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【 ORIGINAL ARTICLE 】

Catheter-induced Spasm in the Proximal Right Coronary Artery

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Abstract:

Objectives The clinical characteristics in patients with catheter-induced spasm in the proximal right coronary artery (RCA) are controversial. We performed a clinical analysis of catheter-induced spasm in the RCA.

Methods We retrospectively analyzed 5,296 consecutive patients who underwent diagnostic or follow-up angiography during a 26-year period. During this period, we found 40 patients with catheter-induced spasm in the RCA. We compared the clinical characteristics and procedures of cardiac catheterization in patients with catheter-induced spasm in the RCA with those in patients without such spasm.

Results The frequency of catheter-induced spasm in the RCA was 0.75% (40/5,296). We performed pharmacological spasm provocation tests in 36 of 40 patients after spasm relief. Positive spasm was observed in 32 patients (88.9%), and 25 patients (78.1%) had multiple spasms. The catheter procedures, including the approach sites (radial/brachial/femoral), catheter size (4/5/6Fr) and catheter type (Judkins right/Sones/Shared/Judkins left 3.5/Amplatz) were not markedly different between the two groups. A multivariate analysis showed that positive spasm [odds ratio (OR): 7.030, 95% confidence interval (CI): 1.920-25.700], a younger age (OR: 0.937, 95% CI: 0.910-0.965) and diabetes mellitus (OR: 0.278, 95% CI: 0.083-0.928) were the determinant factors for the catheter-induced spasm.

Conclusion Approximately 80% of patients with catheter-induced spasm in the proximal RCA had coronary spastic angina. Positive provoked spasm was the most powerful determinant factor for catheter-induced spasm.

Key words: catheter-induced spasm, coronary spastic angina, right coronary artery, chest pain, ischemic ECG change

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Introduction

We sometimes encounter the catheter-induced spasm in the proximal right coronary artery (RCA) when we perform diagnostic or follow-up coronary angiography in the cardiac catheterization laboratory. The majority of catheter-induced spasms in the RCA are silent, and spontaneous relief is recognized after the removal of the catheter from the right coronary ostium (1-4). When cardiologists experienced catheter-induced spasm in the RCA, they often administer nitrates to achieve relief. However, cardiologists cannot ascertain the presence or absence of a provoked spasm, even if they perform pharmacological spasm provocation tests after the administration of nitrates for relief. The incidence of catheter-induced spasm may also be related to the size of the catheter used, the catheter approach site, the type of catheter used or the skill of the angiographer. The frequency of catheter-induced spasm may be lower in recent years in the past because the catheters in use have become smaller over time, and the quality of the catheter material has improved. The rate of catheter-induced spasm in a previous report was 0.26-3.0% (5-10), and no relationship between catheter-induced spasm and provoked spasm induced by pharmacological spasm provocation tests was noted.

In this article, we reexamined the incidence of catheter-

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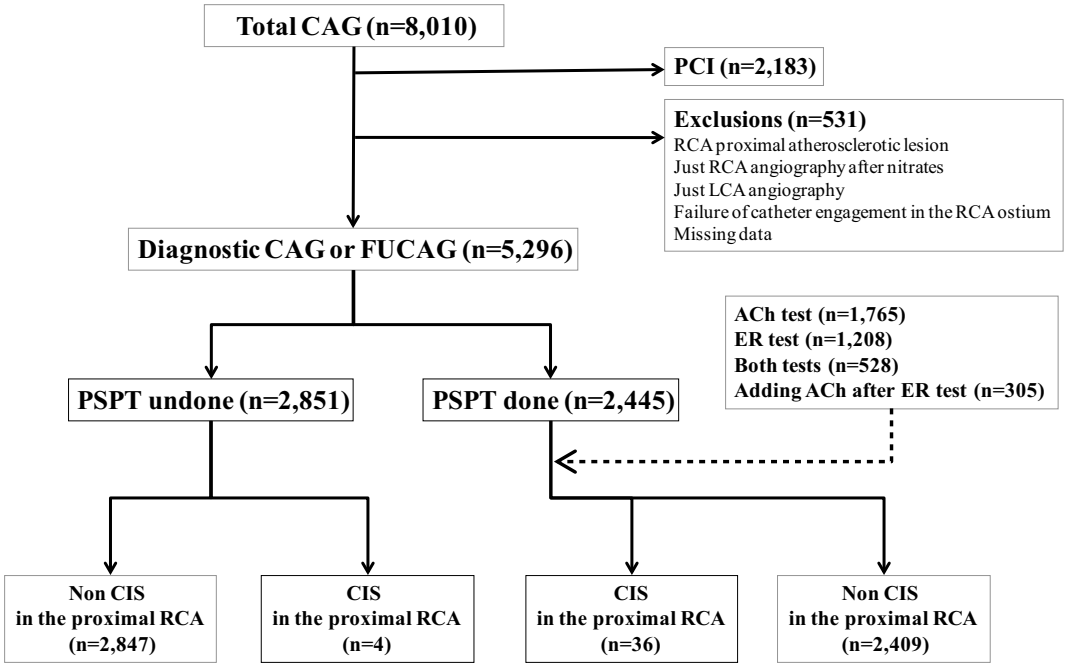

Figure 1. **Study flow chart. CAG: coronary angiography, PCI: percutaneous coronary intervention, RCA: right coronary artery, LCA: left coronary artery, FUCAG: follow-up coronary angiography, PSPT: pharmacological spasm provocation test, ACh: acetylcholine, ER: ergonovine, CIS: catheter-induced spasm**

induced spasm in the RCA and compared the clinical characteristics and procedures of cardiac catheterization in patients with catheter-induced spasm in the RCA with those in patients without such spasm.

