Differences in clinical significance of atrial tachyarrhythmias in idiopathic ventricular fibrillation vs Brugada syndrome: A multicenter study

Tomofumi Mizuno, MD,[1] Nobuhiro Nishii, MD, PhD,[2] Hiroshi Morita, MD, PhD,[2] Takuro Masuda, MD,[1] Akira Ueoka, MD, PhD,[1] Saori Asada, MD, PhD,[1] Yoshimasa Morimoto, MD,[3] Masakazu Miyamoto, MD,[1] Satoshi Kawada, MD, PhD,[1] Tadashi Wada, MD, PhD,[4] Shigeki Hiramatsu, MD, PhD,[5] Keisuke Okawa, MD,[6] Motoki Kubo, MD, PhD,[7] Koji Nakagawa, MD, PhD,[1] Atsuyuki Watanabe, MD, PhD,[1] Kazufumi Nakamura, MD, PhD,[1] Shinsuke Yuasa, MD, PhD[1]

From the [1]Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan, [2]Department of Cardiovascular Therapeutics, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan, [3]Department of Cardiovascular Medicine, Fukuyama City Hospital, Fukuyama, Japan, [4]Department of Cardiovascular Medicine, Iwakuni Clinical Center, Iwakuni, Japan, [5]Department of Cardiovascular Medicine, Fukuyama Cardiovascular Hospital, Fukuyama, Japan, [6]Department of Cardiovascular Medicine, Kagawa Prefectural Central Hospital, Takamatsu, Japan, and [7]Department of Cardiovascular Medicine, Tsuyama Central Hospital, Tsuyama, Japan.

BACKGROUND Atrial tachyarrhythmias (ATAs) are the primary cause of inappropriate implantable cardioverter-defibrillator (ICD) therapy in patients with idiopathic ventricular fibrillation (IVF) and are associated with decreased quality of life and increased mortality. Nonetheless, the incidence of ATAs in IVF cases has not been clarified.

OBJECTIVE The study sought to determine the incidence and clinical significance of ATAs in patients with IVF compared with those with Brugada syndrome (BrS).

METHODS Patients diagnosed with IVF or BrS and receiving ICDs in 6 hospitals were enrolled between February 1997 and July 2020 to compute data regarding the incidence of ATAs, appropriate/inappropriate ICD therapy frequency, and independent predictors of ATAs.

RESULTS Overall, 137 patients (51 in the IVF group and 86 in the BrS group) were enrolled. ATAs were detected in 22 (43.1%) patients in the IVF group and 17 (19.8%) in the BrS group (P = .006). Inappropriate ICD therapies due to ATAs were more frequently observed in the IVF group than in the BrS group (12 [23.5%] vs 7 [8.1%]; P = .020). Conversely, there was no significant difference in appropriate ICD therapies between the IVF and BrS groups (14 [27.5%] vs 23 [27.1%]; P = 1.000). Cox regression analysis revealed no predictive factors for the development of ATAs in the IVF group.

CONCLUSION ATA events were observed more frequently in patients with IVF than in those with BrS, and ATAs led to inappropriate ICD therapy in patients with IVF. Clinicians need to consider the recurrence of not only ventricular arrhythmias, but also the development of atrial arrhythmias for better management of IVF cases.

KEYWORDS Idiopathic ventricular fibrillation; Brugada syndrome; Atrial tachyarrhythmias; Atrial fibrillation; Implantable cardioverter-defibrillator; Inappropriate therapy

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Introduction

Idiopathic ventricular fibrillation (IVF) is a rare cause of out-of-hospital cardiac arrest, with 1.2% of out-of-hospital cardiac arrests without structural heart disease reportedly being related to a shockable rhythm.[1] IVF is defined in an individual who has experienced a cardiac arrest, preferably with documented ventricular fibrillation (VF), after excluding cardiac, respiratory, metabolic, and toxicological causes.[2]

Previous reports indicate that 17%–31% of patients with IVF experience recurrent ventricular arrhythmias.[3,4] An

Address reprint requests and correspondence: Dr Tomofumi Mizuno, Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan. E-mail address: me18076@s.okayama-u.ac.jp.

