

[ORIGINAL ARTICLE]

Optimal Medications and Appropriate Implantable Cardioverter-defibrillator Shocks in Aborted Sudden Cardiac Death Due to Coronary Spasm

Shozo Sueda¹ and Hiroaki Kohno²

Abstract:

Objective Life-threatening ventricular arrhythmias are recognized in patients with coronary spastic angina. Implantable cardioverter-defibrillators (ICDs) are effective in patients with structural heart disease and ventricular fibrillation. However, the optimal medication for patients with aborted sudden cardiac death (SCD) due to coronary artery spasm after the implantation of ICD remains controversial.

Methods We investigated the medications and the numbers of appropriate ICD shocks in 137 patients with a history of aborted SCD due to coronary spasm.

Results Appropriate ICD shocks were observed in 24.1% (33/137) of patients with aborted SCD due to coronary spasm during 41 months of follow-up. Only 15 (15.6%) of the 96 patients with ICDs received aggressive medical therapy, including two or three calcium-channel antagonists. The rate of appropriate ICD shocks was significantly higher in Western countries than in Asian countries (42.9% vs. 19.3%, $p < 0.01$), whereas the medications did not differ between the two regions. Appropriate ICD shocks successfully resuscitated 33 patients. Three patients died due to second serious fatal arrhythmias.

Conclusion Appropriate ICD shocks were recognized in a quarter of patients with aborted SCD due to coronary spasm and ICD implantation was effective for suppressing the next serious fatal arrhythmia in these patients. We should reconsider prescribing more medications after ICD implantation in patients with aborted SCD due to coronary artery spasm.

Key words: implantable cardioverter-defibrillator, coronary artery spasm, aborted sudden cardiac death, ventricular fibrillation, coronary spastic angina

(Intern Med 57: 1361-1369, 2018)

(DOI: 10.2169/internalmedicine.8796-17)

Introduction

Life-threatening ventricular arrhythmias after resuscitation from aborted sudden cardiac death (SCD) in patients with coronary artery spasm are a major problem in the clinical setting (1). Under optimal medical therapy, including calcium-channel antagonists or nitrates, in the majority of cases, coronary spastic angina shows a good clinical course, whereas patients with aborted SCD due to coronary artery spasm may have a poor prognosis (2-6). Implantable cardioverter-defibrillators (ICDs) have been effective in patients with structural heart disease and ventricular fibrilla-

tion (7). The majority of the clinical reports published in the recent era concluded that ICDs were useful in patients with aborted SCD due to coronary artery spasm (8-11). However, although these patients received optimal medical therapy, we had no data about the appropriate ICD shocks that were administered to patients with aborted SCD due to coronary spasm after ICD implantation. We analyzed the past reports about appropriate ICD shocks and the medications that were administered after ICD implantation in patients with aborted SCD due to coronary artery spasm. We also compared the rates of appropriate ICD shocks and medications in patients from Western and Asian countries.

¹Department of Cardiology, Ehime Prefectural Niihama Hospital, Japan and ²Department of Cardiology, Tsukazaki Hospital, Japan

Received: January 6, 2017; Accepted: June 12, 2017; Advance Publication by J-STAGE: January 11, 2018

Correspondence to Dr. Shozo Sueda, EZF03146@nifty.com

Table 1. Appropriate Implantable Cardioverter-defibrillator Shocks in Patients with Aborted Sudden Cardiac Death Due to Coronary Artery Spasm.

Reference	Patient number of ICD implantation	Follow-up duration	Patient number with appropriate ICD shocks
12	2	4 m/11 m	2 (100%)
13	1	2 m	0
14	1	-	1 (100%)
11	7	3.5±3.2 year	4 (57.1%)
15	1	6 m	0*
16	1	18 m	0
17	1	4 m	1 (100%)
18	1	1 day	1 (100%)
19	1	14 m	0
20	1	18 m	0
10	1	6 m	0
21	1	2 m	0
22	1	24 m	0
23	1	3 m	1 (100%)
24	12	19 m (1-48 m)	1** (8.3%)
25	1	12 m	1*** (100%)
26	14	32 m (17-46 m)	2 (14.3%)
8	23	2.9 years (median 2.1 year)	4 (17.4%)
27	13	17±14 m (1-40 m)	1 (7.7%)
28	14	69±82 m	5 (35.7%)
29	1	24 m	1 (100%)
30	2	12 m	0
31	1	12 m	0
32, 33	2	36 m	1 (50%)
34	1	-	0*
35	6	18±23 m (6-60 m)	0
36	1	24 m	0*
37	1	-	1**** (100%)
38	24	7.5 years (4.0-11.8 years)	6 (25%)
Total	137	41±28 m	33 (24.1%)

*: after percutaneous coronary intervention, **: with Burgada syndrome, ***: cocaine induced, ****: after SES (Cypher)

ICD: implantable cardioverter-defibrillator, m: month

Materials and Methods

Study subjects

We extracted the papers published about ICD implantation in patients with coronary spastic angina from the PubMed database. We were able to analyze 137 patients who underwent the implantation of an ICD after the aborted SCD due to coronary artery spasm. Among the 137 patients, one patient had coronary artery spasm and Burgada syndrome, another patient had cocaine-induced spasm and one underwent ICD implantation after the implantation of a sirolimus-eluting stent (Cypher). We investigated the frequency of appropriate ICD shocks and compared the coronary risk factors, arteries with proven spasm, the medications and the prognosis after the implantation of ICD between patients with and without appropriate ICD shocks. Moreover, we compared Western and Asian patients with aborted SCD due

to coronary artery spasm after ICD implantation, because coronary artery spasm has been reported to occur more frequently in Asian countries than in Western countries.