Materials and Methods

Study patients

The study flow chart is shown in Fig. 1. From January 1991 to November 2016, we performed a total of 8,010 coronary angiography procedures, including 2,183 percutaneous coronary intervention procedures and 5,827 diagnostic and follow-up cardiac catheterization procedures. During the same period, we experienced 40 patients with catheter-induced spasm in the proximal RCA. We excluded 531 patients from this study due to right proximal atherosclerotic lesions, angiography only being performed in the right coronary artery after the administration of nitrates, angiography only being performed in the left coronary artery (LCA), failure of catheter engagement in the right ostium or missing data. This resulted in a final study population of 5,296 patients.

We performed intracoronary acetylcholine (ACh) testing in 1,765 patients and intracoronary ergonovine (ER) tests in 1,208 patients. Both ACh and ER tests were performed in 528 patients, while intracoronary injections of adding ACh just after the intracoronary ER tests were performed in 305 patients. We examined the sheath size (4/5/6 French), approach site (radial/brachial/femoral) and catheter type (Judkins right catheter/Sone catheter/Judkins left 3.5 catheter/Shared catheter/Amplatz catheter) in patients with and without catheter-induced spasm. The risk factors for coronary artery disease were hypertension (>140/90 mmHg or taking antihypertensive medications), dyslipidemia (total cholesterol ≥220 mg/dL, low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol <40 mg/dL or, triglycerides ≥150 mg/dL or taking medications for dyslipidemia), diabetes mellitus (causal plasma glucose concentration ≥200 mg/dL, fasting plasma glucose concentration ≥126 mg/dL, glycohemoglobin >6.2% or taking medications for diabetes mellitus) and a history of smoking (habitual smoking >5 years).

Definition of catheter-induced spasm

In general, we defined positive catheter-induced spasm as ≥90% transient stenosis around the catheter tip within 1-2 cm with or without chest symptom or ischemic ECG changes. After the administration of sublingual/intracoronary nitroglycerin or spontaneous relief after the removal of the catheter from the right ostium, catheter-induced spasm was reversed without angiographical fixed stenosis. We also defined positive provoked spasm as ≥90% transient narrowing and usual chest pain or ischemic ECG changes on pharmacological spasm provocation tests. The degree of ST-segment depression was measured 80 mseconds after the J point. We considered a result to be positive when at least 1 of the following ischemic ECG changes was demonstrated during and/or after the ACh test: 1) ST-segment elevation of ≥0.1 mV in at least 2 contiguous leads or 2) ST-segment depres-

sion of 0.1 mV in at least 2 contiguous leads. We also considered a negative U wave as a positive ischemic ECG change.

Spasm provocation test

All drugs except for nitroglycerine were discontinued for ≥24 hours before the study, and nitroglycerine was also discontinued ≥4 hours before the study. Cardiac catheterization was performed from 9:00 am to 4:00 pm in the fasting state, as previously reported (11-15). We also attempted to perform the ACh or ER spasm provocation tests whenever possible. After control coronary arteriograms of the LCA in the right anterior oblique with caudal projection and of the RCA in the left anterior oblique with cranial projection were obtained by injection of 8-10 mL of contrast medium, provocation of coronary artery spasm was performed with an intracoronary injection of ACh and ER, as previously reported (16-18). ACh chloride (Neucholin-A, 30 mg/2 mL; Zeria Seiyaku, Tokyo, Japan) was injected in incremental doses of 20, 50 and 80 μg into the RCA and 20, 50 and 100 (200) μg into the LCA over 20 seconds with at least a 3-minute interval between each injection. ER (ergometrine by injection F, 0.2 mg/mL; Fuji Seiyaku, Tokyo, Japan) in a 0.9% warm saline solution was injected at 10 μg/min for 4 minutes for a maximum dose of 40 μg into the RCA and 16 μg/min over 4 minutes for a total dose of 64 μg into the LCA, with at least a 5-minute interval between each injection. We added ACh after the ER tests if no spasm was induced by the ACh and ER tests. The additional doses of ACh were 50/80 μg into the RCA and 50/100/200 μg into the LCA over 20 seconds with at least a 3-minute interval between each injection.

Coronary arteriography was performed when ST-segment changes and/or, chest pain occurred or 1-2 minutes after the completion of each injection. When an induced coronary spasm did not resolve spontaneously within 3 minutes after the completion of ACh and ER injections or when hemodynamic instability occurred as the result of coronary spasm, 2.5 to 5.0 mg of nitrate was injected into the involved vessel. A standard 12-lead electrocardiogram was recorded every 30 seconds. We used the ECG findings when ACh/ER, saline and contrast medium were not injected into the responsible vessels for at least 60 seconds. After the spasm provocation tests were completed, an intracoronary injection of 5.0 mg isosorbide dinitrate was administered, and coronary arteriography was then performed in multiple projections.