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KEY FINDINGS

- Atrial tachyarrhythmias are the primary cause of inappropriate implantable cardioverter-defibrillator therapy in patients with idiopathic ventricular fibrillation and are associated with decreased quality of life and increased mortality.
- The frequency and clinical significance of atrial tachyarrhythmias in patients with Brugada syndrome are well established, but less is known about those in patients with idiopathic ventricular fibrillation.
- In this study, atrial tachyarrhythmias were observed in 43.1% of the patients with idiopathic ventricular fibrillation and 19.8% of the patients with Brugada syndrome ($P = .006$), and inappropriate implantable cardioverter-defibrillator therapies due to atrial tachyarrhythmias were more frequently observed in the idiopathic ventricular fibrillation group than in the Brugada syndrome group (12 [23.5%] vs 7 [8.1%]; $P = .020$).

implantable cardioverter-defibrillator (ICD) is required to prevent sudden cardiac death due to recurrent VF episodes. However, inappropriate ICD therapy in IVF cases is not rare, occurring in 14%–44% of cases.[3,5] The most important cause of inappropriate ICD therapy is atrial tachyarrhythmias (ATAs), including atrial fibrillation (AF).[5] Nonetheless, the incidence of ATAs in patients with IVF has not been clarified.

Brugada syndrome (BrS) was initially reported as a type of IVF because of normal cardiac function. BrS has specific electrocardiogram (ECG) characteristics and has been differentiated from "pure" IVF. The clinical significance of ATAs in patients with BrS has been well established: the occurrence of ATAs is more common in those with BrS than in the age- and gender-matched general population.[6] The incidence of AF in patients with BrS ranges between 13% and 39%.[7–10] Furthermore, ATAs in these patients also make an important contribution to inappropriate ICD therapies.[6]

The clinical significance of ATAs in patients with IVF is not well established. Here, we aimed to compare the clinical significance of ATAs in patients with IVF and BrS using the data of the ICD, especially remote monitoring data, and to identify the predictors of ATAs.

Methods

Patient population

Patients diagnosed with IVF or BrS who underwent ICD implantation between February 1997 and July 2020 were enrolled from 6 hospitals in the western territory of Japan including Okayama University Hospital, Tsuyama Central Hospital, Fukuyama Cardiovascular Hospital, Kagawa Prefectural Central Hospital, Fukuyama City Hospital, and Iwakuni Clinical Center. This study was approved by the Ethics Committee on Human Research and Epidemiology of Okayama University and each hospital. This study adhered to ethical principles consistent with the Declaration of Helsinki.

IVF was defined as documented VF or highly suspected syncope caused by VF and meeting the following criteria: (1) normal cardiac function without evidence of structural heart disease on transthoracic echocardiography, (2) absence of any coronary artery stenosis, (3) absence of any electrolyte abnormalities in blood tests at the time of initial presentation, and (4) absence of evidence of known primary electrical disease (eg, BrS, long or short QT syndrome, or catecholaminergic polymorphic ventricular tachycardia [VT]). We included patients with inferolateral J waves in the IVF group. The J-wave was defined as a notch or slur of the terminal part of the QRS complex in at least 2 consecutive leads in inferior (II, III, aVF) or lateral (I, aVL, V4–V6) leads, or both, with a peak amplitude of $\geq$0.1 mV.[11] BrS was diagnosed based on the J-wave syndrome expert consensus conference report published in 2016.[12]

Transvenous ICD (TV-ICD) or subcutaneous ICD (S-ICD), single or dual chamber, were implanted at the discretion of the attending physician. Data were collected from ICD remote monitoring records and medical records up to the date of the last visit. All patients gave their written informed consent for using the remote monitoring system.

Clinical investigation for IVF patients

Patients enrolled in the study underwent a detailed interview to obtain medical history data, 12-lead ECG, laboratory tests, transthoracic echocardiography, and coronary angiography (or computed tomography angiography). At the discretion of clinicians, additional tests were performed if underlying disease was suspected; these tests included sodium-channel blocker challenge test (pilsicainide hydrochloride, 1 mg/kg/10 min), coronary spasm induction with acetylcholine or ergonovine, cardiac magnetic resonance imaging, electrophysiological study, endomyocardial biopsy, adrenaline provocation, gallium scintigraphy, signal-averaged ECG, and exercise stress test.

