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Role of fragmented QRS and Shanghai score system in recurrence of ventricular fibrillation in patients with early repolarization syndrome

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Abstract

Background: The Shanghai Score System, which weighs electrocardiogram (ECG) findings reflecting repolarization abnormalities, has been proposed for diagnosis of early repolarization syndrome (ERS). However, recent studies have suggested the involvement of depolarization abnormalities in some ERS patients. The aim of this study was to validate the Shanghai Score System in predicting the recurrence of ventricular fibrillation (VF) in ERS patients. The predictive value of fragmented QRS (fQRS) was also investigated.

Methods: Fifteen consecutive ERS patients (14 males, median age of 47 years) with a history of VF were retrospectively reviewed. The Shanghai Score System points were calculated, and the presence of fQRS was evaluated.

Results: During the median follow-up period of 79.2 months, five patients experienced VF recurrence. In the VF recurrence group, two patients showed augmented amplitude of J waves with horizontal ST-segment, while the other three patients had dynamic changes in J-wave amplitude. The Shanghai Score System points in the VF recurrence group were higher than those in the VF non-recurrence group (6.5 [range: 5.8–6.8] vs. 4.5 [range: 4.0–4.5], $p = 0.002$). The presence of fQRS on standard 12-lead ECG was more frequently observed in the VF recurrence group compared with the non-recurrence group (100% vs. 10%, $p = 0.002$).

Conclusions: The present study demonstrated that the Shanghai Score System could effectively identify ERS patients at high risk for VF recurrence. The results also suggested that the presence of fQRS, a marker of depolarization abnormalities, may be useful for predicting VF recurrence in ERS patients.

KEYWORDS
cardiac arrest/sudden death, electrocardiography, ventricular tachycardia/fibrillation

1 | INTRODUCTION

The Shanghai Score System has been proposed as a diagnostic scoring system for early repolarization syndrome (ERS; Antzelevitch et al., 2017). The scoring system consists of clinical history, 12-lead electrocardiogram (ECG), ambulatory ECG monitoring, family history, and genetic test results. For 12-lead ECG findings, two points are given for early repolarization (ER) ≥0.2 mV in two or more inferior and/or lateral ECG leads with horizontal/descending ST-segment. One and a half points are given for dynamic changes in J-point elevation (≥0.1 mV) in two or more inferior and/or lateral ECG leads. One point is given for J-point elevation (≥0.1 mV) in at least two inferior and/or lateral ECG leads. These 12-lead ECG findings reflect repolarization abnormality. However, based on a multicenter study to evaluate mapping and ablation of ventricular fibrillation (VF) substrates or VF triggers in ERS patients, Nademanee et al. recently demonstrated that there are two distinct phenotypes: ERS patients with and without late depolarization abnormalities (Nademanee et al., 2019). These observations led to a hypothesis that 12-lead ECG findings reflecting depolarization abnormalities such as fragmented QRS (fQRS) could also be useful for identifying ERS patients at high risk for VF recurrence in addition to the Shanghai Score System. The present study thus retrospectively evaluated the predictive value of the Shanghai Score System and the presence of fQRS in VF recurrence in VF-experienced ERS patients.

2 | METHODS

2.1 | Study design and patients

We performed a retrospective chart review of 15 consecutive ERS patients with a history of spontaneous VF who were admitted to Oita University Hospital between 2005 and 2020. All patients were diagnosed with ERS according to the 2013 HRS/EHRA/APHRS expert consensus statement (Priori et al., 2013). Implantable cardioverter-defibrillators (ICDs) were implanted in all patients. Probable pathogenic ERS susceptibility gene mutations (*AKAP9*, *KCNH2*, *KCNJ8*, *KCNQ1*, *CACNA1C*, *CACNB2*, *CACNA2D1*, *SCN5A*, and *SCN10A*) were analyzed. Of these 15 patients, eight patients agreed to genetic testing. Therefore, all of the patients were scored using the Shanghai Score System (Shanghai ERS score) excluding genetic test results (Antzelevitch et al., 2017). The 15 patients were divided into the VF recurrence group that received appropriate ICD shock delivery due to VF (n = 5) and the VF non-recurrence group (n = 10). Patients were followed up every 3–6 months for regular clinical review and device interrogation with a median of 79 months (range 43–107 months). Patient characteristics including medical history, laboratory data, 12-lead ECG, and coronary angiography (CAG) were collected from the medical records. No patient had organic heart disease based on physical examination, chest radiography, 12-lead ECG, echocardiography, treadmill exercise ECG, ^{201}Tl cardiac scintigraphy, and CAG (including coronary spasm provocation test). This study was approved by Oita University Faculty of Medicine Ethics Committee.