During the study, arterial blood pressure and ECG were continuously monitored on an oscilloscope by Nihon-Kohden Polygraphy (Tokyo, Japan). In the present study, coronary arteriograms were analyzed separately by two independent observers. The percent luminal diameter narrowing of coronary arteries was measured using an automatic edge-counter detection computer analysis system. The size of the coronary catheter was used to calibrate the images in millimeters and the measurement was performed in the same projection of coronary angiography at each stage. Focal spasm was defined as a discrete transient vessel narrowing ≥ 90% localized in a major coronary artery, whereas diffuse spasm was diagnosed when transient vessel narrowing ≥ 90%, compared with baseline coronary angiography, was observed from the proximal to distal segment in all 3 major coronary arteries. The spasm provoked site was classified according to the America College of Cardiology (ACC)/ American Heart Association (AHA) classification Significant organic stenosis was defined as >75% luminal narrowing according to the ACC/AHA classification (19).

The study protocol complied with the Declaration of Helsinki. Written informed consent to perform the pharmacological spasm provocation tests was obtained from all patients, and the protocol of this study was in agreement with the guidelines of the ethical committee at our institution.

Statistical analyses

Data analyses were carried out with SPSS (version 22.0, IBM Japan, Tokyo, Japan). All data were presented as the mean±1 standard deviation (SD). The clinical characteristics and procedures of cardiac catheterization of patients with and without catheter-induced spasm were analyzed by Fisher's exact test with correction or the Mann-Whitney U test. We also analyzed these issues by univariate and multivariate logistic regression analyses. $p<0.05$ was considered significant.

Results

Incidence of catheter-induced spasm in the proximal RCA

Catheter-induced spasm in the proximal RCA was observed in 40 (0.75%) of 5,296 patients undergoing diagnostic and follow-up coronary angiography in this study.

Coronary risk factors and medications before the pharmacological spasm provocation test in patients with catheter-induced spasm in the proximal RCA

Among the 40 patients, the mean age was 56±11.1 years old and 31 (77.5%) patients were men. A history of smoking was found in 37 (92.5%) patients, while hypertension was recognized in 11 (27.5%) patients. Dyslipidemia was found in 21 (52.5%) patients. Pharmacological spasm provocation tests were performed in 36 (90%) patients including 32 ACh tests and 11 ER tests. We also performed the addition of ACh just after the intracoronary ER tests in three patients. No vasodilators were administered in 23 patients (57.5%) before the pharmacological spasm provocation tests, while 1 vasodilator and 2 vasodilators were administered in 7 (calcium channel antagonist: 4 patients and nitrate: 3 patients) and 10 patients (all calcium channel antagonists and nitrates/nicorandils), respectively. Angiotensin receptor blocker or angiotensin-converting enzyme inhibitor was administered in four patients and just two patients had taken

Table 1a. Comparisons of Clinical Characteristics between Patients with and without Catheter-induced Spasm in the Right Coronary Artery.

	Total patients	With catheter induced spasm	Without catheter induced spasm	p value
Number	5,296	40 (0.8%)	5,256 (99.2%)	
Male (%)	3,570	31 (77.5%)	3,539 (67.8%)	0.1717
Age (year)	67.9±10.6	56.0±11.1	68.0±10.6	<0.001
Smoking	3,360	37 (92.5%)	3,323 (63.2%)	0.0001
Hypertension	2,868	11 (27.5%)	2,857 (54.4%)	0.0006
Dyslipidemia	2,189	21 (52.5%)	2,168 (41.2%)	0.1499
Diabetes mellitus	1,388	3 (7.5%)	1,385 (26.4%)	0.0117
4 Fr catheter	2,452	18 (45.0%)	2,434 (46.3%)	0.8686
5 Fr catheter	1,722	16 (40.0%)	1,706 (32.5%)	0.3103
6 Fr catheter	1,122	6 (15.0%)	1,116 (21.2%)	0.3365
Radial approach	1,272	9 (22.5%)	1,263 (24.0%)	0.8215
Brachial approach	3,313	27 (67.5%)	3,286 (62.5%)	0.5166
Femoral approach	711	4 (10.0%)	707 (13.5%)	0.6854
Left approach (radial & brachial)	425	1 (2.5%)	424 (8.1%)	0.3178
Judkins right catheter	1,083	10 (25.0%)	1,073 (20.4%)	0.4738
Shared catheter	798	3 (7.5%)	795 (15.1%)	0.2621
Judkins left 3.5 catheter	2,667	23 (57.5%)	2,644 (50.3%)	0.3645
Sones catheter	711	4 (10.0%)	707 (13.5%)	0.6854
Amplatz catheter	37	0	37 (0.7%)	0.6743
Acetylcholine test	1,765	32 (80.0%)	1,733 (33.0%)	<0.001
Ergonovine test	1,208	11 (27.5%)	1,197 (22.8%)	0.4779
Both acetylcholine and ergonvine test	528	7 (17.5%)	521 (9.9%)	0.1832
Adding acetylcholine after ergonovine test	305	3 (7.5%)	302 (5.7%)	0.8935
Undone pharmacological test	2,851	4 (10.0%)	2,847 (54.2%)	<0.001

Fr: french

beta-blockers. Statins were administered in three patients.

Comparisons of clinical characteristics between patients with and without catheter-induced spasm in the RCA

As shown in Table 1a, patients with catheter-induced spasm in the RCA had a significantly lower age (p<0.001) and lower incidence of hypertension (27.5% vs. 54.4%, p= 0.0006) and diabetes mellitus (7.5% vs. 26.4%, p=0.0117) than those without catheter-induced spasm in the RCA. However, there were no marked differences between the two groups in the catheter size, approach site or catheter type. ACh spasm provocation test (80% vs. 33.0%, p<0.001) was more frequently performed in patients with catheter-induced spasm than in those without it.