Outcomes and definitions

The primary endpoint was the occurrence of ATAs, and secondary endpoints were defined as the occurrence of appropriate/inappropriate ICD therapies. The ATA events include AF, atrial flutter, atrial tachycardia, and other supraventricular tachycardias, and are defined as follows: (1) ATAs with atrial rate of $>$190 beats/min and lasting $>$6 minutes, as detected by a dual-chamber ICD[13]; (2) ventricular high-rate episodes lasting $>$6 minutes with irregular RR intervals, and with the ventricular electrogram similar to that of sinus rhythm, as detected by a single-chamber ICD or S-ICD; (3) ATAs that caused inappropriate ICD therapies; and (4) those documented on a 12-lead ECG at regular outpatient visits. Because the primary objective of this study was to examine the incidence of ATAs, patients with a history of AF were also included in the calculation of ATAs incidence. However, ATAs recorded immediately after resuscitation from VF and

those occurring during electrophysiological studies were excluded from the calculation of the incidence of ATAs due to the special circumstances under which they occurred.

Appropriate ICD therapies were defined as shocks or antitachycardia pacing delivered for VT or VF, whereas inappropriate ICD therapies were defined as shocks or antitachycardia pacing delivered for causes other than VT/VF. In patients with a single-chamber ICD or S-ICD, therapy episodes were classified as inappropriate ICD therapies for ATAs if the ventricular electrogram was sufficiently similar to that of sinus rhythm.

The start date of the follow-up was defined as the date of ICD implantation in patients with an ICD for primary prevention and the date of VF onset in patients with an ICD for secondary prevention.

We evaluated the differences in the occurrences and significance of ATAs and ICD events between the IVF and BrS groups.

ICD programming

The ICD was programmed at the discretion of physicians. Discrimination algorithms were also used in this study. In more than 85% of patients, the VF zone was set to >220 beats/min in both TV-ICD and S-ICD: TV-ICD was programmed with at least 1 train of antitachycardia pacing before the ICD-delivered shock; the VT zone was set to >190 beats/min, with at least 3 trains of antitachycardia pacing before the TV-ICD–delivered shock. However, modifications were permitted based on the background of each patient. The single zone included only the VF zone, whereas the multiple zones included both VF and VT zones.

Follow-up

ICD follow-up was performed 1 month after ICD implantation, with regular follow-up intervals ranging from 3 to 6 months in the outpatient clinic at each hospital. During each visit, physical examination, 12-lead ECG, and ICD interrogations were performed. Remote monitoring data were collected every 1–4 months. All ICD interrogation data, remote monitoring of intracardiac electrograms, and 12-lead ECGs were reviewed by at least 2 electrophysiologists.

Statistical analysis

Continuous data were presented as median (interquartile range) and categorical data as frequency and percentage. Statistical comparisons were performed using the Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables. Survival curves were plotted using the Kaplan-Meier method, and differences were compared using the log-rank test. Hazard ratios with 95% confidence intervals were derived using the Cox regression model. All tests were 2-sided, and a P value of $<.05$ was considered statistically significant. All data analyses were conducted using R version 4.2.1 (R Foundation for Statistical Computing) and RStudio version 1.4.1717 software.

Results

Patient characteristics

Fifty-one patients in the IVF group and 86 in the BrS group admitted to Okayama University Hospital and 6 associated hospitals between February 1997 and July 2020 were enrolled in this study. The baseline characteristics of the patients are presented in Tables 1 and 2. The IVF group was younger and comprised fewer males than the BrS group. There were no differences in comorbidities and CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category) score between the 2 groups. Most patients in the IVF group had indications for ICD as secondary prevention, whereas primary prevention was indicated for the BrS group. The implanted ICD types were not different between the 2 groups. The PR interval, QRS duration, and QT interval were longer in the BrS group than in the IVF group. J waves were frequently observed in 23 (45.1%) patients in the IVF group. There were no significant differences between the 2 groups regarding left atrial/ventricular size, B-type natriuretic peptide, and renal function. Additional testing was performed to diagnose IVF and BrS (Table 3). Imaging studies, such as coronary angiography, gallium scintigraphy, and myocardial biopsies, revealed no abnormalities. VF inducibility with programmed ventricular stimulation in electrophysiology studies was observed in 13 (31.7%) of 41 cases in the IVF group and 62 (80.5%) of 77 cases in the BrS group.

