Electrocardiographic Parameters and Fatal Arrhythmic Events in Patients with Brugada Syndrome: Combination of Depolarization and Repolarization Abnormalities.

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Abbreviated title: ECG markers in high-risk Brugada syndrome

Abstract

Objectives: This study aimed to determine the usefulness of the combination of severalelectrocardiographic (ECG) markerson risk assessment of ventricular fibrillation (VF) in patients withBrugadasyndrome (BrS).

Background: Detection of high/low-risk BrSpatientsusing a noninvasive method is animportant issuein the clinical setting. Several ECG markers related to depolarization and repolarization abnormalities have been reported, butthe relationship and usefulness of these parametersin VF events are unclear.

Methods: Baseline characteristics of 246 consecutive patients (236 males; mean age, 47.6±13.6 years) with Brugada type ECG, including 13 patients witha history of VF and 40 patients with ahistory of syncopalepisodes,were retrospectively analyzed. During the mean follow-up period of 45.1 months, VFin 23 patients and sudden cardiac death(SCD) in one patientwere observed. Clinical/geneticand electrocardiographic parameterswere compared with VF/SCD events.

Results: Byunivariate analysis, history of VF, history of syncopal episodes, paroxysmal atrial fibrillation , spontaneous type1 pattern in the precordial leads, ECG markers of depolarization abnormalities(PQ >200ms, QRS duration ≥120ms,and fragmented QRS [f-QRS]),and those of repolarizationabnormalities(infero-lateral early repolarization [ER] pattern and QT prolongation)were associated with later cardiac events. By multivariable analysis,history of VF, history of syncopal episodes, infero-lateral ER pattern,f-QRS wereindependent predictors of documented VF and SCD (odds ratio, 19.61, 28.57, 2.87, and 5.21, respectively, $P<0.05$). Kaplan-Meier curves showed thatthe presence/absence ofinfero-lateral ER and f-QRS provided a worse/better prognosis (log-rank test, $P<0.01$).

Conclusions: The combination of depolarization and repolarization abnormalitiesin BrSis associated with later VF events. The combination of these abnormalities is useful for detecting high-and low-riskBrSpatients.

Keywords: Brugada syndrome, fragmented QRS, early repolarization, ventricular fibrillation, noninvasive risk assessment

Abbreviations:

BrS: Brugada syndrome

ECG: electrocardiogram

EP: electrophysiology

ER: early repolarization

f-QRS: fragmented QRS

ICD: implantable cardioverter defibrillator

PAF: paroxysmal atrial fibrillation

SCD: sudden cardiac death

SCN5A: pore-forming region of the human cardiac sodium channel

VF: ventricular fibrillation

Introduction

Brugada syndrome (BrS) is a distinct form of idiopathic ventricular fibrillation (VF).BrS is characterized by a unique electrocardiogram (ECG) pattern consisting of a right bundle branchblock-like morphology and ST-segment elevation in precordial leads. Results of many studies(1-10)have suggested that patients with syncope, particularly patients with a spontaneous type1 ECG pattern, have a significant risk ofsudden cardiac death (SCD)or VF.In the remaining population of asymptomatic subjects, the risk is lower, but not negligible(1,5). Therefore, assessment ofthe risk of SCD and VF in patients with Brugada type ECGis clinically important, especially when sporadic cases are detected during routine medical check-ups.

Many markersfor development of VFin BrS have been reported, including clinical markers ofa family history of sudden cardiac death (11), syncope with nonprodromal episodes(12),episodes of paroxysmal atrial fibrillation (PAF)(13), electrocardiographic markers of spontaneous type1 ECG pattern, existence of late potential (14), fragmented QRS (f-QRS)(15),T-wave alternans after sodium channel blocker injection (16),aninfero-lateral early repolarization (ER) pattern(17,18), agenetic marker of *SCN5A*, a gene encoding the cardiac sodium channel(19),electrophysiological markers of VF inducibility by programmed electrical stimulation, abnormal restitution properties,and ventricular effective refractory period <200ms(20). However, the relationship of these markers and the usefulness of their combination have not been sufficiently examined.

In this study, we examinedrisk markers, with a focus on noninvasive surface ECGmarkers categorized by depolarization and repolarization abnormalities, and attempted to improve the accuracy of prediction and classification of high- and low-risk

BrSpatients.

Methods

Patient population and clinical data collection

We retrospectively analyzeddata from246consecutive patients(236 males; mean age,47.6±13.6 years) with Brugada type ECG in Okayama University Hospital. All patients showed a typical ECG "Brugada pattern" with or without a sodium channel blocker (pilsicainide), which was defined previously(11). Informed consent was obtained from all subjects, andclinical data, including data on age, sex, family history of SCD (less than 45 years old), history of syncopal episodes,history of VF episodes, and VF induction during electrophysiological (EP) studywere obtained from patient records.Follow-up data defined that the start of follow-up was taken as first visit,and the end of follow-up was set to death, arrhythmic events, or the last visit.

