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Relationship between the early repolarization pattern and a history of suicide attempts among drug-free psychiatric patients

Hiroshi Kameyama[1] | Kenichi Sugimoto[2] | Fumitoshi Kodaka[1] | Kyoko Ito[3] | Kazutaka Nukariya[1,4] | Tomohiro Kato[3] | Masahiro Shigeta[1]

[1]Department of Psychiatry, The Jikei University School of Medicine, Tokyo, Japan

[2]Department of Cardiology, The Jikei University School of Medicine, Tokyo, Japan

[3]Centre for Preventive Medicine, The Jikei University Hospital, Tokyo, Japan

[4]Department of Psychiatry, The Jikei University Kashiwa Hospital, Chiba, Japan

Correspondence
Hiroshi Kameyama, Department of Psychiatry, The Jikei University School of Medicine, 3-19-18, Nishi-Shimbashi, 105-8471 Minato-Ku, Tokyo, Japan.
Email: h27kameyama@jikei.ac.jp

Abstract

Aim: Suicide attempts are an important severe psychiatric symptom and a clear outcome for mental disorders. Although the relationship between the early repolarization pattern in electrocardiogram and psychiatric disorders has recently been reported, these reports have not been able to exclude the influence of psychiatric drugs. This study aimed to investigate the relationship between the early repolarization pattern and a history of suicide attempts among patients not receiving psychiatric medication.

Methods: A total of 71 patients with a history of suicide attempts were investigated, 38 of whom were analyzed for this study. We compared the frequency of the early repolarization pattern between a suicide attempt group and a control group. Then, we investigated the association between the early repolarization pattern and the suicide attempt group by logistic regression analysis, including electrocardiographic findings associated with psychiatric disorders.

Results: The findings indicated that the frequency of the early repolarization pattern was significantly higher in the suicide attempt group (n = 20; 52.6%) than in the control group (n = 4; 10.5%) ($P < 0.001$), and the results of the logistic regression analysis indicated that the early repolarization pattern was associated with suicide attempts.

Conclusions: These findings suggest that the early repolarization pattern is associated with a history of suicide attempts.

KEYWORDS
early repolarization pattern, electrocardiogram, mental health, psychiatric disorders, suicide

1 | INTRODUCTION

Multidisciplinary studies have been conducted among the fields of psychiatry and cardiology, and a psychosomatic correlation is known to exist between psychiatric and cardiac disorders based on reports regarding the impact of the mental state on cardiac disease[1] or the impact of cardiac disease on the mental state.[2]

Recently, relationships between several psychiatric disorders and the early repolarization pattern (ERP) on electrocardiogram (ECG) have been reported. ERP is characterized by elevation of J-point in

two or more contiguous electrocardiogram leads. J point is located in the end of the QRS wave to the beginning of the ST segment. ERP has been shown to be associated with schizophrenia and schizoaffective disorder.[3,4] Similarly, a high prevalence of the ERP has been reported in patients with attention deficit/hyperactivity disorder (ADHD)[5,6] and eating disorders[7] compared with healthy controls. The severity of these disorders can lead to serious psychiatric symptoms such as suicide attempts.

The ERP is observed in 10% of healthy individuals in Asian regions.[8] In recent years, the relationship between the ERP and sudden death has been recognized and is currently being investigated[9]; however, the clinical significance of the ERP remains unclear because sudden cardiac death is not observed in most cases.

Previous studies have reported associations between ECG findings and psychiatric symptoms. The severity of anxiety and obsessive–compulsive symptoms has been reported to be associated with prolongation of P wave dispersion,[10,11] and the QTc interval may be significantly prolonged at an early stage in active mental stress.[12]

Although previous studies have suggested an association between the prevalence of the ERP and schizophrenia, schizoaffective disorder, or ADHD, disease specificity remains unclear. Taken together with the fact that other ECG findings may be associated with psychiatric symptoms, the ERP may be associated with the severity of psychiatric symptoms.

Given this background, the present study aimed to compare the ERP in drug-free patients with a history of suicide attempts with that in healthy individuals. We also investigated predictors of suicide attempts by analyzing the association between ERP, prolongation of P wave dispersion, and QTc time, which are reportedly associated with psychiatric symptoms, and the history of suicide attempts.