2.2 | Twelve-lead ECG findings

The ER pattern was defined as "notch" or "slur" with an amplitude ≥0.1 mV on the terminal QRS portion in two or more inferior (II, III, $_aV_F$) or lateral (I, $_aV_L$, and $V_{4\text{-}6}$) leads as previously proposed (Macfarlane et al., 2015; Priori et al., 2013). The J-wave amplitude in notch was measured at the peak of the positive deflection relative to the QRS onset. In slur, it was measured at the inflection point of the QRS complex relative to the QRS onset. Late potentials on signal-averaged ECG were defined as positive when two of the following criteria were satisfied: (1) filtered QRS duration >105 ms; (2) root mean square voltage of the signals in the last 40 ms of the total filtered QRS complex <15 μV; and (3) duration of low-amplitude signals <40 μV of the filtered QRS complex >39 ms. The fQRS in 12-lead ECG was defined as the presence of spikes within the QRS complex of two or more consecutive leads (QRS <120 ms) according to the ECG criteria for fQRS (Das et al., 2006). With the subject lying supine, standard 12-lead surface digital ECGs (with leads I, II, III, $_aV_R$, $_aV_L$, $_aV_F$, and $V_{1\text{-}6}$) and right precordial ECGs (V_3R to V_6R) were recorded using Cardiofax (Nihon Kohden, Tokyo, Japan) with a 150 Hz low-pass filter. ECGs were analyzed at 400% size, and each parameter and fragmentation of the QRS complex were measured. Patients with a short QT interval (corrected QT interval using Bazett's formula <340 ms) or long QT interval (corrected QT interval using Bazett's formula >440 ms) were excluded. All patients underwent drug provocation tests using intravenous pilsicainide (1 mg/kg per 10 min) and standard and high intercostal (2nd and 3rd intercostal). ECGs were recorded to exclude Brugada syndrome (BrS). This study did not include any patients with type 1 Brugada ECG (coved type ST elevation) in the right precordial leads.

2.3 | Statistical analysis

Data were expressed as median (25th–75th percentile) for continuous variables or as numbers and percentages for categorical variables. Univariate analysis was performed with Fisher's exact test. The Shapiro–Wilk test was performed to determine whether the continuous variables were normally distributed. Normally distributed continuous variables were compared using the unpaired Student's *t* test. Otherwise, continuous variables were compared using the Mann–Whitney *U* test. Sensitivity and specificity for predicting VF recurrence were calculated using receiver operating characteristic (ROC) analysis. A *p*-value <0.05 was considered

statistically significant. All statistical analysis was performed with JMP v9.0.0/Windows software (SAS).

3 | RESULTS

3.1 | Baseline clinical characteristics and VF recurrence

The baseline clinical characteristics of all 15 patients are listed in Table 1. The median age was 47 years (range: 35–58 years) and 14 of them (93%) were male. None of the patients had a family history of sudden cardiac death (SCD) before the age of 45 years. None of the patients took any medications, including antihypertensive drugs. During the median follow-up period of 79.2 months (range: 43.0–107.1 months), five patients experienced appropriate ICD shock delivery due to the recurrence of VF (VF recurrence group). The recurrence of VF was observed 17.7 months (median, range: 5.5–33.3 months) after the ICD implantation. Three patients (20%) developed newly atrial fibrillation (AF) during follow-up period.

3.2 | Comparison of Shanghai Score between VF recurrence and VF non-recurrence groups

Table 2 shows a detailed comparison of the Shanghai Scoring System between VF recurrence and VF non-recurrence groups. Based on the 12-lead ECG findings in the VF recurrence group, two patients showed augmented amplitude of the J waves with a horizontal ST-segment, while the remaining three patients showed dynamic changes in the J-wave amplitude without a horizontal ST-segment (Figure 1A and B). In intracardiac electrograms of ICD recordings and ECG monitoring, short-coupled PVCs often preceded the development of VF in patients with the VF recurrence group than in the non-recurrence group (80 vs. 10%, $p = 0.02$). As a result, the Shanghai Scoring System scores in the VF recurrence group were significantly higher than those in the VF non-recurrence group (6.5 [range: 5.8 to 6.8] vs. 4.5 [range: 4.0 to 4.5] points, $p = 0.002$). Figure 2 illustrates the distribution of the Shanghai scores in all of the patients. Four patients in the VF recurrence group had a score of ≥6.5 points. None of the patients with a score <5.0 points had VF recurrence. In order to predict the recurrence