Statistical analysis

All of the data were presented as the mean±1 standard deviation (SD). All of the categorical variables were analyzed by Fisher's exact test with correction or by the Mann-Whitney U test. p values of <0.05 were considered to indicate statistical significance.

Results

Appropriate ICD shocks

As shown in Table 1, 137 patients underwent ICD implantation after aborted SCD due to coronary artery spasm (8-38). During the follow-up period (41±28 months), appropriate ICD shocks were observed in 33 patients

Table 2. Comparisons of Coronary Risk Factors between Patients with and without Appropriate Implantable-cardioverter Defibrillator Shocks.

	With appropriate ICD shocks	Without appropriate ICD shocks	p value
Number of patients	7	36	
Age (y)	46.7±10.1	50.3±13.3	0.075
Male	3 (42.9%)	32 (88.9%)	0.019
History of smoking	3 (42.9%)	31 (86.1%)	0.038
Hypertension	3 (42.9%)	11 (30.6%)	0.845
Dyslipidemia	1 (14.3%)	10 (27.8%)	0.783
Diabetes mellitus	0	1 (2.8%)	0.355

ICD: implantable-cardioverter defibrillator

(24.1%). However, the remaining 104 patients (75.9%) had no ICD shocks. All 33 patients had second ventricular tachycardia, fibrillation, or pulseless electrical activity, and appropriate ICD shocks successfully resuscitated 33 patients. Three patients were not successfully resuscitated. Inappropriate ICD shocks were observed in four patients (2.9%) for sinus tachycardia (n=2) or the double counting of the QRS by the ICD. Multiple appropriate ICD shocks were observed in 10 (30.3%) of the 33 patients; the mean number of appropriate ICD shocks among these 10 patients was 2.6±1.1.

Coronary risk factors

As shown in Table 2, we could only analyze the coronary risk factors in 43 (31.4%) patients; the records of the remaining 94 patients were missing data about coronary risk factors. Appropriate ICD shocks were observed in 7 (16.3%) of 43 patients, while the remaining 36 patients (83.7%) received no ICD shocks. The rates of male sex and a history of smoking in patients without appropriate ICD shocks were significantly higher than in those with appropriate ICD shocks.

Provable artery spasm

We could only analyze the 63 (45.6%) cases involving provable artery spasm. These included 24 Western patients and 39 Asian patients. Appropriate ICD shocks were observed in 19 patients, while 44 patients had no appropriate ICD shocks. The incidence of provable spasm in each of the three coronary arteries did not differ between the patients with and without appropriate ICD shocks [right coronary artery (RCA): 68.4% (11/19) vs. 50.0% (22/44), ns, left circumflex artery (LCX): 57.9% (11/19) vs. 50.0% (22/44), ns, left anterior descending artery (LAD): 63.2% (12/19) vs. 72.7% (32/44), ns]. Moreover, the rates of provable spasm in each of the three coronary arteries of patients with appropriate ICD shocks did not differ between Western and Asian patients [RCA: 81.8% (9/11) vs. 50.0% (4/8), ns, LCX: 45.5% (5/11) vs. 75.0% (6/8), ns, LAD: 54.5% (6/11) vs. 75.0% (6/8), ns].

Pharmacological spasm provocation tests

Pharmacological spasm provocation tests were performed in 55 (40.1%) patients, including 4 Western and 51 Asian

patients. Invasive spasm provocation tests were performed significantly more frequently in Asian countries than in Western countries [46.8% (51/109) vs. 14.3% (4/28), $p < 0.01$], while spasm provocation tests in both the RCA and LCA were performed significantly more frequently in Asian countries than in Western countries [22.0% (24/109) vs. 3.6% (1/28), $p < 0.05$]. However, angiographic spontaneous spasm observed significantly more frequently in Western countries than in Asian countries [35.7% (10/28) vs. 0.9% (1/109), $p < 0.001$].

Medications in patients with appropriate ICD shocks

Table 3 shows the medications in 33 patients with appropriate ICD shocks. We could not analyze the medications in 11 patients (33.3%) because of missing data. Only 5 patients (15.2%) received 2 or 3 calcium-channel antagonists, while 17 patients (51.5%) had been treated with a single calcium-channel antagonist. Nitrates or nicorandils were administered to 13 patients (39.4%). Only one patient (3%) was treated with triple calcium-channel antagonists. Seven patients (31.8%) were treated with 1 vasodilator, 10 (45.5%) patients were treated with 2 vasodilators and 5 (22.7%) patients were treated with 3 vasodilators.