Comparisons of provoked spasm by the pharmacological tests between patients with and without catheter-induced spasm

As shown in Table 1b, the rates of provoked spasm in the left circumflex artery (53.1% vs. 30.6%, p=0.0068) and multiple spasm (78.1% vs. 53.0%, p=0.0050) found in patients with catheter-induced spasm in the RCA were markedly higher in than those without catheter-induced spasm in the RCA. However, no marked differences except in the use of a 6 Fr catheter (13.9% vs. 30.9%, p=0.0277) were noted between the two groups with regard to the cardiac catheterization procedures.

Comparisons of the incidence of catheter-induced spasm

As shown in Fig. 2A, the rate of using a 5 Fr catheter was higher than the rates of using catheters of other sizes, but not to a significant degree. Fig. 2B shows that the rate of using a femoral approach was those of using other approaches, but no significant differences were noted among the three groups. Fig. 2C shows that the 4 types of catheter used induced spasm in the proximal RCA in 0.82-1.68% of cases. No significant differences were observed among the four types of catheters.

Chest pain, ischemic ECG changes and necessity of nitrates during the catheter-induced spasm

As shown in Table 2, chest pain and ischemic ECG changes were observed in 22 and 18 patients, respectively, and nitrates were needed to relieve catheter-induced spasm in the RCA was recognized in 9 patients. We were unable to perform the pharmacological spasm provocation tests in nine patients.

Result of pharmacological spasm provocation

We were unable to perform the pharmacological spasm

Table 1b. Comparisons of Clinical Characteristics between Patients with and without Catheter-induced Spasm in the Right Coronary Artery.

	With catheter induced spasm	Without catheter induced spasm	p value
Pharmacological spasm provocation test done	36	2,409	
Provoked spasm positive	32 (88.9%)	1,071 (44.5%)	<0.001
In the right coronary artery	26 (81.3%)	760 (71.0%)	0.2050
In the left coronary anterior descending artery	25 (78.1%)	747 (69.7%)	0.3082
In the left circumflex artery	17 (53.1%)	328 (30.6%)	0.0068
One vessel spasm	7 (21.9%)	503 (47.0%)	0.0050
Multi vessel spasm	25 (78.1%)	568 (53.0%)	0.0050
4 Fr catheter	17 (47.2%)	863 (35.8%)	0.1572
5 Fr catheter	14 (38.9%)	801 (33.3%)	0.4762
6 Fr catheter	5 (13.9%)	745 (30.9%)	0.0277
Radial approach	9 (25.0%)	467 (19.4%)	0.3984
Brachial approach	25 (69.4%)	1,620 (67.2%)	0.7803
Femoral approach	2 (5.6%)	322 (13.4%)	0.2608
Left approach (radial & brachial)	1 (2.8%)	115 (4.8%)	0.8695
Judkins right catheter	7 (19.4%)	441 (18.3%)	0.8609
Shared catheter	3 (8.3%)	190 (7.9%)	0.9214
Judkins left 3.5 catheter	22 (61.1%)	1,285 (53.3%)	0.3535
Sones catheter	4 (11.1%)	484 (20.1%)	0.2592
Amplatz catheter	0	9 (0.4%)	0.3082

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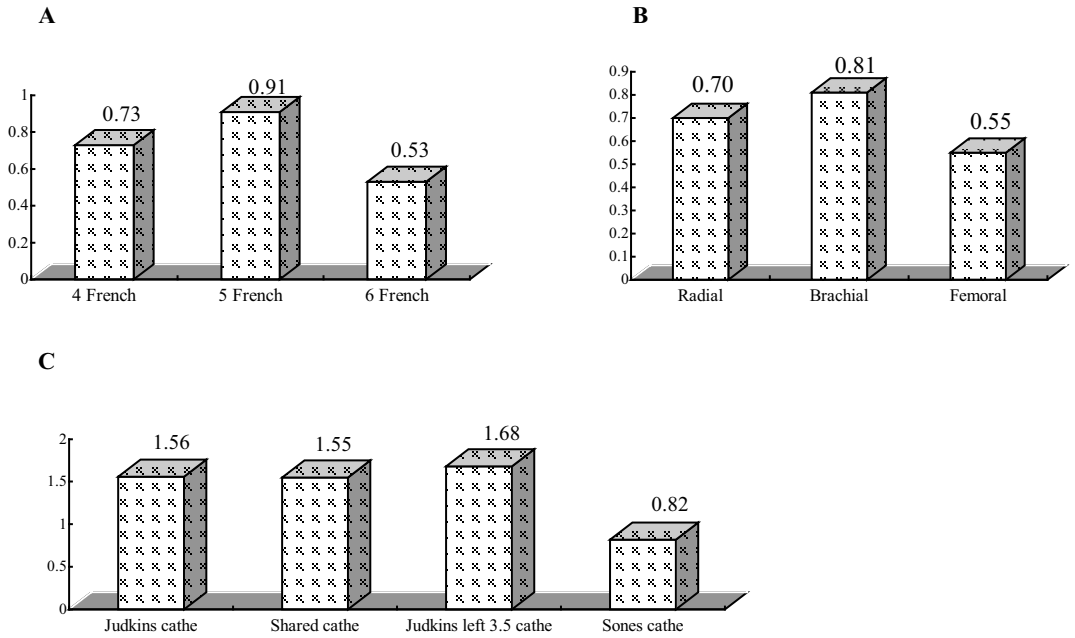