Incidence of ATAs and ICD events

The ATAs were observed in 43.1% of the patients with IVF and 19.8% of the patients with BrS ($P = .006$). Four (7.8%) patients in the IVF group and 3 (3.5%) in the BrS group had previous AF. During the follow-up period, ATAs occurred more frequently in the IVF group than in the BrS group (annual event ratio: 4.9% and 1.7%, respectively; $P = .006$) (Figure 1 and Table 4). After ICD implantation, ATAs were newly detected more frequently in the IVF group (n = 18 of 47 [39.1%]) than in BrS group (n = 14 of 83 [16.9%]) ($P = .013$) (Table 4 and Supplemental Figure 1). Eight patients in the IVF group and 7 in the BrS group were diagnosed with AF using a 12-lead ECG. The occurrence of overall inappropriate ICD therapies was not different between the groups, but inappropriate ICD therapies triggered by ATA events more frequently occurred in the IVF group (n = 12 [23.5%]) than in the BrS group (n = 7 [8.1%]) (Table 4 and Figure 2). Some interventions for ATAs were required for 17 (33.3%) patients in the IVF group and 12 (14.0%) in the BrS group ($P = .010$). Treatments of ATAs in the IVF and BrS groups were initiation of beta-blocker (16 patients [31.4%] vs 8 patients [9.3%]; $P = .002$), catheter ablation for AF (7 patients [13.7%] vs 4 patients [4.7%]; $P = .100$), and atrial lead implantation (2 patients [3.9%] vs 2 patients [2.3%]; $P = .628$). Other causes of inappropriate ICD therapies in the IVF and BrS groups were T-wave oversensing (4 patients [7.8%] vs 6 patients

Table 1 Baseline characteristics

	IVF (n = 51)	BrS (n = 86)	*P* value
Age, y	38 (29–52)	46 (36–56)	.008
Male	38 (74.5)	84 (97.7)	<.001
Body mass index, kg/m^2	22.1 (19.7–24.9)	23.1 (20.7–25.4)	.236
Family history of sudden death	7 (13.7)	41 (47.7)	<.001
Follow-up duration, mo	107 (58–161)	137 (78–184)	.139
Hypertension	9 (17.6)	19 (22.4)	.662
Diabetes mellitus	3 (5.9)	7 (8.2)	.743
Previous stroke	3 (5.9)	0 (0.0)	.051
Previous vascular disease	1 (2.0)	3 (3.5)	1.000
CHA_2DS_2-VASc score	0 (0–1)	0 (0–1)	.074
ICD indication			<.001
Asymptomatic primary prevention	0 (0.0)	31 (36.0)	
Primary prevention with syncope	2 (3.9)	32 (37.2)	
Secondary prevention	49 (96.1)	23 (26.7)	
Type of ICD			.153
Dual-chamber ICD	24 (47.1)	45 (52.3)	
Single-chamber ICD	13 (25.5)	29 (33.7)	
S-ICD	14 (27.5)	12 (14.0)	
Antiarrhythmic drugs			
Beta-blocker	23 (45.1)	15 (17.4)	.001
Bepridil	3 (5.9)	6 (7.0)	1.000
Quinidine	1 (2.0)	6 (7.0)	.257
Disopyramide	2 (3.9)	5 (5.8)	1.000
Amiodarone	1 (2.0)	1 (1.2)	1.000
Mexiletine	0 (0.0)	1 (1.2)	1.000
Flecainide	0 (0.0)	1 (1.2)	1.000

Values are median (interquartile range) or n (%).

BrS = Brugada syndrome; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category; ICD = implantable cardioverter-defibrillator; IQR = interquartile range; IVF = idiopathic ventricular fibrillation; S-ICD = subcutaneous implantable cardioverter-defibrillator.

[7.0%]; $P = 1.000$), sinus tachycardia (1 patient [2.0%] vs 4 patients [4.7%]; $P = .651$), and lead noise (2 patients [3.9%] vs 2 patients [2.3%]; $P = .628$). In contrast, there was no significant difference in the occurrence of appropriate ICD therapies between the groups (Table 4 and Figure 3). The mean ventricular rates during inappropriate ICD therapy by ATAs were 230 and 209 beats/min in the IVF and BrS groups, respectively ($P = .103$).

We subsequently chose patients with documented VF from the BrS group and compared their ATA events with those in the IVF group. Despite narrowing the comparison with patients with BrS who experienced VF, the Kaplan-Meier survival analysis demonstrated a higher incidence of ATAs (Supplemental Figure 2), along with a higher occurrence of inappropriate ICD therapies for ATAs in the IVF group than those in the BrS group (Supplemental Figure 3).

