluded: those age >60 years; patients with structural heart disease or coronary heart disease; patients with genetic cardiac ion channel diseases including Brugada syndrome, congenital long QT interval, or short QT interval syndrome; deaths caused by multiple organ failure; pre-excitation syndrome; complete left bundle branch block or complete right bundle branch block; hyperkalemia, and others. Finally, 57 patients (43 males; mean age, 18–60 years) with cardiac arrest and ERP were enrolled, and 100 cases (83 males; mean age, 18–60 years) with ERP but without cardiac arrest, unexplained syncope, family history of unexplained sudden death, or any exclusion criteria mentioned above, were randomly selected from the health physical examination center in the same period to form the control group. The ECG and laboratory data were collected on the first day of admission if cardiac arrest occurred during the hospitalization period. If cardiac arrest occurred outside the hospital, we used previous ECG and laboratory results or data from >1 week after the cardiac event when patients were in stable condition. At the same time, we made sure drugs that could affect ECG—such as class Ia, Ic, and III antiarrhythmia drugs; antidepressants; and some antitumor drugs—were not used within 1 month before the ECGs were collected.

2.2 | Electrocardiographic Characteristic Analysis

According to the leads with J point ≥ 0.1 mV, ERP leads can be divided into 3 groups: inferior leads (II, III, and aVF), lateral leads (V₄ through V₆), and both inferior and lateral leads. The P-R interval was used as reference baseline for measuring magnitude of J-point elevation, and the lead with the highest-amplitude J-point elevation was chosen. The ratio of magnitude of J-point elevation and the R-wave amplitude in all leads was measured and the maximum value was chosen for the comparison of J/R

ratio. Methods for the measurement of J-point elevation magnitude and J/R ratio are shown in Figure 1A. The QT interval and corrected QT interval (QTc) were calculated on the leads with the highest magnitude of J-point elevation. To determine the morphology of the ST segment after the J point, the ST segment that was 40 ms after the J point was chosen, and the morphology of the ST segment was divided into 3 types: ascending/upsloping, horizontal, and descending (Figure 1B).

2.3 | Statistical Analysis

Continuous variables are shown as mean $\pm$ SD. Specified variation was shown as proportion and rate. The *t* test of 2 independent samples was adopted in measurement data that obeyed normal distribution. Count data were compared using the χ^2 test or Fisher exact test. The effects of covariates on cardiac arrest in patients with ERP were analyzed using multivariate logistic regression. Statistical analyses were conducted using SPSS version 22 (IBM Corp., Armonk,

FIGURE 1 ERP morphologies and J/R ratio. (A) ERP with notching (left) or slurring (right) morphology. J/R is the ratio of J-point elevation magnitude and R-wave amplitude on the same ECG lead. (B) ERP with notching or slurring morphology, and with ascending, horizontal, and descending ST segment. Abbreviations: ECG, electrocardiographic; ERP, early repolarization pattern.

TABLE 1 Clinical Characteristics of Patients With ERP, With and Without Cardiac Arrest

	With Cardiac Arrest, n = 57	Without Cardiac Arrest, n = 100	P Value
Sex, M/F	43/14	83/17	0.252
Age, y	44.9 ± 12.6	43.9 ± 12.4	0.605
HTN	10 (17.5)	19 (19)	0.821
DM	8 (14.0)	10 (10)	0.445
Smoker	18 (31.6)	35 (35)	0.663
Serum K concentration, mmol/L	3.96 ± 0.43	4.08 ± 0.44	0.113
Serum Ca concentration, mmol/L	2.25 ± 0.13	2.27 ± 0.12	0.370

Abbreviations: Ca, calcium; DM, diabetes mellitus; F, female; HTN, hypertension; K, potassium; M, male; SD, standard deviation.

Data are presented as n (%) or mean ± SD.