TABLE 1 Comparison between VF recurrence and non-recurrence groups

	All (n = 15)	VF recurrence (n = 5)	VF non-recurrence (n = 10)	*p* Value
Age, years	47 (35–58)	38 (29–48)	48 (40–56)	.36
Male, n (%)	14 (93)	5 (100)	9 (90)	1.00
Family history of SCD, n (%)	0 (0)	0 (0)	0 (0)	
Physiological parameters				
Systolic blood pressure, mmHg	109 (103–121)	114 (100–137)	109 (103–120)	.75
Diastolic blood pressure, mmHg	71 (60–85)	74 (63–90)	69 (58–78)	.30
Heart rate, bpm	73 (57–77)	75 (63–100)	68 (53–75)	.10
Left ventricular EF, %	67 (59–73)	59 (55–69)	70 (62–73)	.14
Late potential positive, n (%)	5 (33)	2 (40)	3 (30)	1.00
Electrocardiographic parameters				
PR interval, ms	154 (139–168)	154 (147–169)	152 (138–170)	.62
RR interval, ms	869 (800–1036)	800 (612–955)	913 (809–1162)	.13
PQ interval, ms	144 (140–160)	150 (142–170)	144 (138–165)	.67
QRS duration, ms	101 (96–105)	98 (95–103)	102 (95–116)	.39
QT interval, ms	388 (359–409)	388 (339–416)	390 (360–409)	.76
QTc interval (Bazett), ms	406 (387–431)	410 (398–435)	399 (381–412)	.13
QTc interval (Fridericia), ms	397 (385–422)	413 (389–432)	389 (383–423)	.24
Clinical outcome				
Follow-up period, months	79.2 (43.0–107.1)	107.1 (46.5–144.9)	77.2 (41.6–89.5)	.30
AF occurrence during follow-up, n (%)	3 (20)	2 (40)	1 (10)	.24
VF recurrence, n (%)	5 (33)	5 (100)	0 (0)	
ICD implantation to VF recurrence time, months	N/A	17.7 (5.5–33.3)	N/A	

Note: Data were expressed as median (25th to 75th percentile) for continuous variables, or as numbers and percentages for categorical variables.

Abbreviations: AF, atrial fibrillation; EF, ejection fraction; ICD, implantable cardioverter-defibrillator; N/A, not applicable; SCD, sudden cardiac death; VF, ventricular fibrillation.

TABLE 2 Comparison of Shanghai Score System between VF recurrence and non-recurrence groups.

	Overall (n = 15)	VF recurrence (n = 5)	VF non-recurrence (n = 10)	*p* Value
I. Clinical History				
A. Unexplained cardiac arrest, documented VF or polymorphic VT	15 (100)	5 (100)	10 (100)	
B & C. Suspected arrhythmic syncope & Syncope of unclear mechanism	0 (0)	0 (0)	0 (0)	
II. Twelve-lead ECG				
A. ER ≥0.2 mV in ≥2 ECG leads with horizontal/descending ST-segment	2 (13)	2 (40)	0 (0)	.06
B. Dynamic changes in J-point elevation (≥0.1 mV)	8 (53)	3 (60)	5 (50)	
C. ≥0.1 mV J-point elevation in at least 2 ECG leads	5 (33)	0 (0)	5 (50)	
III. Short-coupled PVCs with R on ascending limb or peak of T wave	5 (33)	4 (80)	1 (10)	.02
IV. Family History	0 (0)	0 (0)	0 (0)	
V. Genetic Test Result Probable pathogenic ERS susceptibility mutation	1 (13) (n = 8)	1 (50) (n = 2)	0 (0) (n = 6)	.25
Shanghai Score System				
Shanghai ERS score excluding genetic test, points	4.5 (4.0–6.5)	6.5 (5.8–6.8)	4.5 (4.0–4.5)	.002

Note: Data were expressed as median (25th to 75th percentile) for continuous variables, or as numbers and percentages for categorical variables.
Abbreviations: ECG, electrocardiogram; ER, early repolarization; ERS, early repolarization syndrome; PVC, premature ventricular contraction; VF, ventricular fibrillation; VT, ventricular tachycardia.

of VF in ERS patients, ROC curve analysis was performed to evaluate the discriminating power of the Shanghai score while excluding genetic test results. A Shanghai score of 5 points while excluding genetic test results was the pivot point (the area under the ROC curve was 0.98), while the cutoff value had 100% sensitivity and 90% specificity. The incidence of VF recurrence was significantly higher in patients with ≥5 points (probable/definite ERS in ERS diagnosis) than in those with scores of 3–4.5 points (possible ERS in ERS diagnosis; $p<0.01$). Of the eight patients who were genetically analyzed, only one patient in the VF recurrence group had an ERS susceptibility genetic mutation (*CACNA2D1*).