Figure 2. Comparisons of catheter-induced spasm in the right coronary artery among the catheter size (A), approach site (B) and catheter type (C).

provocation tests in 4 patients (from no-1 to no-4 in Table 2), but the remaining 36 patients (from no-5 to no-40 in Table 2) underwent pharmacological spasm provocation tests after the spontaneous or nitrate-based relief of their catheter-induced spasm. We performed 32 ACh tests (26 RCA and 32 LCA) and 11 ER tests (9 RCA and 10 LCA). Furthermore, acetylcholine was added after ergonovine tests in three patients (one RCA and three LCA). We recognized a positive response by ACh testing in 29 patients, while 5 patients showed a positive provoked spasm by ER tests. On adding ACh after the ER tests, 2 of 3 patients showed a positive response. Thus, a positive response on pharmacological spasm provocation testing was found in 32 (88.9%) patients, and 25 showed multiple spasms. Typical catheter-induced spasm cases are shown in Figs. 3 and 4.

Multivariate analyses

A multivariate analysis showed that positive spasm,

Table 2. Clinical Characteristics, Angiographical Procedures and Findings in 40 Patients with Catheter-induced Spasm in the Proximal RCA.

No	Age	Sex	Diagnosis	Catheter-induced spasm	Chest pain	ECG changes	ISDN in RCA	Undone RCA	Catheter size	Catheter	Approach	ACh	ER	ER+ ACh
1	39	M	UAP	# 1	(+)	(+)	(+)	(+)	4 Fr	JR 4.0	Brachial	(-)	(-)	(-)
2	41	F	ACS	# 1	(+)	(+)	(+)	(+)	4 Fr	JR 4.0	Femoral	(-)	(-)	(-)
3	62	M	EAP	# 1	(+)	(+)	(+)	(+)	6 Fr	JR 4.0	Femoral	(-)	(-)	(-)
4	35	M	OMI	# 1	-	-	-	(+)	5 Fr	JL 3.5	Brachial	(-)	(-)	(-)
5	73	F	Rest	# 1	(+)	(+)	-	-	4 Fr	Shared	Radial	8(d)	No spasm	(-)
6	72	F	Rest	# 1	(+)	(+)	-	-	5 Fr	JL 3.5	Radial	1(d) 6(d)	No spasm	2-4(d)
7	50	F	UAP	# 1	(+)	(+)	-	-	4 Fr	Shared	Radial	6(d) 11(d)	No spasm	1(d) 4(d)
8	70	M	Atypical	# 1	(+)	(+)	-	-	5 Fr	JL 3.5	Brachial	1(d)	1(d)	(-)
9	52	M	Rest AP	# 2	(+)	(+)	(+)	(+)	4 Fr	JR 4.0	Brachial	11(f)	(-)	(-)
10	67	M	Rest AP	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	(-)	1(f), 7(d) 9(d)	(-)
11	55	F	Atypical	# 1	(+)	-	-	-	4 Fr	JL 3.5	Brachial	(-)	No spasm	(-)
12	51	M	Rest	# 1	(+)	(+)	-	-	4 Fr	JL 3.5	Brachial	1/6/11(d)	(-)	(-)
13	48	M	OMI	# 1	(+)	(+)	(+)	-	5 Fr	JR 4.0	Brachial	(-)	2(t)	(-)
14	41	M	OMI	# 1	(+)	(+)	(+)	(+)	5 Fr	JR 4.0	Brachial	6/11(d)	(-)	(-)
15	52	M	Rest	# 1	(+)	-	-	(+)	4 Fr	JL 3.5	Brachial	6/11(d)	(-)	(-)
16	67	M	Rest	# 2	(+)	(+)	(+)	-	4 Fr	JL 3.5	Brachial	3(t) 8(d) 11(t)	(-)	(-)
17	58	F	EAP	# 1	-	-	-	-	5 Fr	Shared	Brachial	4(d)	(-)	(-)
18	62	F	Syncope	# 1	-	-	-	-	6 Fr	Sones	Brachial	2(d) 7(d)	(-)	(-)
19	52	M	Rest	# 1	(+)	(+)	-	-	5 Fr	JL 3.5	Brachial	4(t) 6(t) 11(d)	(-)	(-)
20	50	M	Rest	# 1	-	-	-	-	5 Fr	JL 3.5	Radial	1(f) 12/13(f)	(-)	(-)
21	65	M	DCM susp	# 1	-	-	-	-	5 Fr	JL 3.5	Radial	4(d) 6(d)	(-)	(-)
22	53	M	Rest	# 1	(+)	-	-	-	5 Fr	JL 3.5	Radial	3(d) 6(d) 11(d)	(-)	(-)
23	62	M	OMI	# 1	-	-	-	(+)	4 Fr	JR 4.0	Brachial	6(d) 11(d)	(-)	(-)
24	57	M	After PCI	# 1	-	-	-	(+)	5 Fr	JL 3.5	Radial	7(d) 11(d)	(-)	(-)
25	72	M	After PCI	# 1	-	-	-	-	5 Fr	JL 3.5	Radial	1/3(d) 8(d) 11(f)	(-)	(-)
26	55	M	Rest	# 1	(+)	(+)	-	-	4 Fr	JR 4.0	Radial	1(t) 7(d) 12(d)	(-)	(-)
27	47	M	EAP	# 1	(+)	-	-	-	5 Fr	JL 3.5	Brachial	2-3(f) 7(d)	(-)	(-)
28	48	M	Rest	# 1	-	-	-	-	5 Fr	JL 3.5	Brachial (L)	1(t) 6(d) 11(d)	(-)	(-)
29	73	F	Rest	# 1	-	-	-	-	4 Fr	JR 4.0	Brachial	No spasm	(-)	(-)
30	52	M	Variant AP	# 1	-	-	-	-	4 Fr	JR 4.0	Brachial	2(f) 6(d) 11(d)	2(d)	(-)
31	59	M	Rest	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	1(d) 3(f) 7(d)	(-)	(-)
32	79	M	Rest	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	3(d) 6(d)	(-)	(-)
33	48	M	ECG ab	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	1(d) 7(f)	(-)	(-)
34	37	M	Rest	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	4(f) 6(d) 11(f)	No spasm	(-)
35	45	M	Rest	# 1	-	-	-	-	4 Fr	JL 3.5	Brachial	2(d) 6(f)	(-)	(-)
36	62	F	UAP	# 1	(+)	(+)	(+)	-	6 Fr	Sones	Brachial	No spasm	No spasm	No spasm
37	53	M	After PCI	# 1	-	-	-	-	6 Fr	Sones	Brachial	4(d)	(-)	(-)
38	59	M	EAP	# 1	(+)	(+)	-	-	6 Fr	JR 4.0	Femoral	2(d) 6(d) 11(d)	(-)	(-)
39	71	F	EAP	# 1	(+)	(+)	-	-	6 Fr	Sones	Brachial	(-)	2(d) 6(d) 11(d)	(-)
40	45	M	OMI	# 1	(+)	(+)	(+)	-	5 Fr	JR 4.0	Femoral	No spasm	(-)	(-)