The medications in patients without appropriate ICD shocks

Table 4 shows the medications that were administered to 104 patients without appropriate ICD shocks. Two or three calcium-channel antagonists were administered to just 10 patients (9.6%), whereas 62 patients (59.6%) were treated with a single calcium-channel antagonist. Nitrates or nicorandils were administered to 55 patients (52.9%). No patients were treated with triple calcium-channel antagonists. Detailed medication information was not available for 30 patients (28.9%). Twelve patients (16.2%) were treated with one vasodilator, while 39 (52.7%) patients received 2 vasodilators or 14 (18.9%) patients received 3 vasodilators. Moreover, 2 (2.7%) patients received no medications, while 3 (4.1%) patients were treated with four vasodilators.

The medications and appropriate ICD shocks in patients from Western and Asian countries

The rate of appropriate ICD shocks was significantly

Table 3. Medications and Spasm Sites in Aborted Coronary Spastic Angina Patients with Appropriate Implantable Cardioverter-defibrillator Shocks.

Reference	Age/ Sex	No of pts	Spasm vessel	Follow-up duration	Medication
Western countries					
12	56/M	1	LAD/ RCA	4 m	CCB (unknown)
	36/F	1	LCX/RCA	11 m	Diltiazem (dose unknown)
14	60/M	1	LAD	unknown	unknown
11	42/M	1	LAD/LCX/RCA	25 m	Diltiazem 60 mg, Verapamil 80 mg, ISDN 80 mg,
	42/M	1	LAD/LCX/RCA	60 m	Diltiazem 60 mg, Verapamil 80 mg, Nifedipine 40 mg
	46/M	1	RCA	18 m	Diltiazem 120 mg
	47/M	1	LAD/RCA	120 m	Nifedipine 30 mg, Verapamil 120 mg, ISMN 20 mg
17	50/M	1	RCA	4 m	Amlodipine
18	40/F	1	RCA/LAD	1 day	unknown
23	38/F	1	LCX	3 m	CCB (unknown), nitrate (unknown)
25	54/M	1	RCA	12 m	CCB & nitrates (maximum dose)
32, 33	52/F	1	LAD/LCX	36 m	Amlodipine 10 mg, Nifedipine 30 mg, Nicorandil 10 mg
Asian countries					
24	57/M	1	unknown	25 m	Benijipine 2 mg
26		2	unknown	unknown	unknown
8		4	LAD(4)/LCX(5)/RCA(3)	unknown	Diltiazem (5), ISMN (2), nicorandil (2)
27	33/M	1	LAD	6 m	Diltiazem 200 mg, ISMN 40 mg
28		5	unknown	unknown	CCBs (5), nitrates or nicorandil (3)
29	53/F	1	RCA/LCX	3 m	Diltiazem 240 mg, ISMN 40 mg, Nicorandil 15 mg, Amiodarone 200 mg
37	57/M	1	LAD	unknown	unknown
38		6	unknown	unknown	unknown

M: male, F: female, No of pts: Number of patients, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, m: month, ISDN: isosorbide dinitrate, ISMN: isosorbide mononitrate, CCB: calcium channel blocker

higher among patients from Western countries than those from Asian countries (42.9% vs, 19.3%, $p < 0.01$), as shown in Fig. 1. However, the medications that were administered after the implantation of an ICD in patients with aborted SCD due to coronary spasm did not differ between patients from Western and Asian countries.

The medications administered to patients with and without appropriate ICD shocks

As shown in Table 5, the medications in patients with appropriate ICD shocks did not differ from those in patients without appropriate ICD shocks. One calcium-channel antagonist was administered to 77.3% of the patients with appropriate ICD shocks, whereas 83.8% of the patients without appropriate ICD shocks were treated with 1 calcium-channel antagonist. In contrast, more than 3 vasodilators were administered to 22.7% of the patients with appropriate ICD shocks, while 24.3% of the patients without appropriate ICD shocks were treated with three or four vasodilators. We could only analyze the dosage of calcium-channel antagonists and nitrates/nicorandils in 45 (32.8%) patients (Table 6). Diltiazem and nicorandil were often administered to patients in Asian countries, while verapamil was most frequently administered in Western countries. However, with the exception of diltiazem, the dosages did not differ between the two countries. Eight patients were treated with amiodarone, including one patient with appropriate ICD

shock.

The prognosis after the appropriate ICD shocks

Appropriate ICD shocks were effective in suppressing ventricular tachycardia in 3 patients, ventricular tachycardia or fibrillation in 9 patients and ventricular fibrillation in 21 patients. Three patients with aborted SCD due to coronary spasm, who had undergone the implantation of an ICD, died during the follow-up period. One patient died due to pulseless electrical activity despite the continuous delivery of electrical therapy by the ICD, the second patient died due to intractable ventricular fibrillation, and the third patient died due to electromechanical dissociation and severely reduced left ventricular contraction despite appropriate ICD therapy. With the exception of the 3 patients who died, all 33 who received appropriate ICD shocks were rescued from second ventricular fibrillation/tachycardia. As shown in Fig. 2, 8 patients each from Western and Asian countries received appropriate ICD shocks. Within 12 months, appropriate ICD shocks were recognized in 10 (62.5%) of 16 patients. The details of the periods in which the appropriate ICD shocks were delivered were not found in 17 patients.