3.3 | Comparison of QRS fragmentation between VF recurrence and VF non-recurrence groups

All five patients in the VF recurrence group had spikes within the QRS complex on two or more consecutive standard 12 leads. When this criterion was applied, the presence of fQRS was significantly higher in the VF recurrence group compared with the VF non-recurrence group (Table 3; 100% vs. 10%, $p = 0.002$). The total number of leads with QRS fragmentation on standard 12-lead ECG was greater in the VF recurrence group than in the VF non-recurrence group (4.0 [range: 2.5 to 4.5] vs. 0 [range: 0 to 0.25] points, $p = 0.001$). Of the 15 ERS patients, thirteen patients underwent ECG including right precordial leads (V_3R to V_6R). The fQRS at right precordial leads was observed more frequently in the VF recurrence group than in the non-recurrence group (Table 3; 80% vs. 13%, $p = 0.03$). The fQRS on the right precordial leads could only be confirmed with V3R and V4R leads (Figure 1C). All five patients in the VF recurrence group had QRS fragmentation on V3R lead.

4 | DISCUSSION

4.1 | Main findings

The main findings of the present study are as follows: First, the Shanghai Score System, which has been proposed as a diagnostic scoring system for ERS, could effectively identify ERS patients at high risk of VF recurrence. Second, the presence of fQRS on standard 12-lead ECG and right precordial ECG was associated with VF recurrence. To the best of our knowledge, this study is the first to evaluate the role of the Shanghai Score System and the presence of fQRS in VF recurrence in VF-experienced ERS patients.

4.2 | Shanghai ERS score for predicting VF recurrence

The 2016 HRS/APHRS/EHRA/SOLAECE J-wave syndrome expert consensus conference report proposed a point scoring system for diagnosis of ERS and BrS (Antzelevitch et al., 2017). Kawada et al. reported that scoring with the Shanghai Score System can not only diagnose BrS, but also be a useful tool for