TABLE 2 ECG Characteristics of Patients With ERP, With and Without Cardiac Arrest

	With Cardiac Arrest	Without Cardiac Arrest	P Value
J-point elevation, mV	0.204 ± 0.089	0.193 ± 0.078	0.447
J/R ratio, %	26.8 ± 18.1	16.3 ± 10.3	<0.001
J-point elevation ≥0.2 mV	16 (28.1)	26 (26.0)	0.778
J-point elevation			0.08
Inferior leads	31 (54.4)	37 (37.0)	
Lateral leads	14 (24.6)	28 (28.0)	
Both inferior and lateral leads	12 (21.1)	35 (35.0)	
QTc >440 ms	11 (19.3)	5 (5.0)	0.004
ST segment			<0.001
Ascending/upsloping	17 (29.8)	71 (71.0)	
Horizontal/descending	40 (70.2)	29 (29.0)	

Abbreviations: ECG, electrocardiographic; J/R, the ratio of J-point elevation magnitude and R-wave amplitude on the same ECG lead; QTc, corrected QT interval; SD, standard deviation.

Data are presented as n (%) or mean ± SD.

TABLE 3 Subgroups Analysis of Patients With ERP, With and Without Cardiac Arrest

	With Cardiac Arrest	Without Cardiac Arrest	P Value
J-point elevation, mV			
Inferior leads	0.192 ± 0.070	0.187 ± 0.083	0.811
Lateral leads	0.232 ± 0.131	0.173 ± 0.070	0.134
Both inferior and lateral leads	0.200 ± 0.071	0.218 ± 0.084	0.514
J/R ratio, %			
Inferior leads	35.6 ± 18.2	21.2 ± 12.1	<0.001
Lateral leads	16.4 ± 14.5	8.8 ± 3.4	0.074
Both inferior and lateral leads	16.1 ± 4.8	17.2 ± 8.6	0.676
J-point elevation ≥0.2 mV			
Inferior leads	6 (19.4)	7 (18.9)	0.964
Lateral leads	6 (42.9)	4 (14.3)	0.040
Both inferior and lateral leads	4 (33.3)	15 (42.9)	0.562
QTc >440 ms			
Inferior leads	8 (25.8)	4 (10.8)	0.106
Lateral leads	2 (14.3)	0 (0)	0.106
Both inferior and lateral leads	1 (8.3)	1 (2.9)	0.450
Horizontal/descending ST segment			
Inferior leads	25 (80.6)	20 (54.1)	0.021
Lateral leads	7 (50)	4 (14.3)	0.013
Both inferior and lateral leads	8 (66.7)	5 (14.3)	<0.001

Abbreviations: ECG, electrocardiographic; ERP, early repolarization pattern; J/R, the ratio of J-point elevation magnitude and R-wave amplitude on the same ECG lead; QTc, corrected QT interval; SD, standard deviation.

Data are presented as n (%) or mean ± SD.

NY). In 2-sided tests, a P value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | General Clinical Features

Fifty-seven patients with cardiac arrest and ERP were included in our study. In 22 patients (38.6%), cardiac arrest occurred outside the hospital; in 35 patients (61.4%), cardiac arrest occurred in the hospital. Within the 30 days after experiencing cardiac arrest, 27 patients (47.4%) died, 30 patients (52.6%) survived, and some survivors were implanted with an implantable cardioverter-defibrillator. Three of them had recurrent syncopal attacks before confirmed as cardiac arrest, and 2 of them had a family history of unexplained sudden death at age <60 years. General clinical characteristics of patients of ERP with and without cardiac arrest are shown in

Table 1. There were no significant differences in average age, sex composition, incidence of hypertension or diabetes mellitus, smoking proportion, or serum potassium and calcium concentration between the 2 groups.