Discussion

During the 41-month follow-up period, appropriate ICD shocks were recognized in 24.1% of the patients with

Table 4. Medications and Spasm Sites in Aborted Coronary Spastic Angina Patients without Appropriate Implantable Cardioverter-defibrillator Shocks.

Reference	Age/Sex	No of pts	Spasm vessel	Follow-up duration	Medication
Western countries					
13	70/M	1	LAD/LCX	2 m	Verapamil 180 mg, ISMN 60 mg
11	40/M	1	LAD	60 m	Nifedipine 30 mg, Diltiazem 60 mg, Verapamil 120 mg, ISDN 20 mg
	53/M	1	LAD	3 m	Verapamil 240 mg, ISDN 50 mg
	68/M	1	LAD	27 m	Diltiazem 60 mg, Amlodipine 10 mg, ISDN 40 mg
15	47/F	1	LAD	6 m	Verapamil 320 mg, Transdermal NTG 15 mg
16	60/M	1	RCA	18 m	Diltiazem dose unknown, Nitrates dose unknown
19	49/M	1	LAD/LCX	14 m	Amlodipine 10 mg, Transdermal Nitrate 5 mg
20	50/M	1	LAD/RCA	18 m	CCB unknown
10	58/F	1	RCA	6 m	Nifedipine dose unknown
21	Middle age/F	1	LCX	2 m	CCB unknown, Nitrates unknown
22	46/M	1	unknown	24 m	Diltiazem dose unknown, ISMN dose unknown
30		2	LAD & LCX	12 m	Amlodipin & metropolo (1), CCB & nitrate (1)
32, 33	54/M	1	LMT	18 m	Nifedipine 30 mg, Verapamil 240 mg
34	54/M	1	LAD	-	CCB unknown. Long-acting nitrate unknown
36	59/M	1	RCA	24 m	Nifedipine 60 mg, ISMN 60 mg
Asian countries					
24		11	unknown	18.5±12.5 m	Benidipine 2/4/8 mg (1/2/2), Benidipine 8 mg/Diltiazem 200 mg (2), Diltiazem 200 mg (1), Amlodipine 5 mg (1), CCB (-) (2)
26		12	unknown	unknown	unknown
8		19	LAD(11)/LCX(12)/RCA(18)	2.9 year (median 2.1 year)	Diltiazem (19), ISMN (13), Nicorandil (10)
27		12	LAD(12)/LCX(6)/RCA(1)	18±14 m	Diltiazem 200 mg & ISMN 40 mg (2), Diltiazem 200 mg/Nicorandil 10-20 mg/ ISMN 20-40 mg (5), Diltiazem 200 mg/Benidipien 8 mg/ Nicorandil 15-20 mg/ISMN 40-80 mg (2), Diltiazem 200 mg/Benidipine 16 mg/ Nicorandil 20 mg (1), Diltiazem 200 mg/Nifedipien 20 mg/ Nicorandil 20 mg/ISMN 40 mg (1), Nifedipine 20 mg & Amlodipine 5 mg (1)
28		9	unknown	69±82 m	CCBs (9), nitrates or nicorandils (6)
31	68/M	1	RCA	12 m	Diltiazem 400 mg, ISDN 40 mg, Nicorandil 15 mg
35		6	unknown	18±23 m	Nifedipine CR 40/60 mg & ISDN 40 mg (2/1), Nifedipine 40 mg & Nicorandil 15 mg (1), Amlodipine 5 mg & ISDN 40 mg (1), Diltiazem R 200 mg ISDN 40 mg Nicorandil 15 mg (1)
38		18	unknown	unknown	unknown

M: male, F: female, No of pts: Number of patients, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, LMT: left main trunk, m: month, ISDN: isosorbide dinitrate, ISMN: isosorbide mononitrate, CCB: calcium channel blocker, (): number of patient

aborted SCD due to coronary artery spasm who underwent ICD implantation. Only 15.6% (15/96) of the patients were treated with aggressive medical therapy including two or three calcium-channel antagonists. The rate of appropriate ICD shocks was significantly higher in patients from Western countries than in those from Asian countries; however, the medications did not differ between the two regions. Appropriate ICD shocks resuscitated 33 patients; 3 patients

died due to second ventricular fibrillations/tachycardia. The implantation of ICDs in patients with aborted SCD due to coronary spasm was effective in resuscitating these patients from their next life-threatening ventricular arrhythmias.