2 | METHODS

2.1 | Study design and patients

This retrospective, case–control study investigated 71 psychotropic drug-free patients with a history of suicide attempts who had visited the Department of Psychiatry (suicide group) at Jikei University Kashiwa Hospital between January 2015 and July 2020. Both outpatient and inpatient consultation cases were included. The inclusion criteria were: (i) patients diagnosed as having a psychiatric disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision; (ii) patients with a history of suicide attempts (patients with any history of non-suicidal self-injury were excluded); (iii) patients who had undergone electrocardiography at Jikei University Kashiwa Hospital; and (iv) patients who had never taken psychotropic drugs or were not using psychotropic drugs during electrocardiography. The exclusion criteria were: (i) patients in a poor general condition that could affect the ECG, such as hypothermia, carbon monoxide poisoning, cardiopulmonary resuscitation, or acute poisoning by medical drugs, pesticides, or over-the-counter drugs; and (ii) patients who were difficult to analyze because of electrocardiographic artifacts.

Age- and gender-matched healthy individuals (control group) with no family history of psychiatric disorders who had undergone medical checkups at the Jikei University School of Medicine Center for Predictive Medicine were also included in the study.

2.2 | Electrocardiogram (ECG) evaluation

The first ECG recorded in the absence of psychotropic medication or exclusion criteria during the study period was selected for
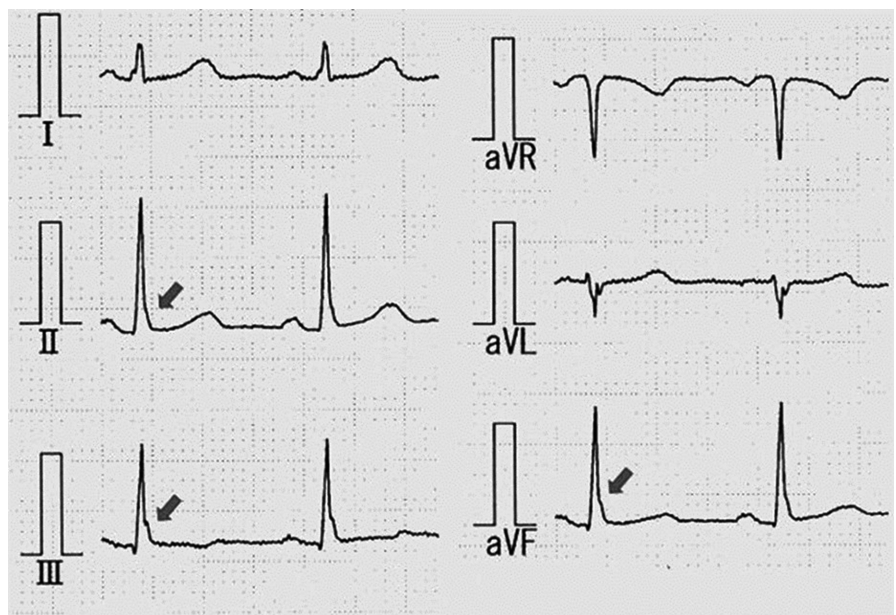

FIGURE 1 Example of electrocardiograms from a patient showing the early repolarization pattern

evaluation if multiple recordings had been taken. All ECGs were recorded at a paper speed of 25 mm/s and amplitude of 1 mV/10 mm. Two independent reviewers (H.K.: medical Doctor and K.S.: cardiologist) blindly analyzed all ECGs. As for the evaluation of the ERP, we followed the evaluation criteria from a previous study.[13] We considered the ERP to be present if all the following criteria were met: (i) an end-QRS notch or slur on the downslope of a prominent R-wave; (ii) if there is a notch, it should lie entirely above the baseline; (iii) the onset of a slur must also be above the baseline; (iv) the J-point peak is ≥0.1 mV in two or more contiguous leads of the 12-lead ECG, excluding leads V1–V3; (v) the QRS duration is <120 ms; (vi) both the slur and notch should occur in the final 50% of the R-wave downslope to be regarded as the ERP to exclude fragmented QRS (Figure 1).

Heart rate, PR interval, P wave duration, QRS interval, and QTc interval (The method for calculating the QTc is the Bazett formula) were measured using the results of the automatic analysis function, and P wave dispersion was defined as the difference between the largest and smallest P wave duration on the ECG.[14]

2.3 | Statistical analyses

We used IBM SPSS 25 [IBM SPSS 25 [IBM, Chicago, IL] for all statistical analyses. All tests were two-tailed, and a P value <0.05 was considered to indicate a significant difference. A t-test was used for continuous variables and a chi-squared test for categorical variables.

2.4 | Comparison of clinical characteristics between the psychotropic drug-free patients with a history of suicide attempts and healthy controls

To compare clinical characteristics between the suicide and control groups, we evaluated gender, age, and coronary risk factors as possible confounders.

2.5 | Comparison of electrocardiographic characteristics in the psychotropic drug-free patients with a history of suicide attempts and healthy controls

To investigate ECG characteristics in the suicide and control groups, we compared the presence of the ERP, heart rate, PR interval, QTc interval, and P wave dispersion.