Electrocardiographic measurements

Standard 12-lead ECGs were recorded inthe same way and were evaluated for the RRinterval, PQ interval, QRS width, QT interval, ST level at the J point,and number of positive spikes within the QRS complex in leads V1through V3.A spontaneous type1 pattern was defined as documentation by ECG of a type 1 pattern in the absence of class I anti-arrhythmic drugs. The presence of a late potential was evaluated by a signal-averaged ECG (ART 1200 EPX, noise level <0.3μV, and high-pass filtering of 40 Hz with a bidirectional 4-pole Butterworth).A late potential was positive when the following two criteria were met: root-mean-square voltage of the terminal 40ms in the filtered QRS complex <20μV and a duration of low-amplitude signals <40μV in the terminal filtered QRS complex >38ms(21).

The presence of f-QRS was defined as an abnormal fragmentation within the QRS complex as ≥four spikes in one or ≥eight spikes in all of the leads V1, V2, and V3 as described previously(15)(Figure 1A).

Aninfero-lateral ER pattern was defined as an elevation of the J point in at least two consecutive leads. The amplitude of the J wave or J-point elevation had to be at least 1 mm above the baseline level, either as QRS slurring or notching in the inferior lead (II, III, and aVF), lateral (I, aVL, and V4–V6) lead, or both as described previously(17,18,22-25)(Figure 1B).

We divided the patients into thedepolarization abnormality (PQ interval >200ms,QRS width≥120ms, positive late potential, and f-QRS)group andtherepolarization abnormality (QT prolongationand infero-lateral ER pattern) group.

EP study

After obtaining written informed consent from patients, an EP study was performed as described previously(1,26) in all patients.The criterion for the induction of ventriculararrhythmia was induction of sustained polymorphic ventriculartachycardia or VF by programmed electrical stimulation from the right ventricularapex, right ventricular outflow tract, or left ventricle with amaximum of threeextrastimuli at two cycle lengths.

Gene mutation analysis of *SCN5A*

This study was performed in compliance with guidelines for human genome studies of the Ethics Committee of Okayama University as described previously(13). In brief, all exons of *SCN5A* were amplified by polymerase chain reaction from DNA isolated from peripheral leukocytes of the patients. Genomic DNA was extracted from peripheral blood leukocytes using a DNA extraction kit (Gentra, Minneapolis,Minnesota, USA)

and was stored at –30°C until use. Twenty-seven exons of the *SCN5A* gene were amplified with previously reported intronic primers(13).

Statisticalanalysis

Statistical analysis was performed using SPSS 17.0 for Windows (SPSS Inc, Chicago, IL, USA).Data are expressed as mean ± SD or median (IQR) values.Student's t test was performed to test for statistical differences between two unpaired mean values, and categorical data and percentage frequencies were analyzed by the chi-square test.Inunivariate analysis, nine predictors were significantly associated with arrhythmic events. Multivariate analysis using Cox proportional-hazards regression analysis estimated thosenine predictors and was performed in search of independent risk factors for arrhythmic events.This analysis was based on a stepwise algorithm, with the p value set at 0.05 for entering and 0.1for exclusion.The effects of ER and f-QRS on arrhythmic events during the follow-up period were evaluated using the log-rank test and were described using a Kaplan Meier curve. $P<0.05$ was considered statistically significant.

Results

Patients' characteristics

Baseline patients' characteristics are summarized in Table 1. Sixty-ninepatients (28.0%) had anfamily history of SCD, 40 (16.3%) had history of syncopal episodes, and 13 (5.3%) had history of VF episodes. Gene analysis showed that *SCN5A* genemutationwas present in 17 patients (13.8%). Spontaneous type1 ECG was observed in 156patients (63.4%). In theEP study, VF was induced in 71patients (45.8%), and 63 of them (25.6%) had received ICD implantation. During the follow-up period of 45.1±44.3months, fatal arrhythmic events occurred in 24 patients(23 appropriate ICD

shocks due to VF and onecardiac arrest duringsleep).

Clinical/genetic/ECG parameters and cardiac events

Clinical and genetic parameters were compared in BrS patients with and those without cardiac events during the follow-up period (Table2). PAF episodes (9/24, 37.5% versus 35/222, 15.8%, P=0.013), ahistory of VF (9/24, 37.5% versus 4/222, 1.8%, P<0.001), a history of syncopal episodes (13/24, 54.2% versus 27/222, 12.2%, P<0.001), VF inducibility during EP study (17/24, 70.8% versus 54/131, 41.2%, P=0.007), and spontaneous type1 ECG (22/24, 91.7% versus 134/222, 60.4%, P=0.002) were observed more oftenin VF/SCD patients than in those without VF/SCD,butother parameters such as age, sex,family history of SCD, and *SCN5A* gene mutation were not different.

Among the ECG parameters of depolarization abnormalities, QRS width≥120ms (8/24,33.3% versus 29/222, 13.1%, P=0.015),and f-QRS (20/24,83.3% versus 58/222, 26.1%,P<0.001) were observed more oftenin patients with VF/SCD than in those without VF/SCD. Among the ECG parameters of repolarization abnormalities, aprolonged QTcinterval>440ms (7/24,29.2% versus 28/222, 12.6%, P=0.036) and infero-lateral ER pattern (8/24,33.3% versus 17/222, 7.7%, P<0.001) were observed moreoften in patients with VF/SCD than in those without VF/SCD.