Although these 33 patients underwent ICD implantation, medications might not have been sufficient for suppressing the patients' next life-threatening ventricular arrhythmias due to coronary artery spasm. We should administer more

calcium-channel antagonists and nitrates/nicorandils in these near-miss patients. We did not find any patients who were treated with aggressive medical therapy among the patients without ICD shocks. Three patients died despite receiving appropriate ICD shocks after aborted SCD. If they had re-

ceived more aggressive medical therapy, such as two or three calcium-channel antagonists, the implantation of an ICD might have rescued them. The optimal medications in patients with aborted SCD due to coronary spasm remain controversial; however, cardiologists should reconsider administering multiple medications to patients who are at high risk of serious fatal arrhythmias due to coronary spasm.

Pharmacological spasm provocation tests were defined as class I according to the Japanese Circulation Society guidelines (39), while the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines defined the tests as class IIa or IIb (40, 41). With the exception of cardiologists who worked in small special institutions, Western cardiologists did not perform the pharmacological spasm provocation tests in cardiac catheterization laboratories. In contrast, Asian cardiologists have been performing these tests for more than 30 years. In this series, Asian cardiologists performed pharmacological spasm provocation tests more frequently than their Western

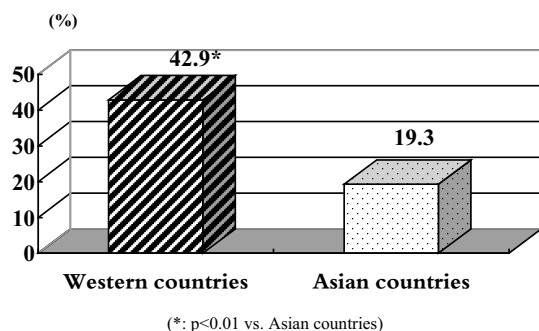


Figure 1. The rates of appropriate ICD shocks in Western and Asian countries. ICD: implantable cardioverter-defibrillator

Table 5. Comparisons of Medications in Patients with Aborted Sudden Cardiac Death with and without Appropriate Implantable Cardioverter-defibrillator Shocks.

	With appropriate ICD shocks				Without appropriate ICD shocks				p value [a] vs. [b]
	Total [a]	Western	Asian	p value	Total [b]	Western	Asian	p value	
Medication unknown	11	2	9		30	0	30		
Medication known	22	10	12		74	16	58		
1 Ca	17 (77.3%)	6 (60.0%)	11 (91.7%)	0.209	62 (83.8%)	13 (81.2%)	49 (84.5%)	0.756	0.482
2 Ca	4 (18.1%)	3 (30.0%)	1 (8.3%)	0.156	10 (13.5%)	3 (18.8%)	7 (12.1%)	0.780	0.733
3 Ca	1 (4.5%)	1 (10.0%)	0	0.925	0	0	0		0.517
Nitrate or nicorandil	13 (59.1%)	5 (50%)	8 (66.7%)	0.721	55 (74.3%)	12 (75.0%)	43 (74.1%)	0.944	0.167
No medication	0	0	0		2 (2.7%)	0	2 (3.4%)	0.906	0.943
1 vasodilator	7 (31.8%)	4 (40.0%)	3 (25.0%)	0.769	12 (16.2%)	2 (12.5%)	10 (17.2%)	0.942	0.106
2 vasodilators	10 (45.6%)	2 (20.0%)	8 (66.7%)	0.078	42 (56.8%)	12 (75.0%)	30 (51.7%)	0.167	0.350
3 vasodilators	5 (22.7%)	4(40.0%)	1 (8.3%)	0.209	14 (18.9%)	1 (6.3%)	13 (22.4%)	0.270	0.693
4 vasodilators	0	0	0		4 (5.4%)	1 (6.3%)	3 (5.2%)	0.865	0.612
Total	33	12	21		104	16	88		

Ca: calcium channel antagonist, ICD: implantable cardioverter-defibrillator

Table 6. Comparisons of Dose of Calcium-channel Antagonists and Nitrates/nicorandil in Patients with Aborted Sudden Cardiac Death with and without Appropriate Implantable Cardioverter-defibrillator Shocks.

	With appropriate ICD shocks			Without appropriate ICD shocks			Total		p value [a] vs. [b]
	Western (n=5)	Asian (n=3)	Total (n=8)	Western (n=9)	Asian (n=28)	Total (n=37)	Western [a] (n=14)	Asian [b] (n=31)	
Diltiazem (mg) (n=23)	80±35	220±28	136±82	60	206±57	190±72	72±27	208±55	0.001
Verapamil (mg) (n=8)	93±23	0	93±23	220±75	0	220±75	173±88	0	1.000
Nifedipine (mg) (n=12)	33±6	0	33±6	40±17	37±15	38±15	38±15	37±15	0.924
Amlodipine (mg) (n=6)	10	0	10	10	5	7±3	10	5	0.095
Benidipine (mg) (n=11)	0	2	2	0	7±4	7±4	0	7±4	1.000
ISMN (mg) (n=14)	20	40	33±12	60	42±15	44±15	40±28	42±13	1.000
ISDN (mg) (n=12)	80	0	80	43±17	40	41±9	50±22	40	0.209
Nicorandil (mg) (n=14)	10	15	13±4	0	17±3	17±3	10	17±3	0.137
Nitrate tape (mg) (n=2)	0	0	0	10±7	30	10±7	10±7	0	1.000
Amiodarone (mg) (n=8)	0	100	100	0	114±38	114±38	0	113±35	1.000