2.6 | Relationship between the psychotropic drug-free patients with a history of suicide attempts and electrocardiographic characteristics

Logistic regression analysis was conducted to estimate the electrocardiological predictor(s) of suicidal attempts. The prevalence of the ERP, P wave dispersion, and QTc interval, which have been reported to be associated with psychiatric disorders, were used as independent variables, and presence of suicide attempts was used as a dependent variable. To avoid multicollinearity, variance inflated factors (VIFs) were calculated for the presence of the ERP, P wave dispersion, and QTc interval; pairs of independent variables that showed VIFs of 10 or higher were excluded from the analysis.

2.7 | Comparison of clinical backgrounds with or without the ERP in the psychiatric patients with a history of suicidal attempts

To investigate the clinical characteristics of patients with the ERP, we performed a post-hoc analysis to compare the demographic data, diagnosis, and suicide methods between the patients with and without the ERP.

3 | RESULTS

Of the 71 psychotropic drug-free patients with a history of suicide attempts, 38 who met the selection criteria were enrolled in this study (Figure 2). There were no specific abnormalities in serum electrolytes which could affect early repolarization.

3.1 | Comparison of clinical characteristics between the drug-free patients with a history of suicide attempts and healthy controls

No significant differences in gender, age, or coronary risk factors were found between the suicide and control groups (Table 1). In the suicide group, the most common psychiatric diagnosis was depression (47.4%), followed by schizophrenia (28.9%).

3.2 | Comparison of electrocardiographic characteristics in the psychotropic drug-free patients with a history of suicide attempts and medical checkups

The rate of occurrence of the ERP was significantly higher in the suicide than in the control group (P < 0.001). Heart rate was faster and QTc time was longer and the PR interval was significantly shorter in the suicide compared with the control group (Table 2).

3.3 | Relationship between the psychotropic drug-free patients with a history of suicide attempts and electrocardiographic characteristics

Because all the VIFs were <10, all the independent variables were adopted. The ERP and a shorter P wave dispersion were significant predictors of a history of suicide attempts (P = 0.01 and P = 0.02, respectively). QTc interval prolongation, which has been reported
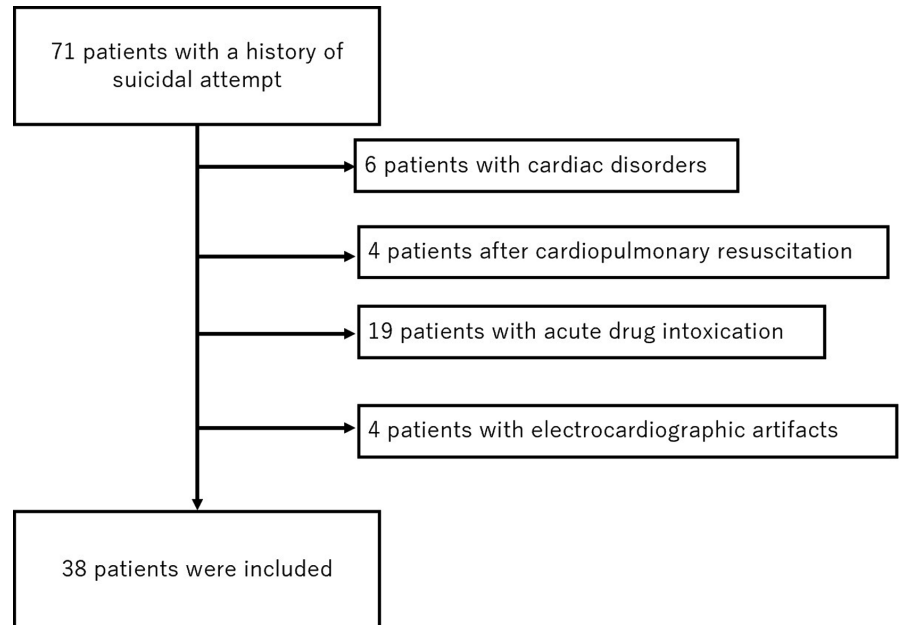
FIGURE 2 CONSORT diagram