Multivariate analysis showed that the following four parameters were independent risk factors for arrhythmic events: f-QRS(hazard ratio, 5.21; 95% confidence interval [CI], 1.69 to 16.13; P=0.004),infero-lateral ER pattern (hazard ratio, 2.87; 95% CI, 1.16 to 7.14; P=0.023), a history of VF episodes (hazard ratio, 19.61; 95% CI, 4.12 to 90.91; P<0.001),and a history of syncopal episodes (hazard ratio, 28.57; 95% CI, 6.14 to 142.86; P<0.001) (Table 2).

Patients' characteristics withf-QRS

In multivariate analysis, depolarization abnormalitiesof f-QRS were an independent risk factor for arrhythmic events. Therefore, clinical, genetic, and electrocardiographic data for patients with and those without f-QRS wereanalyzed again (Table 3). There were no significant differences in age, family history of SCD, and incidence of the*SCN5A* gene mutationbetween patients with and those without f-QRS. However, ahistory of syncopal episodes, a history of VF episodes, and VF inducibilityduring EP studywere more frequentlyobserved in patients with f-QRS than in those without f-QRS(P=0.002, 0.005, and0.002, respectively).PQ interval, QRS duration and QTc interval werelonger in patients with f-QRS than in those without f-QRS (P=0.037, 0.001, and 0.042, respectively), but the ER pattern was not different between the groups. Spontaneous type1 ECG and PAF episodes were more frequently observed in patients with f-QRS than in those without f-QRS (P<0.001and P=0.031, respectively). VF/SCD episodes during follow- up were more frequently observed in patients with f-QRS than in those without f-QRS (P<0.001).

Patients' characteristics with anER pattern

In multivariate analysis, repolarization abnormality of the ER pattern was an independent risk factor for arrhythmic events. Therefore, clinical, genetic, and electrocardiographic data with and without an ER pattern wereanalyzedagain (Table 4). There were no significant differences in age, family history of SCD, incidence of *SCN5A* gene mutation, positive late potential, a history of syncopal episodes, f-QRS,and VF inducibility during the EP study. However, VF/SCD episodes during followup and a

history of VF episodeswere more frequentlyobserved in patients with ER than in those without ER (P=0.001 and 0.005, respectively).

Follow-up data

We next examined the follow-up data in patients with f-QRS and ER.Twenty-three patients developedVF, one patient died suddenly during sleep,possibly due to VF, and one patient died of a non-arrhythmic cause (pneumonia) during the follow-up period.

Figure 2shows the results of Kaplan-Meier analyses of fatal arrhythmic events in patients with and those without f-QRS (Fig. 2A) oran ER (Fig. 2B) pattern. Patients with f-QRS or ER had a significantly worse prognosis than did patients without those parameters (P<0.001 and <0.001,respectively).

Figure 3 shows results of the combination analysis of f-QRSand ERparameters. Patients with both f-QRS and ER parameters had a significantly higher frequency offatal arrhythmic events than did patients without both parameters (P<0.001). Moreover, patients with both f-QRS and ER parameters had a significantly higher frequency of arrhythmic events than did patients with f-QRS alone (P=0.045,Fig.3).

Discussion

The present study showed that the combination of f-QRSand infero-lateral ER pattern was associated withdevelopment of VFin BrS patients. Additionally,the combination of f-QRS with ER (depolarization and repolarization abnormalities)was useful for identifying high- and low-riskBrS patients.

High-risk clinical parametersof VF development

Previous studies have reported that syncopal episodes (especially in patients with

prodrome), a history of VF, and a family history of sudden death are associated with VF events in BrS patients(3,4,12,20,27-29). In our study, we also observed that syncopal episodes and a history of VF were independent predictors of later VF events. These patients were symptomatic patients, and therefore it is reasonable to classify them as high-risk patients. However, more patients have no symptoms with electrocardiographic evidence of Brugada syndrome (asymptomatic Brugada patients). A recent studysuggested that these asymptomatic patients have a better prognosis, but not negligible (1,5). Therefore, simple risk assessment for these asymptomatic Brugada patients is clinically important, especially when sporadic cases are detected during routine medical check-ups.

Repolarization abnormalities in BrS

Many clinical data support the importance of repolarization abnormalities for VF development, such as T-wave alternans after sodium channel blocker injection (16), and ST elevation after exercise (30) or full-stomach status(31) .

An ER pattern is considered to be a benign ECG phenomenon affecting 2–5% of the general population and is most commonly observed in young men (32,33). Recently, an ER pattern has been shown as an additional risk marker for VF development, especially in infero-lateral leads, in patients with BrS(17,18). Our finding that repolarization abnormalitieswere independently associated with VF development is in agreement with these previous findings.

Depolarization abnormalities in BrS

In addition to repolarization abnormalities, recent observations have suggested that VF development in BrS is associated with conduction disturbances, such as prolongation of the PQ interval (34), a wide QRS complex (35), a positive late potential (36), and

f-QRS (15,20). A recent study showed that f-QRS is the strongest predictor of VF development in BrS(20). The usefulness of f-QRS for identifying patients at high risk for various cardiac diseases, including cardiac sarcoidosis, arrhythmogenic right ventricular cardiomyopathy, and acute coronary syndrome (37), has been reported. Our finding that f-QRS (depolarization abnormality) was an independent predictor for VF development is in agreement with those results. We also found that f-QRS was associated with other depolarization abnormalities, such as a prolonged PQ and QRS interval,indicating that depolarization abnormalities in the atrium and ventricle are an important factor for development of VF in BrS.