Univariate Cox regression analysis did not reveal any predictive factors associated with ATA occurrence in the IVF cohort (Table 5). Left atrial diameter, VF inducibility on

Table 2 Results of electrocardiogram, echocardiography, and blood exam

	IVF (n = 51)	BrS (n = 86)	*P* value
Heart rate, beats/min	72 (63–79)	61 (56–68)	<.001
PR interval, ms	156 (146–173)	172 (158–188)	.001
QRS duration, ms	102 (93–108)	108 (100–118)	<.001
QTc interval, ms	428 (410–448)	414 (395–433)	.005
Right bundle branch block	4 (7.8)	26 (30.2)	.002
Left bundle branch block	0 (0.0)	0 (0.0)	NA
J-wave	23 (45.1)	7 (8.1)	<.001
LA diameter, mm	31 (27–36)	34 (30–36)	.097
Interventricular septum thickness, mm	9 (8–10)	9 (8–10)	.779
LV end-diastolic diameter, mm	46 (43–49)	47 (44–50)	.114
LV ejection fraction, %	66 (61–69)	67 (64–71)	.02
B-type natriuretic peptide, pg/mL	13.0 (6.4–23.1)	9.7 (7.0–16.6)	.142
Creatinine, mg/dL	0.76 (0.62–0.82)	0.78 (0.71–0.87)	.074

Values are median (interquartile range) or n (%).

BrS = Brugada syndrome; IQR = interquartile range; IVF = idiopathic ventricular fibrillation; LA = left atrium; LV = left ventricle; NA = not available.

Table 3 Additional tests performed to confirm the diagnosis

	IVF (n = 51)	BrS (n = 86)	*P* value
ECG	51 (100.0)	86 (100.0)	NA
Transthoracic echocardiography	51 (100.0)	86 (100.0)	NA
Cardiac MRI	34 (66.7)	43 (50.0)	.063
Coronary angiography	50 (98.0)	75 (87.2)	.153
Electrophysiological study	41 (80.4)	77 (89.5)	.087
Signal-averaged ECG	39 (76.5)	72 (83.7)	.453
Coronary spasm induction	39 (76.5)	27 (31.4)	<.001
Pilsicainide challenge test	39 (76.5)	74 (86.0)	.310
Exercise test	32 (62.7)	63 (73.3)	.311
Endomyocardial biopsy	31 (60.8)	46 (53.5)	.359
Gallium scintigraphy	23 (45.1)	4 (4.7)	<.001
Adrenaline provocation	12 (23.5)	7 (8.1)	.018

Values are n (%).
BrS = Brugada syndrome; ECG = electrocardiogram; IVF = idiopathic ventricular fibrillation; MRI = magnetic resonance imaging; NA = not available.

electrophysiological studies, and J-wave presence also showed a lack of correlation with ATA occurrence.

Discussion

Major findings

A major finding of the present study was that ATAs frequently occurred in patients with IVF. ATAs occurred in 43% of patients with IVF, including those with a history of AF. ATAs were newly identified in 39.2% of IVF cases during follow-up. ATAs also caused inappropriate ICD therapies more frequently in the IVF group than in the BrS group.

ATAs in IVF and BrS patients

It has been reported that the incidence of AF and atrial flutter is higher in BrS cases compared with the general population.[6] The incidence of ATAs in the BrS group in the present study