ISMN: isosorbide dinitrate, ISMN: isosorbide mononitrate, ICD: implantable cardioverter-defibrillator

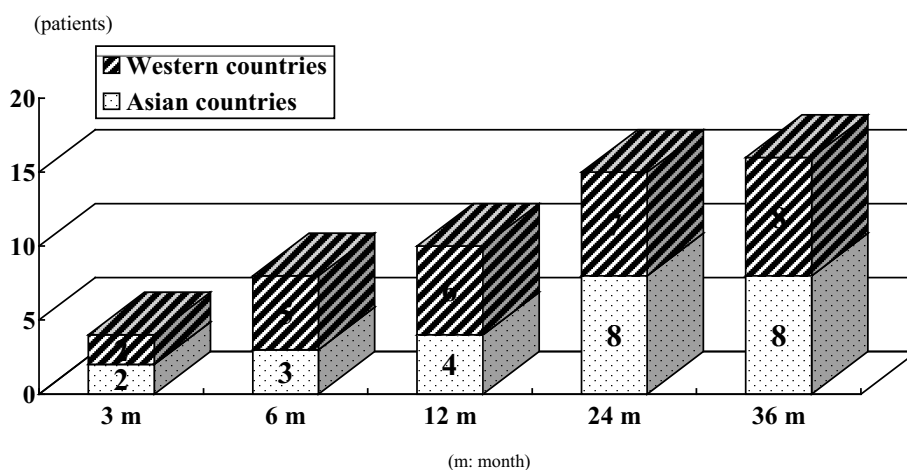


Figure 2. The total population of patients with appropriate ICD shocks in Western and Asian countries. ICD: implantable cardioverter-defibrillator

counterparts. The incidence of ventricular tachycardia or ventricular fibrillation during pharmacological spasm provocation tests in Asian countries was significantly higher than in Western countries, whereas the rates of cardiogenic shock, acute coronary syndrome and death in Asian countries were remarkably lower in comparison to Western countries (42). The incidence of coronary artery spasm was three times higher in Asian countries than in Western countries. We had no data about the precise frequency of ICD implantation in patients with aborted SCD due to coronary spasm in Western and Asian countries. Although the medications after ICD implantation did not differ between Western and Asian countries, the rate of appropriate ICD shocks in patients in Western countries was significantly higher in comparison to those in Asian countries. We did not understand the reasons for the higher incidence of appropriate ICD shocks in Western countries. However, these patients might have higher disease activity than Asian patients. Actually, angiographic spontaneous spasm was more often observed in Western countries than in Asian countries.

According to the Japanese Circulation Society (JCS) guidelines for the non-pharmacotherapy of cardiac arrhythmia (43), ICD implantation was defined as class IIb when patients were at high risk of next fatal arrhythmia, such as ventricular fibrillation or tachycardia due to coronary spasm, irrespective of whether they received appropriate medical therapy. Medical therapy is the first-line treatment for patients with aborted SCD due to coronary spasm. In the clinic, we had no precise strategy for ICD implantation in patients with aborted SCD due to coronary vasospasm. Eschaliier et al. reported the clinical use of ergonovine tests under the optimal medications when cardiologists considered the necessity of ICD implantation in patients with aborted SCD due to coronary spasm (32). We also reported the results of pharmacological spasm provocation testing under patients with refractory spasm who were treated with medical therapy (44). ICD implantation may not be always necessary for patients with aborted SCD who had life-

threatening ventricular arrhythmia and coronary spasm. Actually, in this short article, appropriate ICD shocks were not recognized in three quarters of the patients. Pharmacological spasm provocation tests in patients receiving appropriate medical therapy may become a clinical tool that can be used to differentiate patients with aborted SCD due to coronary spasm require ICD implantation. However, at present, we are of the opinion that ICD implantation in patients with aborted SCD due to coronary spasm may be adequate for classifying a patient as class IIb, because we had no prospective data about the appropriate ICD shocks that were delivered in these patients.

Limitations

The present study was associated with some limitations. First was a retrospective study. Moreover, there were selection and publication biases in the published papers. Second, the same categorical data were not available to compare each of the issues in all of the 137 patients. We were able to analyze the dosage of calcium channel antagonists or nitrate/nicorandil and coronary risk factors in less than a third of the patients. We tried to analyze these data using a multivariate regression analysis. However, we could not obtain statistically significant results due to the data that were missing in each paper. Further prospective studies will be necessary to investigate the optimal treatments for suppressing the next serious fatal arrhythmia after ICD implantation in patients with aborted SCD due to coronary spasm.