A QRS interval in lead V2 ≥120 ms was found to be a possible predictor of life-threatening ventricular arrhythmia and/or syncope. Prolonged QRS duration as measured on a standard 12-lead ECG has been shown to be associated with ventricular arrhythmia (35).Additionally,a prolonged QRS duration in precordial leads is prominent in symptomatic patients, suggesting that delayed conduction of the ventricle (depolarization) is important (29,38). However, in multivariate analysis in our study, there were no significant differences in wide QRS complex between patients with and those without VF/SCD.

Combination of depolarization and repolarization abnormalities

In this study, Kaplan-Mayer analyses showed that the combination of f-QRS (depolarization abnormality) and ER (repolarization abnormality) is useful for predicting VF events in patients with BrS. Recently, f-QRS was reported to be an important marker for the development of VF (Torsade de pointes) in patients with acquired long QT syndrome (typical repolarization abnormality disease) (39), indicating thatthe combination of depolarization and repolarization is important for the

development of lethal arrhythmia. We also found that VF seldom developed in patients without any abnormalities during the follow-up period in this study, suggesting that low-risk BrS patients could also be identified using these markers.

We also investigated the clinical/electrocardiogaphic characteristics of depolarizationand repolarization abnormalities. Interestingly, there were many differences between the groups (Tables 34). Patients with f-QRS had more depolarization abnormalities than those without f-QRS, such as prolonged PQ and QRS intervals. In contrast, patients with an ER pattern had no differences in these markers, suggesting that the genesis of each of these abnormalities is intrinsically different.

Clinical implications

BrSis a heterogeneous disease. Therefore, the mechanism of VF development differs in each patient. Our resultssuggest that the combination of depolarization and repolarization abnormalities (f-QRS, and ER pattern) enables identification of high- and low-risk patients with BrS. In the clinical setting, VF induction during EP study is still considerable to decide the ICD implantation. Thus we think we should recommend EP study in a patient with f-QRS and ER pattern even in an asymptomatic case, or we do not need EP study in an asymptomatic case of neither f-QRS nor ER pattern.

Limitations

This study has several limitations. First, the ECG features of ER and other ECG markers are dynamic, andthus the true prevalence of this coexistence isdifficult to evaluate. Second, we analyzed only the coding regions of *SCN5A* for mutations in this study, and the possibility of mutations occurring in regions of the gene other than

coding regions or other gene mutations cannot be excluded. Third, Nishii et al. reported that *SCN5A*gene mutations are associated with early and frequent VF recurrence(19), but not with initial VF episodes. In our study, we did not find a significant difference. Therefore, further studies on this issue are required.Fourth, this study was a retrospective study.A prospective study to estimate risk factors of BrS is required.And the last, there were a small number of endpoints making it difficult to identify unique predictors in a multivariate model reliably.

Conclusions

Our study shows that ER and f-QRS are independent risk factors for arrhythmic events in patients withBrS. Patients with both ER and f-QRS have a significantly higher frequency of arrhythmic events than do patients who haveneither ER nor f-QRS. Furthermore, when there is neither ER nor f-QRS, arrhythmic events are small.

Clinically, this study shows that the combination of f-QRS (marker of depolarization abnormality) and ER (marker of repolarization abnormality) is useful for estimating the incidence of VF in patients withBrS.

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Figure legends

Figure1: Representative ECGs of fragmented QRS (f-QRS) and early repolarization (ER). (A) Fragmented QRS (f-QRS) was observed in lead V2. Note that there are four