TABLE 1 Comparison of clinical characteristics between the patients and controls

	Patients (N = 38)	Controls (N = 38)	Pvalue
Male (%)	15 (39.4%)	15 (39.4%)	1.000
Age (years)	44.1 ± 18.3	44.0 ± 17.9	0.995
Coronary risk factors			
Diabetes mellitus (%)	3 (7.89%)	1 (2.63%)	0.615
Hypertension (%)	4 (10.5%)	2 (5.26%)	0.674
Dyslipidemia (%)	5 (13.1%)	9 (23.7%)	0.375
Smoker (%)	3 (7.89%)	5 (13.1%)	0.711
Psychiatric diagnosis			
Schizophrenia	11 (28.9%)	0 (0.00%)	
Bipolar disorder	4 (10.5%)	0 (0.00%)	
Depression	18 (47.4%)	0 (0.00%)	
Adjustment disorder	2 (5.26%)	0 (0.00%)	
Panic disorder	1 (2.63%)	0 (0.00%)	
Dissociative disorder	1 (2.63%)	0 (0.00%)	
Personality disorder	1 (2.63%)	0 (0.00%)	

Note: Values are expressed as mean ± standard deviation or N (%).
Abbreviation: ERP, early repolarization pattern.

to be associated with psychiatric disorders, was not a predictor of suicidal attempts (Table 3).

3.4 | Comparison of clinical characteristics between patients with or without the ERP among the psychotropic drug-free patients with a history of suicide attempts

In the post hoc analysis for the suicide group, no difference in clinical findings was found between patients with and without the ERP (Table 4).

TABLE 2 Comparison of the electrocardiographic findings between the patient and controls

	Patients (N = 38)	Controls (N = 38)	Pvalue
Heart rate (bpm)	77.7 ± 18.7	63 ± 9	<0.001
PR interval (ms)	146 ± 23.7	165 ± 29.0	0.002
P wave dispersion (ms)	34.8 ± 19	40.3 ± 23.7	0.264
QRS duration (ms)	94.8 ± 13.1	100 ± 16.9	0.509
QTc intervals (ms)	424 ± 22.9	415 ± 22.2	0.093
ERP (%)	20 (52.6%)	4 (10.5%)	<0.001
Location of ERP			
High lateral leads (%)	2 (5.26%)	2 (5.26%)	
Inferior leads (%)	10 (26.3%)	0 (0.00%)	
Precordial lateral leads (%)	0 (0.00%)	2 (5.26%)	
Inferior and lateral leads (%)	8 (21.0%)	0 (0.00%)	
Amplitude of J wave(mV)	0.18 ± 0.05	0.16 ± 0.05	0.533

Note: Values are expressed as mean ± standard deviation or N (%).
Abbreviation: ERP, early repolarization pattern.

4 | DISCUSSION

The results of present study revealed that the ERP was more frequent in the suicide than in the control group. In addition, ECG findings that have been suggested to be related to other psychiatric symptoms, such as prolonged P wave dispersion and QTc interval, were not associated with severe psychiatric symptoms.

Variables	β	Standard error	OR (95%CI)	Pvalue
ERP (presence)	3.05	0.83	21.2 (4.17–107.3)	<0.01
P wave dispersion (ms)	−0.04	0.17	0.96 (0.93–1.00)	0.02
QTc interval (ms)	0.02	0.01	1.02 (1.00–1.04)	0.09

TABLE 3 Association between the psychiatric patients with a history of suicide attempts and the electrocardiographic findings

Abbreviations: CI, confidence interval; ERP, early repolarization pattern; OR, odds ratio.

	Patients with ERP (N = 20)	Patients without ERP (N = 18)	Pvalue
Age (years)	42.0 ± 18.1	46.4 ± 19.1	0.478
Male (%)	11 (55.0%)	4 (22.2%)	0.052
Heart rate (bpm)	78.3 ± 19.6	77.1 ± 18.7	0.837
PR interval (ms)	146 ± 22.9	146 ± 23.2	0.978
P wave dispersion (ms)	37.8 ± 22.1	31.2 ± 13.5	0.282
QRS interval (ms)	95.6 ± 9.94	93.7 ± 16	0.772
QTc interval (ms)	424 ± 23.9	422 ± 22.3	0.614
Psychiatric diagnosis			
Schizophrenia	6 (30.0%)	5 (27.8%)	0.524
Bipolar disorder	3 (15.0%)	1 (5.56%)	0.895
Depression	7 (35.0%)	11 (61.1%)	0.221
Adjustment disorder	2 (10.0%)	0 (0.00%)	0.527
Panic disorder	1 (5.00%)	0 (0.00%)	0.923
Dissociative disorder	1 (5.00%)	0 (0.00%)	0.923
Personality disorder	0 (0.00%)	1 (5.56%)	0.853
Suicide methods			
Jumping	5 (25.0%)	7 (38.9%)	0.105
Hanging	7 (35.0%)	3 (16.7%)	0.11
Stabbing	6 (30.0%)	2 (18.1%)	0.203
Other or Unknown	2 (10.0%)	6 (33.3%)	0.422

TABLE 4 Comparison of clinical characteristics the patients with or without the ERP

Note: Values are expressed as mean ± standard deviation or N (%).