3.2 | Electrocardiographic Characteristic Analysis

Comparison of ECG characteristics of patients with ERP, with and without cardiac arrest, is shown in Table 2. In patients with ERP and cardiac arrest, the J/R ratio is significantly higher than in patients without cardiac arrest ($26.8\% \pm 18.1\%$ vs $16.3\% \pm 10.3\%$; $P < 0.001$). The proportion of horizontal/descending ST segment in patients with ERP and cardiac arrest (70.2%) was significantly higher than that in patients without cardiac arrest (29.0%), and the proportion of ascending/upsloping ST segment (29.8%) was significantly lower than that in patients without cardiac arrest (71.0%; $P < 0.001$). The proportion of QTc interval >440 ms in patients with ERP and

FIGURE 2 ERP with high J/R ratio and cardiac arrest. (A) A 39-year-old male patient with ERP (inferior leads) and cardiac arrest; J/R ratio was 50% (lead III). (B) A male patient with ERP (inferior leads) but without cardiac arrest; J/R ratio was only 22% (lead III). Abbreviations: ERP, early repolarization pattern.

cardiac arrest (19.3%) was significantly higher than in the no-cardiac arrest group (5.0%; $P = 0.004$). There were no statistical differences in magnitude of J-point elevation and the leads with elevated J point.

Subgroup analysis showed that the J/R ratio of inferior leads in patients with ERP and cardiac arrest was higher than that without cardiac arrest ($P < 0.001$), and the ratio of magnitude of J-point elevation >0.2 mV in lateral lead was higher ($P = 0.04$; Table 3). After adjusting for sex, age, hypertension, diabetes mellitus, and smoking status, multivariate logistic regression analysis revealed that higher J/R ratio (odds ratio: 25.415, 95% CI: 6.863–194.093, $P = 0.001$) and horizontal or descending ST segment (odds ratio: 5.283, 95% CI: 2.457–11.358, $P < 0.001$) were independently associated with increased risk of cardiac arrest in patients with ERP.

4 | DISCUSSION

Our study showed that the ratio of J-point elevation magnitude and R-wave amplitude on the same ECG lead (J/R ratio) in patients with ERP and cardiac arrest was significantly higher than that in patients without cardiac arrest (Figure 2), and the morphology of the ST segment in former patients was mostly the horizontal/descending type, suggesting that the J/R ratio and the morphology of the ST segment may be used as indicators of risk stratification in patients with ERP.

The highlight of the present study is that we applied, for the first time, the J/R ratio in risk stratification of patients with ERP. Experimental study showed that the J wave was formed by transmural voltage difference of 1 and 2 phases in action potential mediated by transient outward (I_{to}) current.^{17–19} The higher the J-wave amplitude was, the stronger the abnormal I_{to} current was, suggesting that the risk of patients suffering malignant arrhythmia may be higher. The QRS wave voltage is affected by multiple factors, such as patients with a slender body type having high voltage of the QRS wave and the recorded voltage of the QRS wave is lower than actual value in patients with obesity, edema, pleural effusion, or ascites, which relates to the distance from the recording electrode to the heart. Similar to the voltage of the QRS wave, the amplitude of the J wave can also be affected by factors mentioned above. The effect may be more obvious in the limb leads with relatively low voltage. Therefore, we believe that, compared with using the magnitude of J-point elevation alone, relative strength of the I_{to} current can be reflected by the J/R ratio. That is, the J/R ratio could suggest the risk of cardiac arrest in patients with ERP. In the morphology of the ST segment, results from our study suggest that risk of suffering cardiac arrest in patients with ERP and horizontal/descending ST segments is higher than in patients with ascending/upsloping ST segments, which is similar to the conclusion reached by Tikkanen and Cappato.^{20,21}

4.1 | Study Limitations

Some limitations exist in our research, including the facts that our study is a retrospective case-control study and the sample size is relatively small. In addition, ECG parameters are of limited value as risk-stratification tools in clinical practice.

5 | CONCLUSION

In patients with ERP and cardiac arrest, J/R ratios were relatively higher and mostly with horizontal/descending ST segments, suggesting that the J/R ratio and morphology of the ST segment may be used as indicators of risk stratification in patients with ERP. Future large prospective studies are needed to confirm these findings.

Conflicts of interest

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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