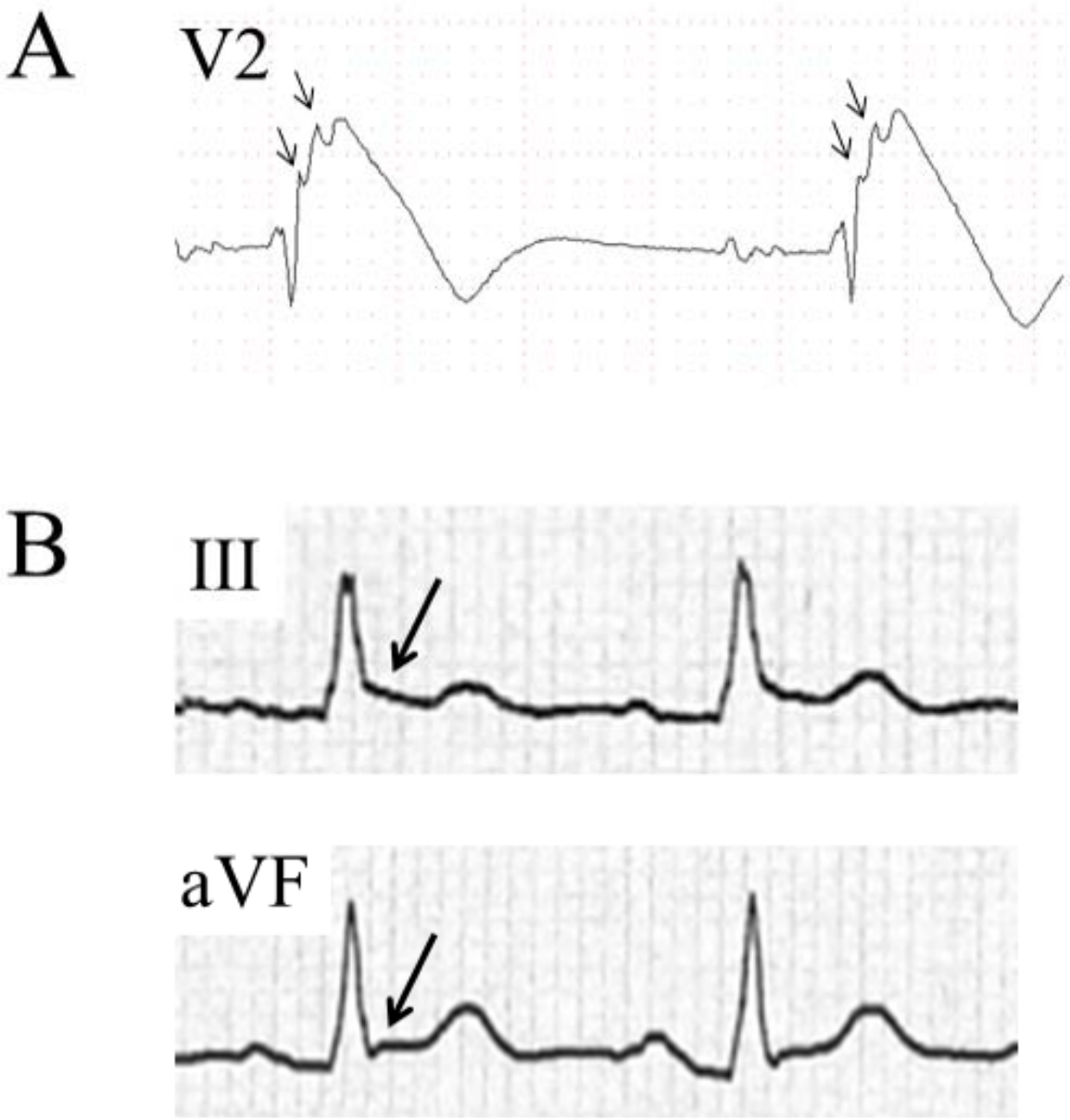
spikes (arrows) in this lead. (B) Early repolarization (ER) pattern in the inferior leads. Note that J-point elevation above the baseline (>1mm) can be seen in leads III and aVF.

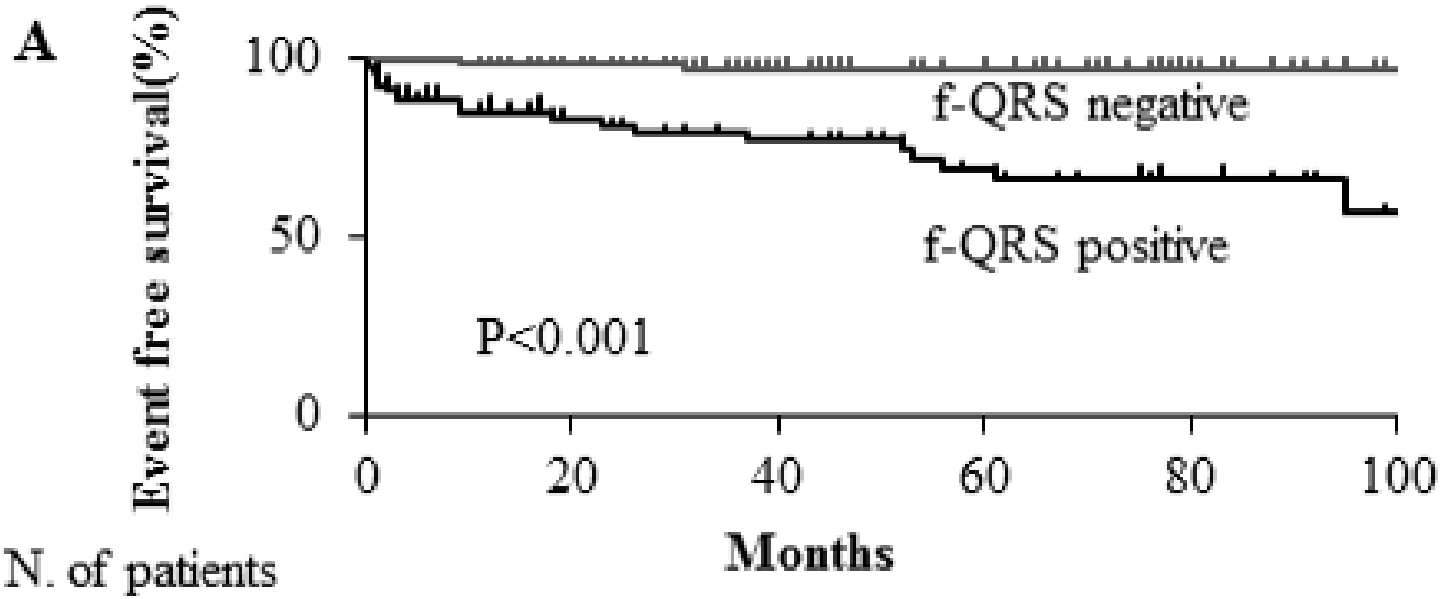
Figure2: Kaplan-Meier analysis of VF/SCD events.