Conclusions

After ICD implantation in patients with aborted SCD due to coronary artery spasm, appropriate ICD shocks were observed in a quarter of these patients during the 41-month follow-up period. Cardiologists should reconsider administering more medications, including two or three calcium channel antagonists, to patients with aborted SCD due to coronary artery spasm as well as ICD implantation.

The authors state that they have no Conflict of Interest (COI).

References

- Modi S, Krahn AD. Sudden cardiac arrest without overt heart disease. *Circulation* **123**: 2994-3008, 2011.
- Miller DD, Waters DD, Szlachcic J, Theroux P. Clinical characteristics associated with sudden death in patients with variant angina. *Circulation* **66**: 588-592, 1982.
- Bott-Silverman C, Heupler FA. Natural history of pure coronary artery spasm in patients treated medically. *J Am Coll Cardiol* **2**: 200-205, 1983.
- Nakamura M, Takeshita A, Nose Y. Clinical characteristics associated with myocardial infarction, arrhythmias, and sudden death in patients with vasospastic angina. *Circulation* **75**: 1110-1116, 1987.
- Yasue H, Takizawa A, Nagao M, et al. Long-term prognosis for patients with variant angina and influential factors. *Circulation* **78**: 1-9, 1988.
- Myerburg RJ, Kessler KM, Mallon SM, et al. Life-threatening ventricular arrhythmia in patients with silent myocardial ischemia due to coronary artery spasm. *N Engl J Med* **326**: 1451-1455, 1992.
- Powell AC, Fuchs T, Finkelstein DM, et al. Influence of implantable cardioverter-defibrillators on the long-term prognosis of survivors of out-of-hospital cardiac arrest. *Circulation* **88**: 1083-1092, 1993.
- Matsue Y, Suzuki M, Nishizaki M, Hojo R, Hashimoto Y, Sakurada H. Clinical implications of an implantable cardioverter-defibrillator in patients with vasospastic angina and lethal ventricular arrhythmia. *J Am Coll Cardiol* **60**: 908-913, 2012.
- Mitchell LB. Use of the implantable cardioverter-defibrillator in patients with coronary artery spasm as the apparent cause of spontaneous life-threatening ventricular tachycardia or ventricular fibrillation. *J Am Coll Cardiol* **60**: 914-916, 2012.
- Hendriks ML, Allaart CP, Bronzwaer JGF, Res JJC, Cock CC. Recurrent ventricular fibrillation caused by coronary artery spasm leading to implantable cardioverter defibrillator implantation. *Europace* **10**: 1456-1457, 2008.
- Meisel SR, Mazur A, Chetboun I, et al. Usefulness of implantable cardioverter-defibrillator in refractory variant angina pectoris complicated by ventricular fibrillation in patients with angiographically normal coronary arteries. *Am J Cardiol* **89**: 1114-1116, 2002.
- Lacroix D, Kacet S, Lekieffre J. Vasospastic angina without flow-limiting coronary lesions as a cause for aborted sudden death. *Int J Cardiol* **43**: 247-249, 1994.
- Fuertes J, Gallego P, Peinado R, Merino JL. Implantable cardioverter as therapeutic option for sudden death secondary to severe coronary vasospasm. *Int J Cardiol* **63**: 181-183, 1998.
- Cheng TO. Implantable cardioverter defibrillator for sudden cardiac death secondary to coronary artery spasm. *Int J Cardiol* **65**: 209-210, 1998.
- Fiocca L, Biasi MD, Bruno N, et al. Coronary vasospasm and aborted sudden death treated with an implantable defibrillator and stenting. *Ital Heart J* **3**: 270-273, 2002.
- Postorino C, Gallagher MM, Santini L, et al. Coronary spasm: a case of transient ST elevation and syncopal ventricular tachycardia without angina. *Europace* **9**: 568-570, 2007.
- Al-Sayegh A, Shukkur AM, Akbar M. Automatic implantable cardioverter defibrillator for the treatment of ventricular fibrillation following coronary artery spasm: a case report. *Angiology* **58**: 122-127, 2007.
- Letsas KP, Filippatos GS, Efremidis M, Sideris A, Kardaras F. Secondary prevention of sudden cardiac death in coronary artery spasm: Is implantable cardioverter defibrillator always efficient? *Int J Cardiol* **117**: 141-143, 2007.
- Mascioli G, Bontempi L, Racheli M, Cerini M, Curnis A, Cas LD. Coronary artery spasm as a cause of ST elevation and inappropriate implantable cardioverter defibrillator intervention. *J Cardiovasc Med* **8**: 1055-1057, 2007.
- Walhout RJ, Winter RJ, Simmers TA, Buijs EM. Aborted sudden death in a 52-year-old man without structural heart disease. *Neth Heart J* **16**: 239-241, 2008.
- Lee CH, Seow SC, Lim YT. Lethal presentations of coronary artery spasm after an event-free period of six years following initial diagnosis. *J Invasive Cardiol* **20**: E30-E32, 2008.
