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Comparison of long-term clinical outcomes of percutaneous coronary intervention in vasospastic angina patients associated with significant coronary artery stenosis

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ABSTRACT

Background: Coronary spasm is the major pathophysiology of vasospastic angina (VA). Medical treatment is usually effective in VA patients without significant stenosis. However, there is little information about the percutaneous coronary intervention (PCI) in VA patients with significant coronary artery stenosis (CAS).
Methods: After retrospective screening of all consecutive VA patients from January 2010 to April 2015, we selected significant CAS (>50% of diameter stenosis) after nitrate injection and divided them into two groups according to the presence of PCI.
Results: A total of 220 VA patients (41 females, mean age: 58 ± 10 years old) were screened, and 85 were included in this study. Males were predominant in the VA with significant CAS group (89 vs 76%, p = 0.020). PCI was done in 43 patients (51%). The most common culprit coronary artery was the left anterior descending coronary artery (18, 42%), diameter stenosis was significantly higher (66 ± 9 vs 61 ± 10%, p < 0.01), and total number of antianginal medication was significantly lower in the PCI group than in the medical group (1.7 ± 0.9 vs 2.1 ± 0.8, p = 0.039). Moreover, 4 patients underwent PCI to control symptoms in the medical treatment group during the follow-up period (26 ± 13 months). However, additional antiplatelet therapy was necessary in patients with coronary angioplasty, and there were 2 cases with complication associated with angioplasty (1 restenosis and 1 bleeding complication).
Conclusion: In VA patients with significant CAS, both treatment modalities showed similar clinical outcomes. Although the PCI can afford symptomatic improvement, it needed additional antiplatelet medications and can be associated with procedural complications.

1. Introduction

Vasospastic angina (VA), also known as Prinzmetal's angina, is characterized by ST-segment elevation on electrocardiogram (ECG) and chest pain at rest usually resulted from sudden vasospasm of the epicardial coronary arteries. Vasospasm may occur in angingraphically normal coronary arteries as well as at the level of significantly stenotic coronary arteries [1]. According to the previous reports, spasms can occur in particular coronary stenotic sites in 90% of the cases, when severe organic stenosis is present [2]. Therefore, the treatment of the stenotic coronary lesions by percutaneous coronary intervention (PCI) can prevent future vasospastic occlusion of the coronary lesions and improve symptoms, theoretically. Although there are several case series describing the efficacy of administering calcium channel blockers with PCI for the treatment of VA patients with severe coronary stenosis [3–5], the long-term clinical outcomes of PCI have not been studied well in these patients. We compared the long-term clinical outcomes of PCI versus conventional medical treatment in VA patients with significant coronary artery stenosis.

2. Methods

2.1. Patients

We retrospectively screened all consecutive patients who underwent coronary angiography with the spasm provocation test at the Chungnam National University Hospital between January 2010 and April 2015. VA was defined as the presence of severe coronary vasospasm (more than 90% occlusion of segment) with transient ST-segment elevation and chest pain during the coronary angiography with the provocation test or spontaneously. Also, the spastic coronary lesions were resolved after the injection of nitrate into the causative lesions with an improvement of chest pain and ECG changes associated

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with the spasm. We included all patients with VA with significant coronary arterial stenosis (diameter stenosis >50%) after the resolution of the spasm into this study. The exclusion criteria were catheter induced spasm during the coronary angiography and patients with previous coronary stenting. We divided our study patients into two groups according to the presence of PCI of the causative lesions. We retrospectively investigated the medical records of the participants in order to observe their long-term clinical features. This study protocol was approved by Chungnam National University Hospital Institutional Review Board.

2.2. Coronary angiography with provocation test

Coronary angiography was performed with a radial or femoral artery route. After the subcutaneous injection of lidocaine sufficiently, we inserted an introducing sheath into the arteries by using the Seldinger technique. Left and right coronary angiograms were taken usually with 5-Fr sized Judkins left and right catheters using the standardized technique. After taking baseline coronary angiograms, intravenous ergonovine was used as the spasm introducing agent to provoke coronary vasospasm. The dose of the ergonovine was sequentially increased following the dosing schedule with 50 μg, 100 μg, and 200 μg in every 3-minute intervals. Positive coronary vasospasm was defined as ≥90% decrease in the coronary lumen diameter upon the visual inspection with a transient change of ST segment and/or chest pain. When spasm was induced, sufficient amount of nitrate (up to 1000 μg) was injected intra-coronary in order to identify the resolution of the spasm, improvement of chest pain, and normalization of ST segment change. During the procedure, arterial blood pressure, pulse rate, arterial oxygen saturation and 12-lead ECG were continuously monitored.