Ventricular fibrillation (VF)/ sudden cardiac death (SCD) events were observed often in the presence of (A) fragmented QRS (f-QRS), and (B) early repolarization (ER).

Figure3: Kaplan-Meier analysis of VF/SCD events.

Ventricular fibrillation (VF)/ sudden cardiac death (SCD) events were observed often inthe combination of depolarization (f-QRS) and repolarization abnormalities (ERpattern).


A
V2
B
III
aVF



N. of patients						
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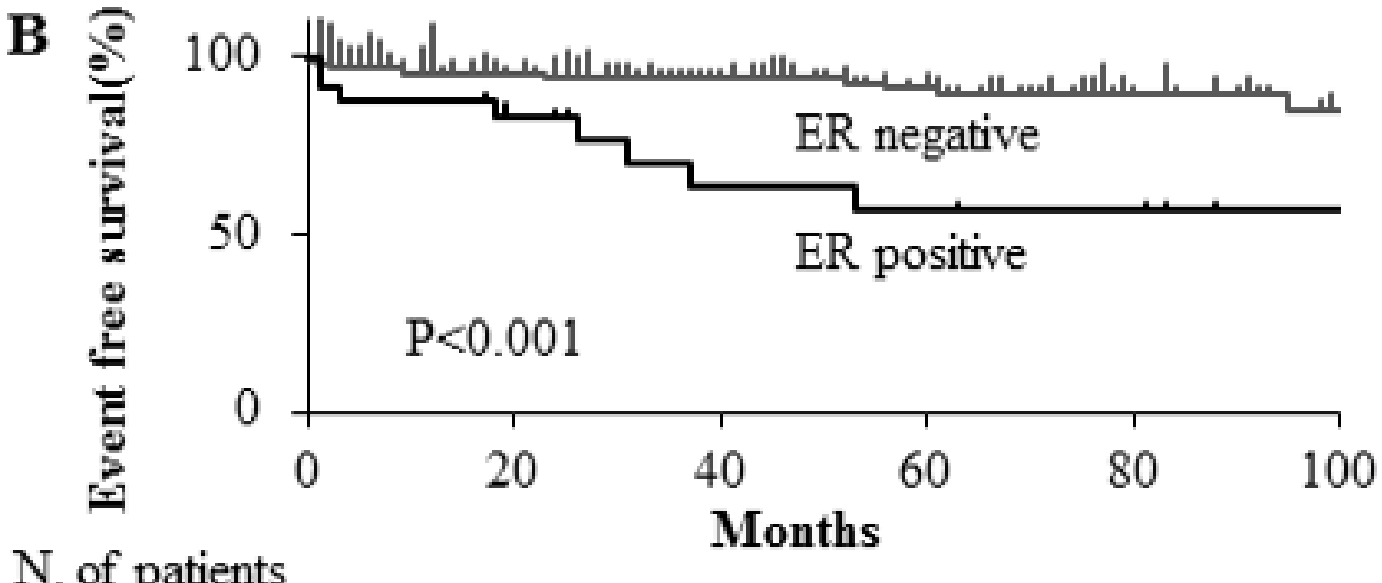
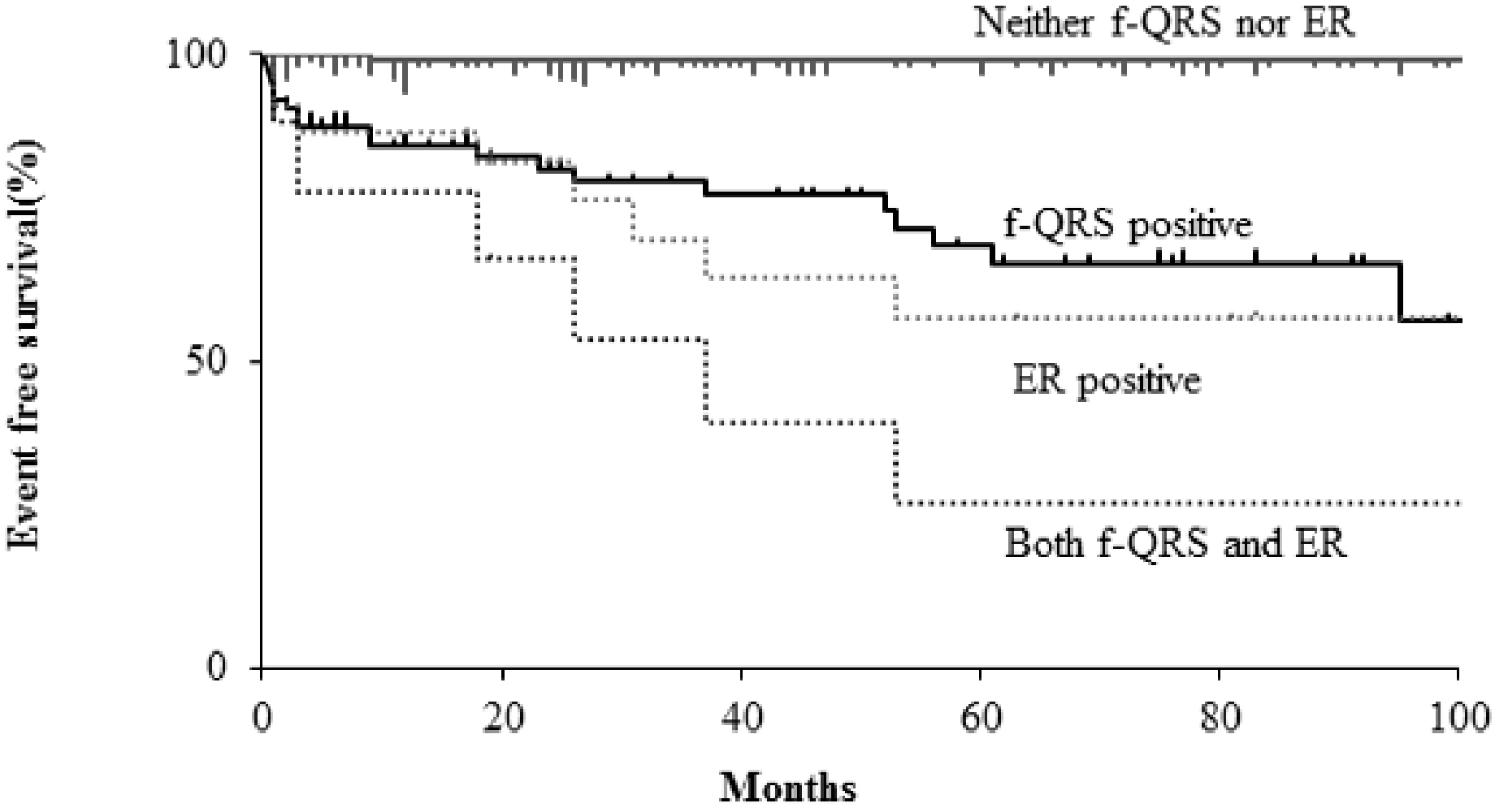
f-QRS pos.	78	43	35	23	12	5