Abbreviation: ERP, early repolarization pattern.

4.1 | Comparison of electrocardiographic findings between the psychotropic drug-free patients with a history of suicide attempts and medical checkups

The ERP was more frequent in the suicide than the control group, indicating an association between the ERP and severe psychiatric symptoms. In previous studies, the ERP has been shown to be associated with schizophrenia, schizoaffective disorder,[3,4] and ADHD.[5,6] Schizophrenia and ADHD are known to be associated with impaired social functioning and high comorbidity, and some patients can also present with severe psychiatric symptoms.[15] The results of the present study are consistent with these previous reports.

4.2 | Relationship between the psychotropic drug-free patients with a history of suicide attempts and electrocardiographic characteristics

Logistic regression analysis revealed that the ERP and P wave dispersion were predictors of a history of suicidal attempts.

The reasons why the presence of the ERP is the most significant predictor of a history of suicide attempts are unclear, but the following can be inferred. A previous study reported that the ERP appeared as a result of intraventricular conduction delay caused by a high heart rate.[16] Intraventricular conduction delay is known to be observed in patients with psychiatric disorders,[17] and it is possible that the ERP became apparent because of the effect of a high heart rate. In addition to the ERP, conduction disturbances such as right and left bundle branch block may also appear as a result of a higher heart rate; however, in this study, none of the psychotropic drug-free patients with a history of suicide attempts showed bundle branch block. Another possible mechanism for ERP in patients with psychiatric disorders who have a history of suicide attempts is as follows. Inflammation and ion channel abnormalities have been reported as common features of ERP and psychiatric disorders.[18,19,20,21] It has been reported that the more severe the psychiatric symptoms, the more enhanced the inflammatory response,[22] which may be related to the results of this study. The common pathophysiology of psychiatric disorders and ECG abnormalities may have influenced the results of this study.

P wave dispersion is known to be associated with anxiety symptoms in panic disorder[10] and with the severity of obsessive–compulsive symptoms.[11] However, in the present study, paradoxically, P wave dispersion was shortened, which was found to be an independent predictor of a history of suicide attempts among the psychotropic drug-free patients. In this study, the psychotropic drug-free patients with a history of suicide attempts were not receiving psychiatric treatment or had self-interrupted psychiatric treatment. It is possible that subjective symptoms such as anxiety were absent in the suicide group, and it can be inferred that they did not seek psychiatric visits and self-interrupted psychiatric treatment.

4.3 | Comparison of clinical backgrounds with and without the ERP in the psychotropic drug-free patients with a history of suicide attempts

No significant differences were found in the clinical backgrounds between the patients with and without the ERP. In general, the ERP is known to be more common in males.[23] Differences in suicide attempts between men and women are also widely known, with more men reported to have completed suicide by lethal methods.[24] In the suicide group in the present study, to exclude the effects of drug intoxication, ECGs performed under acute intoxication were not included. Considering that the ERP is generally more common in males, this result may reflect gender differences in suicide attempts.

4.4 | Limitations

This study did have some limitations. First, this was a single-center, retrospective study. Second, the results cannot be applied clinically because of the small sample size. Third, because this was a preliminary study, we did not compare the ECG findings with those of psychiatric patients without a history of suicide attempts. In addition, we did not use a psychological rating scale. Therefore, the pathophysiology between the ERP and severe psychiatric symptoms remains unclear. Although we applied one in 10-rule for logistic regression analysis, statistical power could be insufficient when compared to the one in 20-rule in terms of shrinkage of regression coefficient. It can be derived from high variance of cases per independent variable. In the future, larger multicenter studies are needed to investigate the relationship between early repolarization pattern and patients with psychiatric disorders with a history of suicide attempts.

5 | CONCLUSION

In the present study, we found that a history of the suicide attempts was associated with the ERP.

CONFLICT OF INTEREST
None.

ETHICAL APPROVAL
This study was approved by the Jikei University School of Medicine Ethics Committee (Approval No. 30–152).

INFORMED CONSENT
Using the public website and in-hospital posters, we disclosed the prescribed information and told the participants or, where appropriate, their nearest relatives, that participation in the study was voluntary.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL
n/a.

ANIMAL STUDIES
n/a.

DATA AVAILABILITY STATEMENT
Public availability of raw data was not planned in the research protocol approved by an Institution Reviewer Board.

ORCID
Hiroshi Kameyama https://orcid.org/0000-0002-9843-7766

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