After the injection of plenty of nitrate, the follow-up coronary angiograms were taken to find any stenotic coronary arterial lesions and evaluate the degree of organic stenosis. The proximal and distal vessel diameters were measured and used as a reference diameter in the quantitative angiographic measurement. According to the algorithm in the dedicated software, lesion length, reference diameter, minimal lumen diameter, and diameter stenosis were measured. Angiographically significant coronary stenosis was defined as >50% diameter stenosis. If with significant coronary artery stenosis, coronary angioplasty was done with the standard technique by the attending physician's decision. After the predilation with a balloon, the optimal stent was inserted in the stenotic coronary lesions.

2.3. Medical treatment and follow up

All VA patients were initially given with a combination of antianginal medications. After the discharge, medications were modified based on their frequency of chest pain. If patients complained chest discomfort despite increasing doses and/or numbers of antianginal medications, they could be treated with the coronary angioplasty by the attending physician's decision. Information on the frequency of chest pain, number and type of antianginal medications, repeated coronary angiography, readmission due to chest pain, and the presence of coronary revascularization during the follow-up period were gathered with the review of the medical records. Also, the data of bleeding, and restenosis were also obtained. All study population was followed at an average of 26 ± 13 months.

2.4. Statistical analysis

Data are expressed as mean ± standard deviation (SD) for continuous variables and as frequencies (percentages) for the categorical variables. Statistical analysis was performed using the SPSS 21.0 (SPSS Inc., Chicago, IL, USA) software. A Student's t-test was performed for statistical comparison between the nominal measures, while a chi-square test was performed for the categorical data. Statistical significance level was established as a p-value < 0.05.

3. Results

3.1. Baseline characteristics

We initially screened a total of 220 patients with VA. Of them, 85 patients had significant coronary stenosis. Their baseline characteristics were summarized at Table 1.

The mean age was significantly higher (61 ± 10 vs 57 ± 10 years old, p = 0.006) and male patients were more predominant (89 vs 76%, p = 0.015) in the stenotic coronary artery group. There were no statistical differences in the presence of hypertension and diabetes mellitus in the two groups. The rate of current smokers was higher in the coronary artery stenosis group (60 vs 44%, p = 0.029).

Of total 85 patients with significant coronary stenosis, 43 were treated by the PCI. There was no statistical difference of baseline characteristics in those with and without PCI (Table 2).

3.2. Coronary angiographic findings

Results of coronary angiography and quantitative coronary analysis data were summarized in Table 2. There was no statistical difference of reference vessel diameter, minimal luminal diameter and total lesion length between two groups. TIMI flow grade after spasm also did not show significant differences between the two groups (p = 0.742). However, diameter stenosis was higher in the PCI group (66 ± 9 vs 61 ± 10%, p = 0.006).

3.3. Medical treatment and clinical follow up

All patients with significant coronary stenosis were treated with various combinations of antianginal medications, such as calcium channel blockers, long acting oral nitrates, nicorandil, and molsidomine. However, the patients with coronary stenting had received dual antiplatelets to prevent stent thrombosis at least 1 year. Patients without coronary stenting were prescribed with more antianginal medications to control their symptoms (1.7 ± 0.9 vs 2.1 ± 0.8, p = 0.039, Table 3).

Table 1
Baseline characteristics of total variant angina patients.

	Variant angina (n = 220)		p-Value
	Coronary artery stenosis (+) (n = 85)	Coronary artery stenosis (−) (n = 135)	
Age (year)	61 ± 10	57 ± 10	0.006
Male gender	76 (89%)	103 (76%)	0.015
Cardiovascular risk factors			
Hypertension	36 (42%)	62 (46%)	0.604
Diabetes mellitus	10 (12%)	12 (9%)	0.489
Current smoker	31 (37%)	60 (44%)	0.029
Dyslipidemia	45 (53%)	63 (47%)	0.365
Blood chemistry			
BUN (mg/dL)	15.5 ± 4.7	15.1 ± 4.5	0.484
Cr (mg/dL)	0.95 ± 0.92	0.82 ± 0.17	0.083
Total cholesterol (mg/dL)	167 ± 36	169 ± 36	0.662
TG (mg/dL)	162 ± 103	164 ± 99	0.859
HDL-C (mg/dL)	49 ± 13	47 ± 12	0.168
LDL-C (mg/dL)	98 ± 31	102 ± 34	0.398
Pattern of spasm			
Single-vessel spasm	69 (81%)	108 (80%)	0.830
Multi-vessel spasm	16 (19%)	27 (20%)	0.830
Causative spastic vessel			
LM	2 (2%)	0 (0%)	0.829
LAD	47 (55%)	63 (47%)	0.213
LCx	27 (32%)	33 (24%)	0.235
RCA	28 (33%)	73 (54%)	0.002

BUN: blood urea nitrogen, Cr: creatinine, TG: triglyceride, HDL-C: high-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein-cholesterol, LM: left main coronary artery, LAD: left anterior descending coronary artery, LCx: left circumflex coronary artery, RCA: right coronary artery.