- Sovari AA, Cesario D, Kocheril AG, Brugada R. Multiple episodes of ventricular tachycardia induced by silent coronary vasospasm. *J Interv Card Electrophysiol* **21**: 223-226, 2008.
- Bhat PK, Quan KJ. Implantable cardioverter defibrillator (ICD) for polymorphic ventricular tachycardia (VT) due to coronary vasospasm. *J Hosp Med* **4**: E23-E25, 2009.
- Takagi Y, Yasuda S, Takahashi J, et al. Importance of dual induction tests for coronary vasospasm and ventricular fibrillation in patients surviving out-of-hospital cardiac arrest. *Circ J* **73**: 767-769, 2009.
- Yildirim AB, Basaric I, Kucuk M. Recurrent ventricular arrhythmias and myocardial infarctions associated with cocaine induced reversible coronary vasospasm. *Cardiol J* **17**: 512-517, 2010.
- Takagi Y, Yasuda S, Tsunoda R, et al. Clinical characteristics and long-term prognosis of vasospastic angina patients who survived out-of-hospital cardiac arrest. *Circ J Arrhythm Electrophysiol* **4**: 295-302, 2011.
- Ishihara A, Tanaka T, Otsu Y, et al. Prognosis of patients with coronary vasospasm after successful resuscitation from ventricular fibrillation. *J Arrhythm* **28**: 105-110, 2012.
- Nishida J, Kawaukai M, Mochizuki A, et al. Prognosis of vasospastic angina patients who survived cardiac arrest: dose implantable cardioverter-defibrillators have an impact? *J Am Coll Cardiol* **59**(Suppl): E1484, 2012.
- Hiki M, Tokano T, Nakazato Y, Daida H. Recurrent ventricular fibrillation under sufficient medical treatment with coronary artery spasm. *BMJ Case Rep* **2013**: 2013.
- Mullertz KM, Hansen HS. Cardiac arrest caused by coronary arterial vasospasm. *Ugeskr Laeger* **174**: 1676-1677, 2012.
- Kawasaki Y, Kato T, Minamino E, Inoko M. Syncope caused by coronary artery spasm without chest pain leading to ventricular fibrillation. *BMJ Case Rep* **2013**: 2013.
- Eschaliel R, Souteyrand G, Jean F, et al. Should an implanted defibrillator be considered in patients with vasospastic angina? *Arch Cardiovasc Dis* **107**: 42-47, 2014.
- Eschaliel R, Motreff P, Bordachar P. Risk of recurrence after life threatening ventricular arrhythmias in coronary spasm. *Arch Cardiovasc Dis* **107**: 205-206, 2014.
- Mousa TM, Akinseye OA, Goldberg SE. Severe coronary artery spasm and sudden cardiac death : Is there a consensus for management? *J Innov Cardiac Rhythm Manag* **5**: 1657-1660, 2014.
- Yamashina Y, Yagi T, Namekawa A, et al. Favorable outcomes of patients with vasospastic angina associated with cardiac arrest. *J Cardiol* **63**: 41-45, 2014.
- Gullsen K, Ayca B, Cerit L, Okuyan E. Coronary vasospasm-induced periodic ventricular fibrillation and successful ablation through coronary stenting. *Postepy Kardiol Interwencyjnej (Adv Interventional Cardiol)* **42**: 337-340, 2015.
- Goto K, Kurabayashi M, Nakamura T, et al. Aborted sudden cardiac death due to intractable ventricular fibrillation caused by coronary spasm refractory to implantable cardioverter defibrillator therapy. *Int J Cardiol* **176**: e133-e134, 2014.
- Ahn JM, Lee KH, Yoo SY, et al. Prognosis of variant angina manifesting as aborted sudden cardiac death. *J Am Coll Cardiol* **68**: 137-145, 2016.
- JCS joint working group. Guidelines for diagnosis and treatment of patients with vasospastic angina (Coronary spastic angina) (JCS

- 2013). *Circ J* **78**: 2779-2801, 2014.
40. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* **34**: 2949-3003, 2013. Erratum in: *Eur Heart J* **35**: 2260-2261, 2014.
41. Anderson JL, Adams CD, Antman EM, et al. 2012 ACCF/AHA focused update incorporated into the ACCF/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* **127**: e663-e828, 2013. Erratum in: *Circulation* **127**: e863-e864, 2013.
42. Sueda S, Kohno H. Overview of the complications during the pharmacological spasm provocation tests. *J Cardiol* **68**: 1-6, 2016.
43. JCS joint working group. Guidelines for non-pharmacotherapy of cardiac arrhythmia (JCS 2011). [Internet]. [cited 2017 May 8]. Available from: http://www.j-circ.or.jp/guideline/pdf/JCS2011_okumura_h.pdf
44. Sueda S, Kohno H, Miyoshi T, Sasaki Y, Sakaue T, Habara H. Spasm provocation tests performed under medical therapy: a new approach for treating patients with refractory coronary spastic angina on emergency admission. *Intern Med* **53**: 1739-1747, 2014.

The Internal Medicine is an Open Access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

© 2018 The Japanese Society of Internal Medicine
Intern Med 57: 1361-1369, 2018