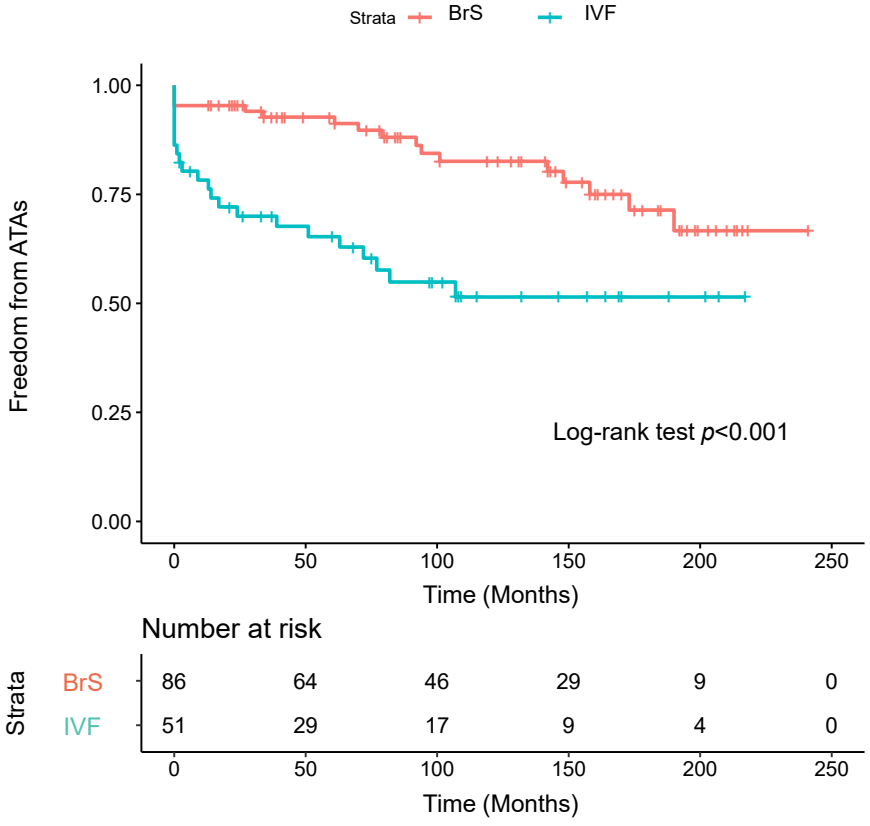

Figure 1 Kaplan-Meier curve analyzing freedom from atrial tachyarrhythmias (ATAs). ATA-free survival is significantly higher in patients with Brugada syndrome (BrS) than in those with idiopathic ventricular fibrillation (IVF).

Table 4 Incidence of ATAs and inappropriate and appropriate ICD therapies

	IVF (n = 51)	BrS (n = 86)	*P* value
Overall ATAs	22 (43.1)	17 (19.8)	.006
ATAs detected after ICD implantation*	20 (39.2)	14 (16.3)	.004
ATAs detected before ICD implantation†	4 (7.8)	3 (3.5)	.424
New ATA occurrence after ICD implantation‡	18 (39.1)	14 (16.9)	.013
Inappropriate ICD therapy	17 (33.3)	17 (19.8)	.101
Inappropriate ICD therapy for ATAs	12 (23.5)	7 (8.1)	.020
Appropriate ICD therapy	14 (27.5)	23 (27.1)	1.00

Values are n (%).

ATA = atrial tachyarrhythmia; BrS = Brugada syndrome; ICD = implantable cardioverter-defibrillator; IVF = idiopathic ventricular fibrillation.

*Number of patients developing ATAs during the follow-up period, with or without previous atrial fibrillation.

†Number of patients with previous atrial fibrillation.

‡Number of patients developing ATAs during the follow-up period without previous atrial fibrillation.

was 19.8%, consistent with the previously reported incidence. Previous studies reported that the interatrial conduction delay and atrial vulnerability was significantly increased in patients with BrS and AF compared with those in individuals without AF.[7,9] Furthermore, Toh and colleagues[14] reported that patients with high-risk BrS had increased left atrial volume and interatrial conduction time, even in the absence of AF.

In contrast to BrS, there are few reports on the incidence and significance of ATAs in IVF. [15] Both patients with BrS and those with IVF have normal cardiac function and do not have a significant organic heart disease; therefore, electrophysiological characteristics of arrhythmias could be similar. In our study, ATAs were found in 43.1% of patients with IVF, despite their younger median age (38 years), and this incidence was higher than in those with BrS. The observations from the present study suggest that patients with IVF may have greater atrial vulnerability to ATAs than those with BrS. Atrial electrical abnormalities could be more severe in patients with IVF than in