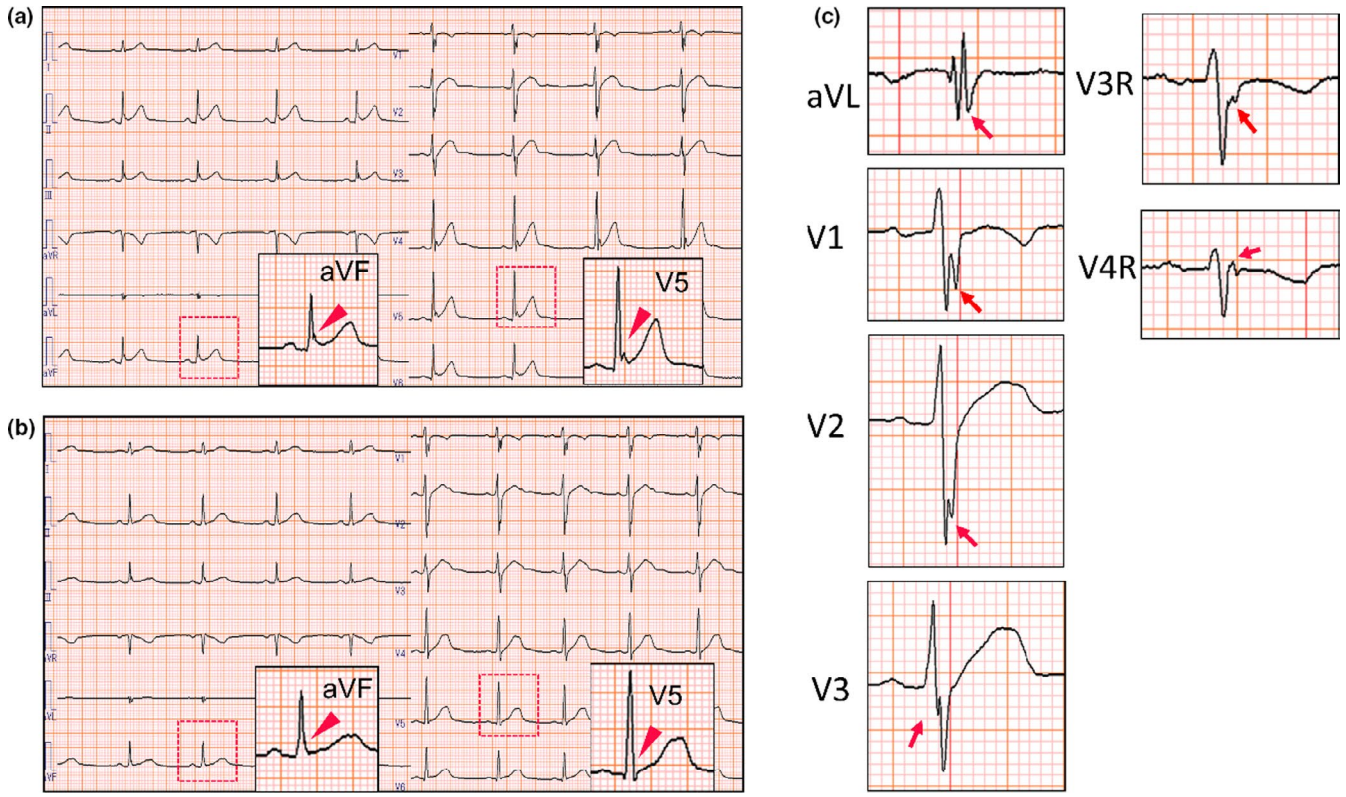

FIGURE 1 J-wave dynamicity and fragmented QRS on 12-lead ECG. a: Twelve-lead ECG showing clear accentuation of early repolarization (ER) pattern in inferior (II, III, and $_aV_F$) and lateral (V_{5-6}) leads. Red arrowheads indicate augmentation of J waves. b: Twelve-lead ECG without ER patterns. c: Fragmented QRS was identified in anterior (V_{1-3}), lateral ($_aV_L$), and right precordial ($V_{3-4}R$) leads. Red arrows indicate spikes within QRS complex

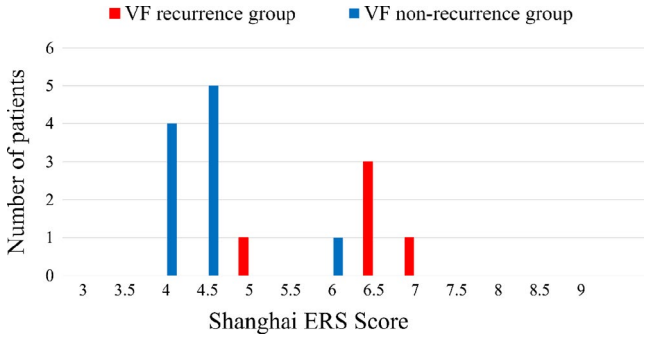

FIGURE 2 Distribution of Shanghai ERS score in VF recurrence and non-recurrence patients with ERS. Patients in VF recurrence group have higher Shanghai ERS scores excluding genetic test results. ERS =early repolarization syndrome; VF =ventricular fibrillation

stratification of SCD risk (Kawada et al., 2018). However, its value in ERS patients remains unknown. The Shanghai ERS score attaches weight to ECG findings reflecting repolarization abnormalities. In this regard, Tikkanen et al. showed that J-point elevation ≥0.2 mV had a markedly elevated risk of SCD (Tikkanen et al., 2009). Furthermore, a horizontal or descending ST-segment was reportedly associated with SCD compared to an ascending ST-segment (Tikkanen et al., 2011). We have previously reported a case of ERS with diurnal and day-to-day variations of the J wave and a marked increase in J-wave amplitude toward the onset of VF (Shinohara et al., 2006). In that case, the J-wave amplitude was accentuated by intravenous injection of verapamil and propranolol (Shinohara et al., 2006). Thereafter, using Holter ECG recordings, it was demonstrated that ERS patients have larger circadian variations in the J-wave amplitude (i.e., higher at night and lower during the day) compared with healthy subjects (Miyazaki et al., 2013). The slope of the J-wave amplitude/(low frequency [LF]/high frequency [HF]) relationship was significantly steeper in ERS patients compared with healthy subjects. These observations suggest that the exaggerated dynamic change in repolarization abnormality in response to cardiovascular autonomic tone may play an important role in the occurrence of VF in ERS patients. Family history of SCD has also been identified as a risk factor for VF in ERS patients (Gourraud et al., 2013). However, Watanabe et al. demonstrated that only 10% of Japanese ERS patients had a family history of SCD (Watanabe et al., 2012). In fact, no patient in this study had a family history of SCD before the age of 45 years. Moreover, among the eight patients who underwent genetic testing, only one patient was positive for the ERS susceptibility gene mutation. Thus, the difference in the Shanghai ERS score between VF recurrence and VF non-recurrence groups in the present study is mainly based on the scores of J-wave findings, which may reflect repolarization abnormality, and the presence of short-coupled PVCs.