M: male, F: female, UAP: unstable angina, EAP: effort angina, AP: angina pectoris, OMI: old myocardial infarction, DCM: dilated cardiomyopathy, ECG ab: ECG abnormal, #: segment, Fr: french, JR: Judkins right, JL: Judkins left, d: diffuse, f: focal, t: total, ISDN: isosorbide dinitrate, ECG; electrocardiogram, RCA: right coronary artery, ACh: acetylcholine, ER: ergonovine, susp: suspected

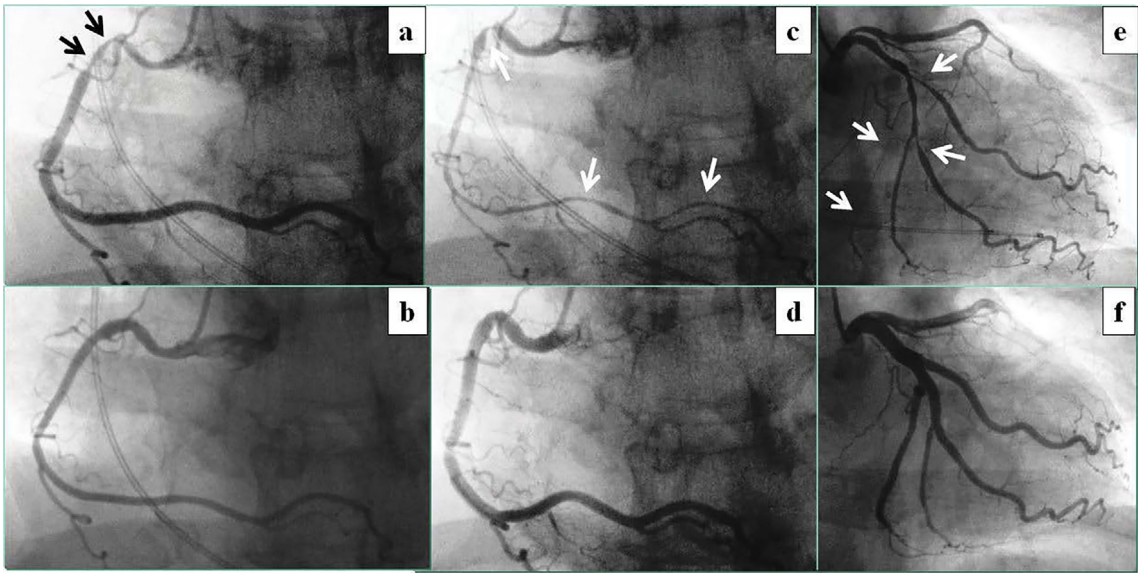

Figure 3. **Angiographical and pharmacological findings in patients with catheter-induced spasm (case 20). Coronary angiography was performed via a right radial approach due to rest angina in a 50-year-old man. When a 5-Fr Judkins left catheter 3.5 was engaged into the right ostium, catheter-induced spasm was recognized around the catheter tip at segment 1 without chest symptoms or ischemic electrocardiographic changes (a: black arrows). We again engaged the Judkins left catheter 3.5 into the right ostium 8 minutes after the removal of the catheter, and catheter-induced spasm disappeared (b). The intracoronary injection of 100 μg acetylcholine provoked spasm in the left circumflex artery (e: white arrows) accompanied by usual chest pain and the appearance of horizontal ST segment depression in the inferior and V56 leads (1.5 mm). After the spontaneous relief of left circumflex artery spasm without the use of nitrates, we administered the 20 μg acetylcholine into the right coronary artery. Provoked positive spasm was found in the proximal and distal right coronary arteries (c: white arrows) accompanied by usual chest pain and the appearance of negative T in the inferior leads. After the administration of nitrates into the responsible artery, no stenosis was found in either coronary artery (d, f).**

younger age, and diabetes mellitus were the determinant factors for catheter-induced spasm in the RCA (Table 3). This means that patients with catheter-induced spasm tended to be younger, have a low incidence of diabetes mellitus and tended to have coronary spastic angina. Provoked spasm was the most powerful determinant factor for catheter-induced spasm in the RCA.