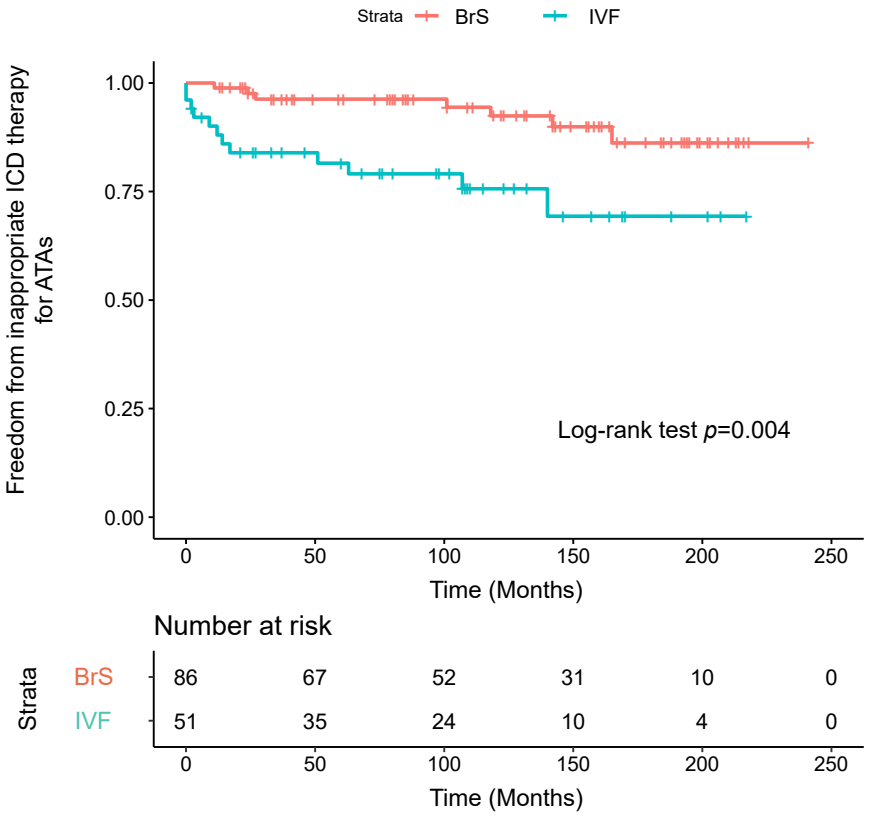

Figure 2 Kaplan-Meier curve analyzing freedom from inappropriate implantable cardioverter-defibrillator (ICD) therapies for atrial tachyarrhythmias (ATAs). Inappropriate ICD therapies for ATAs-free survival is significantly higher in patients with Brugada syndrome (BrS) than in those with idiopathic ventricular fibrillation (IVF).

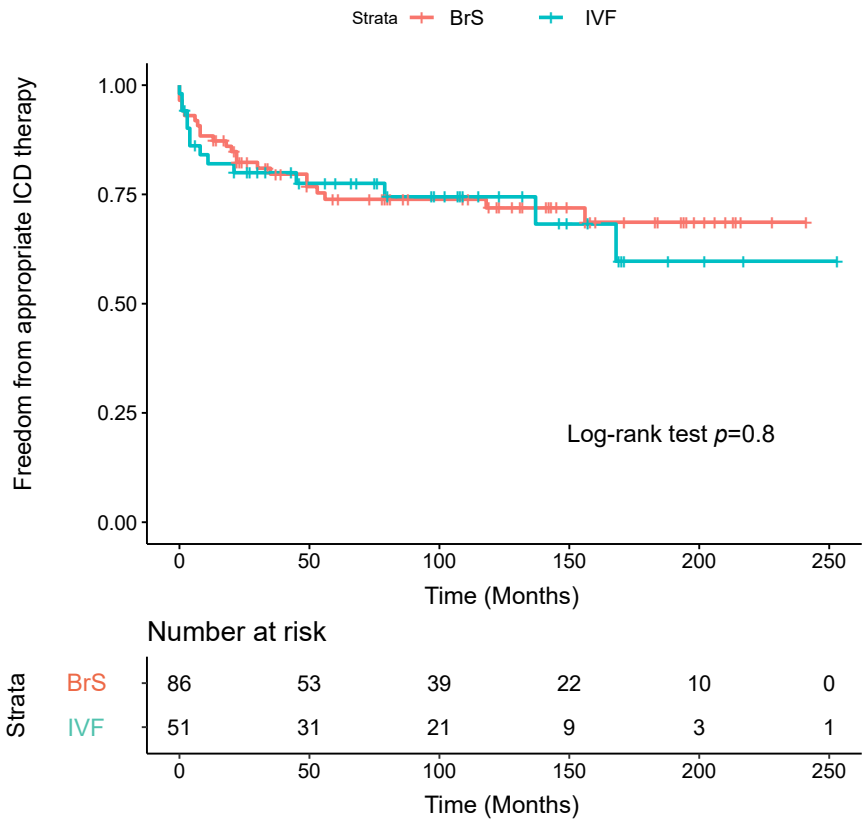

Figure 3 Kaplan-Meier curve analyzing freedom from appropriate implantable cardioverter-defibrillator (ICD) therapies. Appropriate ICD therapy–free survival is significantly higher in patients with Brugada syndrome (BrS) than in those with idiopathic ventricular fibrillation (IVF).

those with BrS, while the atrial structure evaluated by imaging modalities was similar in both groups. We could not determine the risk factor for ATAs in patients with IVF, and the mechanisms underlying this difference remain unclear.