TABLE 3 Comparison of QRS fragmentation between VF recurrence and non-recurrence groups

	All (n = 15)	VF recurrence (n = 5)	VF non-recurrence (n = 10)	*p* Value
Standard 12-lead ECG				
fQRS (QRS fragmentation in ≥2 consecutive leads), n (%)	6 (40)	5 (100)	1 (10)	.002
QRS fragmentation on any of the standard 12-lead ECG, n (%)	7 (47)	5 (100)	2 (20)	.007
Total number of leads with QRS fragmentation, n	0 (0–3.0)	4.0 (2.5–4.5)	0 (0–0.25)	.001
Right precordial leads				
fQRS at right precordial leads (V_3R to V_6R), n (%)	5 (38) (n = 13)	4 (80) (n = 5)	1 (13) (n = 8)	.03
QRS fragmentation at V_3R lead, n (%)	7 (54) (n = 13)	5 (100) (n = 5)	2 (25) (n = 8)	.02
Total number of leads with QRS fragmentation including right precordial leads, n	1.0 (0–5.0) (n = 13)	6.0 (3.5–6.5) (n = 5)	0.5 (0–1.8) (n = 8)	.006

Note: Data were expressed as median (25th to 75th percentile) for continuous variables, or as numbers and percentages for categorical variables.
Abbreviations: fQRS, fragmented QRS; VF, ventricular fibrillation.

4.3 | Fragmented QRS on 12-lead ECG for predicting VF recurrence

Since the 2008 Haïssaguerre et al. report (Haïssaguerre et al., 2008), various ECG markers have been proposed as risk factors for VF in patients with ERS. From the viewpoint of depolarization abnormality, Morita et al. reported that fQRS is a marker for the substrate for spontaneous VF in patients with BrS (Morita et al., 2008). Additionally, regarding the generation mechanism of fQRS, they demonstrated that activation delay in the epicardium could reproduce similar fQRS in the transmural ECG using canine right ventricular tissues (Morita et al., 2008). Accordingly, they proposed that fQRS might represent delayed conduction on the epicardium in patients with BrS. The same group thereafter demonstrated that the progression of fQRS appearance was associated with the occurrence of VF in patients with BrS (Morita et al., 2018). However, to the best of our knowledge, the significance of fQRS on a 12-lead ECG for the risk stratification of VF occurrence in ERS patients has not been reported. Nademanee et al. recently demonstrated that ERS has two phenotypes with and without late depolarization abnormalities in the epicardium. The findings of late depolarization abnormalities contribute to the underlying mechanism in some patients with ERS (Nademanee et al., 2019). Thus, it is conceivable that fQRS in ERS patients represents a conduction delay in the epicardium, contributing to the genesis of VF. The repolarization and depolarization hypotheses have been widely discussed as the mechanisms for BrS or ERS (Haïssaguerre et al., 2019). Some reports suggest that depolarization abnormality plays an important role in VF occurrence in patients with BrS or ERS (Nademanee et al., ,2011, 2019; Pappone et al., 2017). Tokioka et al. showed that the combination of inferolateral ER pattern and fQRS is useful for predicting VF occurrence in BrS patients (Tokioka et al., 2014). In the present study, all five patients with VF recurrence had inferolateral ER pattern and fQRS in anterior (V_1, V_2) and right precordial leads (V_3R), which suggested the presence of depolarization abnormality in right ventricular outflow tract as reported in BrS (Nademanee et al., 2011; Pappone et al., 2017). Although an electrophysiological study was not carried out in our patients, the present study suggested that findings of depolarization abnormality reflected in the presence of fQRS may be useful for predicting VF recurrence in ERS patients, at least in those with a history of VF. As shown in Table 1, there was no significant difference between the two groups in the positive late potential, which was another abnormal depolarization finding. Priori et al. demonstrated in the PRELUDE registry that fQRS is the strongest predictor of VF in patients with BrS (Priori et al., 2012). Our findings are consistent with previous reports (Morita et al., 2008; Tokioka et al., 2014) that fQRS and not positive late potential can predict VF events in BrS patients. Therefore, even in ERS patients, fQRS may be more useful than the positive late potential to predict a substrate for VF.

4.4 | Limitations

This study was a retrospective single-center study and was restricted to ERS patients with a history of VF. Therefore, there may be patient selection bias.

5 | CONCLUSIONS

The present study demonstrated that the Shanghai Score System could effectively identify ERS patients at high risk for VF recurrence. The results also suggested that the presence of fQRS, a marker of depolarization abnormalities, may be useful for predicting VF recurrence in ERS patients.

CONFLICT OF INTEREST

All authors have no conflict to disclose.