Discussion

In this article, we reported the frequency of catheter-induced spasm in the RCA in patients who had undergone diagnostic or follow-up coronary angiography. The incidence was just 0.75% among patients undergoing diagnostic or follow-up coronary angiography. Compared with patients who had no catheter-induced spasm in the RCA, the age and incidence of diabetes mellitus were significantly lower in patients with catheter-induced spasm in the RCA. Furthermore, 78.1% of patients with catheter-induced spasm in the RCA had multiple spasms on pharmacological spasm provocation testing. This is the first report concerning catheter-induced spasm in consecutive cases with pharmacological testing. More than 80% of patients with catheter-induced spasm in the proximal RCA had coronary spastic angina. Aspects of the angiographical procedures, including the catheter size, approach sites and catheter type, did not markedly influence the occurrence of catheter-induced spasm in the proximal RCA. A multivariate analysis showed that coronary spastic angina was the most powerful determinant factor for catheter-induced spasm.

Comparisons of coronary spastic angina

Previous reports found that the clinical characteristics of catheter-induced spasm were similar to those in variant angina or coronary spastic angina (5). Patients with angiographical spontaneous coronary spasm at middle or distal sites rather than the proximal right coronary ostium were diagnosed with coronary spastic angina. Patients with catheter-induced spasm in the proximal RCA had the same clinical characteristics as those with coronary spastic angina. Cardiologists did not perform the pharmacological spasm provocation tests in these patients with catheter-induced spasm in the proximal RCA. We first reported that approximately 80% of patients with catheter-induced spasm in the proximal RCA were diagnosed with coronary spastic angina by performing pharmacological spasm provocation tests. Patients

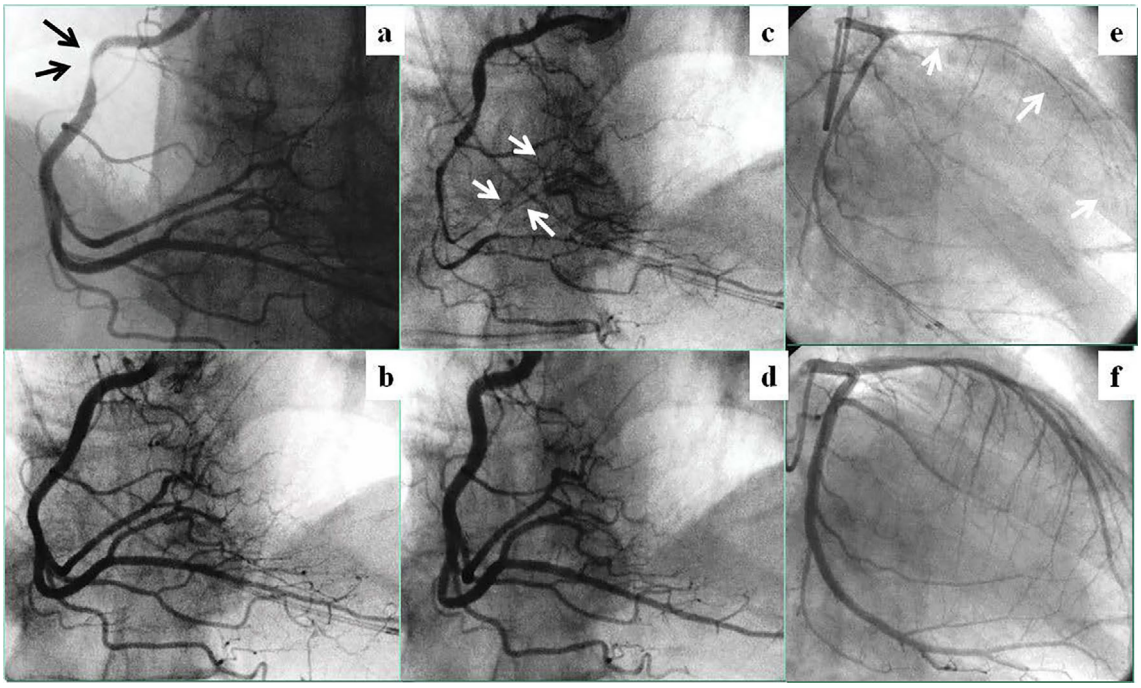

Figure 4. **Angiographical and pharmacological findings in patients with catheter-induced spasm (case 21). Coronary angiography was performed by a right radial approach due to suspicion of dilated cardiomyopathy in a 65-year-old man. When a 5-Fr Judkins left catheter 3.5 was engaged into the right ostium, catheter-induced spasm was recognized around the catheter tip at segment 1 without chest symptoms or ischemic electrocardiographic changes (a: black arrows). We again engaged the Judkins left catheter 3.5 into the right ostium 6 minutes from the removal of the catheter, and catheter-induced spasm disappeared (b). The intracoronary injection of 200 μg acetylcholine provoked spasm in the left anterior descending artery (e: white arrows) accompanied by chest oppression and the appearance of down-sloping ST segment depression in the V56 leads (1.0 mm). After the spontaneous relief of left anterior descending artery spasm without the use of nitrate, we administered the 50 μg acetylcholine into the right coronary artery. Provoked positive spasm was found in the distal right coronary artery (c: white arrows) accompanied by chest pressure and the appearance of horizontal ST segment depression in the inferior leads (2.0 mm). After the administration of nitrates into the responsible artery, no stenosis was found in either coronary artery (d, f).**