N. of patients						
ER neg.	221	121	87	60	32	14
ER pos.	25	15	10	9	8	5



N. of patients						
Neither	152	83	55	39	22	11
fQRS pos.	78	43	35	23	12	5
ER pos.	25	15	10	9	8	5
Both	9	5	3	2	2	2

Table1 . Patients' Characteristics		
Male/Female		236/10
Age, yrs		47.6±13.6
Mean follow up period, months		45.1±44.3
History of syncopal episode (%)	40	(16.3%)
History of VF episode (%)	13	(5.3%)
Family history of SCD (%)	69	(28.0%)
Paroxysmal AF (%)	44	(17.9%)
Spontaneous type-1 ECG (%)	156	(63.4%)
ER pattern (%)	25	(10.2%)
fragmented QRS (%)	78	(31.7%)
Positive LP (%)	166/235	(70.6%)
SCN5A gene mutation (%)	17/123	(13.8%)
VF induction during EP study (%)	71/155	(45.8%)
ICD implantation (%)	63	(25.6%)
VF or SCD event during follow-up period (%	24	(9.8%)

Values are mean ±SD or number of patients.
AF=atrial fibrillation; ECG=electrocardiogram; EP=electrophysiology;
ER=early repolarization; ICD=implantable cardioveter defibrillator;
LP=late potential; SCD=sudden cardiac death;
SCN5A =pore-forming region of the human cardiac sodium channel;
and VF=ventricular fibrillation.

Table2. Characteristics of patients with and without VF/SCD during follow-up p

					Univariate Analys	
	VF/SCD (+)		VF/SCD(-)		Odds Ratio	95%CI
Clinical/genetic parameters						
Number of patients (male/femal	23/1		213/9		1.029	0.125-8.490
Age, yrs	47 (15)		48 (21)			
History of syncopal episode (%)	13	(54.2)	27	(12.2)	8.535	3.477-20.955
History of VF episode(%)	9	(37.5)	4	(1.8)	32.700	.012-118.645
Paroxysmal AF (%)	9	(37.5)	35	(15.8)	3.206	1.301-7.899
Family history of SCD (%)	8	(33.3)	61	(27.5)	1.320	0.537-3.241
SCN5A gene mutation (%)	4/23	(17.4)	3/100	(13.0)	1.409	0.414-4.799
VF induction during EP study	17/24	(70.8)	54/131	(41.2)	3.463	1.344-8.293
Spontaneous type-1 ECG (%)	22	(91.7)	134	(60.4)	7.224	1.657-31.491
Depolarization parameters						
Positive f-QRS (%)	20	(83.3)	58	(26.1)	14.138	4.638-43.093
Positive LP (%)	20/24	(83.3)	46/211	(69.2)	2.226	0.732-6.772
PQ >200msec (%)	8	(33.3)	40	(18.0)	2.275	0.911-5.681
QRS ≧120msec (%)	8	(33.3)	29	(13.1)	3.328	1.307-8.469
Repolarization parameters						
ER pattern (%)	8	(33.3)	17	(7.7)	6.029	2.258-16.103
QTc >440msec (%)	7	(29.2)	28	(12.6)	2.853	1.087-7.490