AUTHOR CONTRIBUTIONS

Dr. Yonezu acquired, analyzed, interpreted the data, and drafted the manuscript. Drs. Sato, Hirota, Kondo, Fukui, Teshima, Yufu, and Nakagawa assisted in acquiring, analyzing the data, and interpreting results. Drs. Shinohara and Takahashi conceived and designed the research as the supervision. All co-authors have read and approved the submission of this manuscript.

ETHICS STATEMENT

This study was approved by Oita University Faculty of Medicine Ethics Committee.

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REFERENCES

Antzelevitch, C., Yan, G. X., Ackerman, M. J., Borggrefe, M., Corrado, D., Guo, J., Gussak, I., Hasdemir, C., Horie, M., Huikuri, H., Ma, C., Morita, H., Nam, G. B., Sacher, F., Shimizu, W., Viskin, S., & Wilde, A. A. M. (2017). J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge. *Europace*, *19*, 665–694.

Das, M. K., Khan, B., Jacob, S., Kumar, A., & Mahenthiran, J. O. (2006). Significance of a fragmented QRS Complex Versus a Q wave in patients with coronary artery disease. *Circulation*, *113*(21), 2495–2501. https://doi.org/10.1161/CIRCULATIONAHA.105.595892.

Gourraud, J.-B., Le Scouarnec, S., Sacher, F., Chatel, S., Derval, N., Portero, V., Chavernac, P., Sandoval, J. E., Mabo, P., Redon, R., Schott, J.-J., Le Marec, H., Haïssaguerre, M., & Probst, V. (2013). Identification of large families in early repolarization syndrome. *Journal of the American College of Cardiology*, *61*(2), 164–172. https://doi.org/10.1016/j.jacc.2012.09.040

Haïssaguerre, M., Derval, N., Sacher, F., Jesel, L., Deisenhofer, I., de Roy, L., Pasquié, J.-L., 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., … Clémenty, J. (2008). Sudden cardiac arrest associated with early repolarization. *New England Journal of Medicine*, *358*(19), 2016–2023. https://doi.org/10.1056/NEJMoa071968

Haïssaguerre, M., Nademanee, K., Hocini, M., Cheniti, G., Duchateau, J., Frontera, A., Sacher, F., Derval, N., Denis, A., Pambrun, T., Dubois, R., Jaïs, P., Benoist, D., Walton, R. D., Nogami, A., Coronel, R., Potse, M., & Bernus, O. (2019). Depolarization versus repolarization abnormality underlying inferolateral J-wave syndromes: New concepts in sudden cardiac death with apparently normal hearts. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, *16*(5), 781–790. https://doi.org/10.1016/j.hrthm.2018.10.040

Kawada, S., Morita, H., Antzelevitch, C., Morimoto, Y., Nakagawa, K., Watanabe, A., Nishii, N., Nakamura, K., & Ito, H. (2018). Shanghai score system for diagnosis of Brugada syndrome. *JACC: Clinical Electrophysiology*, *4*(6), 724–730. https://doi.org/10.1016/j.jacep.2018.02.009

Macfarlane, P. W., Antzelevitch, C., Haissaguerre, M., Huikuri, H. V., Potse, M., Rosso, R., Sacher, F., Tikkanen, J. T., Wellens, H., & Yan, G.-X. (2015). The early repolarization pattern. *Journal of the American College of Cardiology*, *66*(4), 470–477. https://doi.org/10.1016/j.jacc.2015.05.033

Miyazaki, H., Nakagawa, M., Shin, Y., Wakisaka, O., Shinohara, T., Ezaki, K., Teshima, Y., Yufu, K., Takahashi, N., Hara, M., & Saikawa, T. (2013). Comparison of autonomic J-wave modulation in patients with idiopathic ventricular fibrillation and control subjects. *Circulation Journal*, *77*(2), 330–337. https://doi.org/10.1253/circj.CJ-12-0749

Morita, H., Kusano, K. F., Miura, D., Nagase, S., Nakamura, K., Morita, S. T., Ohe, T., Zipes, D. P., & Wu, J. (2008). Fragmented QRS as a Marker of Conduction Abnormality and a Predictor of Prognosis of Brugada Syndrome. *Circulation*, *118*(17), 1697–1704. https://doi.org/10.1161/CIRCULATIONAHA.108.770917

Morita, H., Miyamoto, M., Watanabe, A., Tsukuda, S., Morimoto, Y., Kawada, S., Nakagawa, K., Nishii, N., & Ito, H. (2018). Progression of electrocardiographic abnormalities associated with initial ventricular fibrillation in asymptomatic patients with Brugada syndrome. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, *15*(10), 1468–1474. https://doi.org/10.1016/j.hrthm.2018.06.035