Patients with BrS who received an ICD for secondary prevention experienced more arrhythmic events than those who received an ICD for primary prevention.[16,17] The greater number of patients in the IVF group receiving ICDs for secondary prevention compared with the BrS group in this study could be related to the difference in ATA frequency. Therefore, we compared the IVF group with only those patients with BrS who experienced VF. This comparison revealed that the incidence of ATAs was significantly higher in the IVF group than in BrS group, even when limited to patients with BrS who experienced VF (Supplemental Figure 2). Additionally, ATAs caused an important clinical problem: inappropriate ICD therapies.

Inappropriate ICD therapies

ICD implantation is essential for high-risk patients with BrS or IVF to prevent sudden cardiac death. However, inappropriate ICD therapy is not rare in these patients,[3,5] and it reduces their quality of life and increases mortality.[18] Previous studies have shown that patients with BrS are generally younger than those with structural heart disease, and sinus tachycardia or ATAs with rapid ventricular rates frequently trigger inappropriate ICD shocks.[19,20]

This study showed that ATAs caused inappropriate ICD therapies more frequently in the IVF group than in BrS group. Clinicians should be aware of new onset of ATAs when following up IVF patients. Therefore, ICD programming is important. Adjustments such as VF zone change, prolongation of detection intervals, and supraventricular tachycardia discrimination are useful for distinguishing sinus tachycardia or ATAs from true VF events.[21] Nishii and colleagues[22] reported that immediate intervention after the first inappropriate ICD therapy could reduce the risk of the second inappropriate event. In the present study, some interventions were also performed in IVF patients who developed ATAs. However, this study has not evaluated the effectiveness of pharmacological treatment and ablation for ATAs in IVF patients, highlighting the requirement for further investigations in this area.

Limitations

This study has several limitations. First, this was a nonrandomized retrospective observational study. Given the retrospective, observational nature of this study, several diagnostic tests were not systematically conducted. Consequently, there may be a certain number of patients with undiagnosed abnormalities who do not meet the criteria

Table 5 Univariate Cox regression analysis for development of ATAs in patients with IVF

	Unadjusted HR	95% CI	*P* value
Age	0.991	0.963–1.019	.519
Male sex	1.158	0.426–3.140	.774
Family history of sudden death	1.373	0.404–4.668	.611
LA diameter	0.998	0.928–1.073	.948
Positive for late potential	0.543	0.217–1.357	.191
VF inducibility on EPS	1.390	0.448–4.314	.569
Hypertension	1.030	0.348–3.047	.957
Diabetes mellitus	0.844	0.112–6.340	.869
Body mass index	0.950	0.841–1.073	.411
Follow-up duration	0.996	0.989–1.003	.301
Type of ICD	0.751	0.446–1.263	.280
Heart rate	0.980	0.948–1.013	.236
PR interval	0.990	0.971–1.009	.301
QRS duration	0.998	0.976–1.021	.881
QTc interval	1.004	0.983-1.023	.700
J-wave	0.741	0.316–1.734	.489

ATA = atrial tachyarrhythmia; CI = confidence interval; EPS = electrophysiological study; HR = hazard ratio; ICD = implantable cardioverter-defibrillator; IVF = idiopathic ventricular fibrillation; LA = left atrium; VF = ventricular fibrillation.

for IVF. However, echocardiography was performed during the follow-up period, which ruled out progressive cardiomyopathy. Pilsicainide challenge test was not conducted in a few IVF patients because of the absence of spontaneous coved-type ST-segment elevation (type 1 ECG) in the right precordial leads, even immediately before and after VF, and the absence of type 1 ECG in the high intercostal ECG recording during the follow-up period. Second, approximately 50% of patients were implanted with a single-chamber ICD or S-ICD, indicating that the actual ATA occurrence may have been higher than our current data suggest. Third, because ATAs in this study were diagnosed mainly by intracardiac ECGs recorded on ICDs, atrial flutter or atrial tachycardia may have been included along with AF.

Conclusion

ATAs with rapid ventricular response were more frequently observed in patients with IVF than in those with BrS. Moreover, ATAs often induce inappropriate ICD therapies in patients with IVF. Clinicians need to consider the recurrence of not only VF, but also the development of ATAs for better management of IVF cases. Patients with IVF might have higher atrial vulnerability and enhanced atrioventricular conduction compared with those with BrS.

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Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent: All patients gave their written informed consent for using the remote monitoring system.

Ethics Statement: This study was approved by the Ethics Committee on Human Research and Epidemiology of Okayama University and each hospital. This study adhered to ethical principles consistent with the Declaration of Helsinki.

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