Values are mean ± SD, median (IQR), or number of patients.
AF=atrial fibrillation; CI=confidence interval; ECG=electrocardiogram;EP=electrophysiology; ER=
LP=late potential; *SCN5A* =pore-forming region of the human cardiac sodium channel; VF=ventricu

pariod			
is	Multivariate Analysis		
ɔ Value	Hazard Ratio	95%CI	ɔ Value
0.649			
0.835			
<0.001	28.571	6.135-142.857	<0.001
<0.001	19.608	4.115-90.909	<0.001
0.013			0.306
0.554			
0.396			
0.007			0.562
0.002			0.114
<0.001	5.208	1.689-16.129	0.004
0.150			
0.069			
0.015			0.908
<0.001	2.874	1.160-7.143	0.023
0.036			0.608

=early repolarization; f-QRS = fragmented QRS;
ular fibrillation.

Table3. Characteristics of patients with and without f-QRS

	f-QRS(+)	f-QRS(-)
Clinical/genetic parameters		
Number of patients (male/female)	76/2	160/8
Age, yrs	48.5± 12.9	47.2±14.0
History of syncopal episode (%)	21 (26.9)	19 (11.3)
History of VF epsode (%)	9 (11.5)	4 (2.4)
Paroxysmal AF (%)	20 (25.6)	24 (14.3)
Family history of SCD (%)	23 (29.5)	46 (27.4)
SCN5A gene mutation (%)	9/43 (20.9)	8/80 (10.0)
VF induction during EP study (%)	34/54 (63.0)	37/101 (35.9)
ICD implantation (%)	37 (47.4)	26 (15.5)
VF or SCD event during follow-up (%)	20 (25.6)	4 (2.4)
ECG parameters		
Duration of PQ interval, msec	184±29	176±26
Duration of QRS complex, msec	108 (24)	100 (17)
Duration of QTc interval, msec	419±30	411±24
Amplitude at J point V1, mV	0.12 (0.15)	0.11 (0.10)
Amplitude at J point V2, mV	0.21 (0.21)	0.201 (0.17)
Amplitude at J point V3, mV	0.13 (0.12)	0.12 (0.12)
Positive ER pattern (%)	9 (11.5)	16 (9.5)
Spontaneous type-1 ECG (%)	63 (80.8)	93 (55.4)
Positive LP (%)	59/75 (78.7)	107/160(66.9)

Values are mean ±SD, median (IQR), or number of patients.
AF=atrial fibrillation; ECG=electrocardiogram; EP=electrophysiology; ER=early repo
f-QRS=fragmented QRS; ICD=implantable cardioveter defibrillator; LP=late potenci
SCD=sudden cardiac death; SCN5A=pore-forming region of the human cardiac sodiu
VF=ventricular fibrillation

p Value
0.511
0.514
0.002
0.005
0.031
0.732
0.094
0.002
<0.001
<0.001
0.037
0.001
0.042
0.347
0.468
0.929
0.653
<0.001
0.064

)larization;
al;
m channel;

Table4. Characteristics of patients with and without ER

	ER(+)	ER(-)
Clinical/genetic parameters		
Number of patients, men/women	23/2	213/8
Age, yrs	43 (23)	49 (20)
History of syncopal episode (%)	5 (20.0)	35 (15.8)
History of VF episode (%)	5 (20.0)	8 (3.6)
Paroxysmal AF (%)	3 (12.0)	41 (18.6)
Family history of SCD (%)	7 (28.0)	62 (28.1)
SCN5A gene mutation (%)	2/15 (13.3)	15/108 (13.9)
VF induction during EP study (%)	9/21 (42.9)	62/134 (46.3)
ICD implantation (%)	13 (52.0)	50 (22.6)
VF or SCD event during follow-up (%	8 (32.0)	16 (7.2)
ECG parameters		
Duration of PQ interval, msec	190±34	177±26
Duration of QRS complex, msec	99 (17)	104 (20)
Duration of QTc interval, msec	405±27	414±26
Amplitude at J point V1, mV	0.14 (0.14)	0.11 (0.12)
Amplitude at J pointV2, mV	0.21 (0.25)	0.20 (0.16)
Amplitude at J pointV3, mV	0.17 (0.17)	0.12 (0.11)
Positive f-QRS (%)	9 (36.0)	69 (31.2)
Spontaneous type 1 ECG (%)	14 (56.0)	142 (64.3)
Positive LP (%)	17/23 (73.9)	149/212 (70.3)

Values are mean ±SD, median (IQR), or number of patients.
AF=atrial fibrillation; ECG=electrocardiogram; EP=electrophysiology; ER=early repolar
f-QRS=fragmented QRS; ICD=implantable cardioveter defibrillator; LP=late potencial;
SCD=sudden cardiac death;
SCN5A=pore-forming region of the human cardiac sodium channel; VF=ventricular fibri

p Value
0.269
0.820
0.383
0.005
0.584
0.995
1.000
0.770
0.001
0.001
0.053
0.335
0.097
0.306
0.505
0.069
0.653
0.417
0.717

ization;

illation