Nademanee, K., Haissaguerre, M., Hocini, M., Nogami, A., Cheniti, G., Duchateau, J., Behr, E. R., Saba, M., Bokan, R., Lou, Q., Amnueypol, M., Coronel, R., Khongphatthanayothin, A., & Veerakul, G. (2019). Mapping and ablation of ventricular fibrillation associated with early repolarization syndrome. *Circulation*, *140*, 1477–1490. https://doi.org/10.1161/CIRCULATIONAHA.118.039022

Nademanee, K., Veerakul, G., Chandanamattha, P., Chaothawee, L., Ariyachaipanich, A., Jirasirirojanakorn, K., Likittanasombat, K., Bhuripanyo, K., & Ngarmukos, T. (2011). Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over the Anterior Right Ventricular Outflow Tract Epicardium. *Circulation*, *123*(12), 1270–1279. https://doi.org/10.1161/CIRCULATIONAHA.110.972612

Pappone, C., Brugada, J., Vicedomini, G., Ciconte, G., Manguso, F., Saviano, M., Vitale, R., Cuko, A., Giannelli, L., Calovic, Z., Conti, M., Pozzi, P., Natalizia, A., Crisà, S., Borrelli, V., Brugada, R., Sarquella-Brugada, G., Guazzi, M., Frigiola, A., … Santinelli, V. (2017). Electrical substrate elimination in 135 consecutive patients With Brugada Syndrome. *Circ Arrhythm Electrophysiol.*, *10*, e005053. https://doi.org/10.1161/CIRCEP.117.005053

Priori, S. G., Gasparini, M., Napolitano, C., Della Bella, P., Ottonelli, A. G., Sassone, B., Giordano, U., Pappone, C., Mascioli, G., Rossetti, G., De Nardis, R., & Colombo, M. (2012). Risk Stratification in Brugada Syndrome. *Journal of the American College of Cardiology*, *59*(1), 37–45. https://doi.org/10.1016/j.jacc.2011.08.064

Priori, S. G., Wilde, A. A., Horie, M., Cho, Y., Behr, E. R., Berul, C., Blom, N., Brugada, J., Chiang, C.-E., Huikuri, H., Kannankeril, P., Krahn, A., Leenhardt, A., Moss, A., Schwartz, P. J., Shimizu, W., Tomaselli, G., & Tracy, C. (2013). HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, *10*, 1932–1963. https://doi.org/10.1016/j.hrthm.2013.05.014

Shinohara, T., Takahashi, N., Saikawa, T., & Yoshimatsu, H. (2006). Characterization of J wave in a patient with idiopathic ventricular fibrillation. *Heart Rhythm: the Official Journal of the Heart Rhythm Society*, *3*(9), 1082–1084. https://doi.org/10.1016/j.hrthm.2006.05.016.

Tikkanen, J. T., Anttonen, O., Junttila, M. J., Aro, A. L., Kerola, T., Rissanen, H. A., Reunanen, A., & Huikuri, H. V. (2009). Long-term outcome associated with early repolarization on electrocardiography. *New England Journal of Medicine*, *361*(26), 2529–2537. https://doi.org/10.1056/NEJMoa0907589

Tikkanen, J. T., Junttila, M. J., Anttonen, O., Aro, A. L., Luttinen, S., Kerola, T., Sager, S. J., Rissanen, H. A., Myerburg, R. J., Reunanen, A., &

Huikuri, H. V. (2011). Early repolarization. *Circulation*, *123*(23), 2666–2673. https://doi.org/10.1161/CIRCULATIONAHA.110.014068

Tokioka, K., Kusano, K. F., Morita, H., Miura, D., Nishii, N., Nagase, S., Nakamura, K., Kohno, K., Ito, H., & Ohe, T. (2014). Electrocardiographic Parameters and Fatal Arrhythmic Events in Patients With Brugada Syndrome. *Journal of the American College of Cardiology*, *63*(20), 2131–2138. https://doi.org/10.1016/j.jacc.2014.01.072

Watanabe, H., Nogami, A., Ohkubo, K., Kawata, H., Hayashi, Y., Ishikawa, T., Makiyama, T., Nagao, S., Yagihara, N., Takehara, N., Kawamura, Y., Sato, A., Okamura, K., Hosaka, Y., Sato, M., Fukae, S., Chinushi, M., Oda, H., Okabe, M., … Makita, N. (2012). Clinical characteristics and risk of arrhythmia recurrences in patients with idiopathic ventricular fibrillation associated with early repolarization. *International Journal of Cardiology*, *159*(3), 238–240. https://doi.org/10.1016/j.ijcard.2012.05.091

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