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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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%)                 | 0.8666  |
| 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 ergonovine 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 (88.9%) | 2,049 | 1,071 (44.5%) | <0.001 |
| Provoked spasm positive | 32 | 760 (71.0%) | 0.2050 |
| In the right coronary artery | 26 (81.3%) | 747 (69.7%) | 0.3082 |
| In the left coronary anterior descending artery | 25 (78.1%) | 328 (30.6%) | 0.0068 |
| One vessel spasm | 17 (53.1%) | 350 (47.0%) | 0.0050 |
| Multi vessel spasm | 25 (78.1%) | 568 (53.0%) | 0.0050 |
| 4 Fr catheter | 14 (38.9%) | 801 (33.3%) | 0.4762 |
| 5 Fr catheter | 13 (39.9%) | 754 (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 | 5 (13.9%) | 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 |

Fr: french

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 | 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)       |                | (-)      |      |      | (-)     |
| 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    | (-)        |                | (-)      |      | (-) | (-)     |
| 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(d) 11(d) | (-)      | (-) |      | (-)     |
| 20 | 50  | M   | Rest            | #1 - - - -              | 5 Fr       | JL 3.5      | Brachial    | 1(f) 12/13(f) | (-)      | (-) |      | (-)     |
| 21 | 65  | M   | DCM susp        | #1 - - - -              | 5 Fr       | JL 3.5      | Brachial    | 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(d) | (-)      | (-) |      | (-)     |
| 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    | 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     | (-)      | (-) |      | (-)     |
| 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   | No spasm     | (-)      | (-) |      | (-)     |

M: male; F: female; UAP: unstable angina; EAP: effort angina; AP: angiina pectoris; OMI: old myocardial infarction; DCM: dilated cardiomyopathy; RCA: right coronary artery; ACh: acetylcholine; ER: ergonovine; spur: suspected

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More than 80% of patients with catheter-induced spasm in consecutive cases with pharmacological provocation tests. 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. We first reported that approximately 78.1% of patients with catheter-induced spasm in the proximal RCA had coronary spastic angina. Further, 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 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
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 Kimbris (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
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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