with catheter-induced spasm in the proximal RCA encountered during coronary angiography may be at a highly risk of having coronary spastic angina.

Comparisons of the cardiac catheterization procedures

In the editorial comment by Demany (20), the incidence of catheter-induced spasm was reported to be related to the skill of the angiographer; the author found that the incidence of catheter-induced spasm dropped from 1.0% for the first 750 examinations using the Sones technique to 0.2% for the next 2,000 cases. However, the frequency of catheter-induced spasm was 5% in 200 cases when using the Judkins technique but 1% in 500 cases when using the Schoonmaker-King multipurpose catheter, suggesting that the technique itself may also affect the incidence of spasm. In another editorial comment by Kimbiris (20), the incidence of catheter-induced spasm ranged from 0.26-3% in different laboratories. The reasons for the variation of the incidence of catheter-induced spasm determined the cases or manipulations of the catheter by each angiographer. Kimbris further mentioned that catheter-induced spasm was more frequently seen when the Judkins or Sones techniques were used, or when multipurpose catheters were used via the femoral site. Some reports have described the disappearance of catheter-induced spasm in the same patients when using a different approach site or different catheter type. However, in our experience, there are no marked differences in the incidence of catheter-induced spasm among different catheter types, approach sites or sizes. The present results suggest that the clinical characteristics of the patients may be more important determinant factors for the incidence of catheter-induced spasm than the characteristics of the catheter itself or procedure by each angiographer compared with the old era (30 or 40 years ago). It may be concerned the size down of catheter (from 7/8 Fr to 4/5 Fr) or improvement quality of catheter material.

Clinical implications

More than 80% of cases of catheter-induced spasm in the

Table 3. Multivariate Analysis.

	Odds ratio	95% CI	p value
Spasm positive	7.030	1.920-25.700	0.0032
Positive spasm in the right coronary artery	1.900	0.759-4.780	0.1700
Hypertension	0.528	0.246-1.130	0.1010
Dyslipidemia	1.330	0.660-2.680	0.4250
Smoking	1.460	0.868-2.460	0.1540
Diabetes mellitus	0.278	0.083-0.928	0.0374
Age	0.937	0.910-0.965	<0.0001
Sex	0.455	0.179-1.160	0.0990
Catheter used	0.752	0.539-1.050	0.0947
Catheter size	0.711	0.471-1.074	0.1055
Approach site	1.017	0.706-1.466	0.9240

CI: confidence interval

proximal RCA were in patients with coronary spastic angina. While mechanism underlying catheter-induced spasm in these patients was unclear, they may have had a high disease activity of coronary spasm. Increased coronary reactivity may lead to catheter-induced spasm in the proximal RCA. Catheter engagement into the RCA ostium may cause transient luminal narrowing around the inserted catheter tip. Of note, we seldom experience catheter-induced spasm in the proximal left coronary artery. Because multiple spasms were recognized in approximately 80% of patients with catheter-induced spasm in the RCA, the irritability of both coronary arteries due to some stimulus may have been high in these patients. The mechanism underlying catheter-induced spasm in general is not completely understood, but the anatomic characteristics of the patients may be involved, since the RCA is thought to have a muscular band near its origin. Mechanical stimulation by the catheter tip and myogenic reflexes are also implicated. Cardiologists should be aware of the risk of catheter-induced spasm in the proximal RCA when performing diagnostic coronary angiography or spasm provocation tests. When encountering cases of catheter-induced spasm in the proximal RCA, we should address it by promptly removing the catheter from the RCA ostium or by administering a small amount of nitrate to relieve spasm. Pharmacological spasm provocation tests should also be performed even if nitrate has been administered to relieve catheter-induced spasm in the proximal RCA.

Study limitations

This study had several limitations. One was its retrospective nature, single-center setting and small sample size. Second was that each physician selected their own catheter procedures or manipulations Powerful engagement without soft insertion can cause stimulation of the coronary artery. In the study, we encountered difficulty inserting the catheter into the RCA ostium in two patients (case nos. 36 and 40 in Table 2). These two patients showed no provoked spasm on the pharmacological spasm provocation tests after the administration of nitrates to relieve the catheter-induced spasm in the RCA. Third, we were unable to perform pharmacological spasm provocation testing in all 40 patients. Only four patients underwent coronary angiography after the administration of nitrates. Fourth, we were unable to analyze the medication history before the pharmacological spasm provocation tests in all study subjects. However, all drugs except for nitroglycerine were discontinued for ≥24 hours before the pharmacological spasm provocation tests. Further studies will be necessary to assess the relationship between catheter-induced spasm in the proximal RCA and coronary spastic angina.

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

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