SOLITARY OSTIAL CORONARY ARTERY STENOSIS

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Among 125,000 patients who underwent coronary arteriography at the Cleveland Clinic Foundation from 1960 to 1988, 128 (0.1%) were found to have 50–99% stenosis of one or both coronary ostia. All cases were associated with minimal or no obstruction in the distal coronary arteries. Thirty-six percent were males and 64% were females. Fifty percent had ostial narrowing of the left main trunk, 41% had ostial narrowing of the right coronary artery, and 9% had bilateral ostial stenosis. Based on angiographic appearance, the patients were categorized into three groups: 1) atherosclerotic (77%), 2) primary (unknown etiology) (13%), and 3) secondary to aortic valve disease (10%). Compared with the other groups, primary solitary coronary ostial stenosis was commonly found in middle-aged premenopausal or postsurgical menopausal females who had few coronary risk factors and were experiencing severe angina symptoms. At autopsy, most cases were atherosclerotic, however, fibromuscular dysplasia may be found in primary solitary ostial stenosis. This rare entity is difficult to diagnose, and is associated with increased risk during cardiac catheterization and bypass surgery. Solitary ostial stenosis should be included in the differential diagnosis of ischemic heart disease, especially in young or middle-aged female patients.

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SOLITARY ostial stenosis (SOS) of a coronary artery, in the absence of distal vessel obstructions, is a rare form of coronary artery disease. It can be difficult to diagnose and quantitate angiographically because of its anatomical location. Although few cases have been examined pathologically, the majority have atherosclerosis as the underlying etiology^{1–4}. Other cases of ostial stenosis may occur secondary to syphilitic aortitis^{5,6}, Takayasu's aortitis^{7–9}, aortic valve disease¹⁰, and iatrogenic causes, such as mediastinal irradiation¹¹ or cardiac surgery^{12–15}. Recently, several investigators noted that young or middle-age premenopausal females with few coronary risk factors constitute most cases of SOS, suggesting that a new clinical syndrome might be included as one

of the causes of this entity^{16,17}. In general, the natural history of solitary ostial stenosis, especially that involving the left main trunk, is poor¹⁸. The combination of accurate recognition followed by coronary artery bypass surgery may alter the catastrophic clinical course.

The present study defines the incidence, clinical implications, and pathogenesis of solitary ostial stenosis.

MATERIALS AND METHODS

The study group consisted of 125,172 patients who underwent coronary arteriography at the Cleveland Clinic Foundation from 1960 to 1988. Two hundred forty-three patients (0.19%) were found to have 50–100% isolated stenosis in one or both coronary ostia without evidence of obstructive distal vessel disease. We excluded patients with

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TABLE I SOLITARY OSTIAL STENOSIS IN A CORONARY ARTERY

	Atherosclerotic		Primary		Secondary	
	Male	Female	Male	Female	Male	Female
Number	34	64	3	14	9	4
Male/Female	1	18	1	4.7	2.3	1
Age	57.6±9.9	59.9±9.5	49.3±5.7	45.7±7.2**	59±8.5	54.5±9.2
Functional Class						
I	6	9		1		
II	8	10	2	1	1	1
III	12	17	1	8		1
IV	2	8		4		1
Symptoms other than angina pain	6	20			8	1
Risk Factors						
Hypertension	21 (62%)	30 (47%)	1	5 (31%)	4	
Smoking	27 (80%)	38 (60%)	3	5 (33%)	5	1
Diabetes	4 (11%)	13 (20%)		0 *	2	1
↑ cholesterol	13 (38%)	37 (58%)		2 (13%)**	1	
Obesity	23 (68%)	42 (66%)		5 (33%)*	5	2
Family history	15 (44%)	43 (67%)		9 (60%)	3	
# risk factors	3.4±1.1	3.6±1.4	1.3±0.5	1.8±1.2**	1.6±1.2	
Premenopause		7 (11%)		6 (43%)**		1
Menopause		54 (89%)	8 (57%)		3	
Natural		22 (41%)		0		1
Surgical		32 (59%)		8 (100%)		2
Unknown		3				

* $p < 0.05$ ** $p < 0.01$

complete occlusion of the right coronary (109 patients) or the left main trunk (3 patients). Three patients with secondary ostial stenosis as a result of aortic dissection, cardiac tumor, or mediastinal irradiation, respectively were also excluded. Therefore, 128 patients (0.1%) compromised the basis of this study.

Forty-six (36%) patients were males and 82 (64%) were females. Ages ranged from 32 to 75 years. The patients were divided into 3 groups (Table I) based on the angiographic appearance of the coronary arteries. "Atherosclerotic" SOS had evidence of at least moderate ostial narrowing and mild atheromatous wall irregularities ($\leq 25\%$ stenosis) in the distal coronary arteries (Fig. 1A). "Primary" SOS was characterized by at least moderate ostial narrowing and a completely normal distal coronary artery (Fig. 1B). "Secondary" SOS had at least moderate ostial narrowing, aortic valve disease, and a completely normal distal coronary artery.

Symptoms of angina pectoris, coronary

risk factors, and menstrual history were obtained for all patients. Hysterectomy, bilateral oophorectomy, or tubal ligation were considered to be surgical menopause. Whether postoperative estrogen replacement therapy was administered is not known.

Statistical comparisons were performed by the chi-square analysis or Student t-test, and $p < 0.05$ was considered statistically significant.

RESULTS

Age and gender (Table I)

Ninety-eight patients (77%) were "atherosclerotic", 17 patients (13%) were "primary", and 13 patients (10%) were "secondary" to aortic valve disease. Females predominated in the atherosclerotic group, and especially in the primary group (male: female=1:4.7). Patients with primary SOS were younger than patients in the other groups ($p < 0.01$).

Symptoms, coronary risk factors and men-

Fig.1. A. (Left) Atherosclerotic solitary ostial stenosis, LAO cranial projection. The left coronary ostium has severe concentric stenosis and the distal vessel is mildly irregular.
B. (Right) Primary solitary ostial stenosis, LAO projection. The left coronary ostium has severe narrowing and the distal coronary artery is normal.

TABLE II LOCATION OF SOLITARY OSTIAL STENOSIS

	<i>Atherosclerotic</i>		<i>Primary</i>		<i>Secondary</i>		<i>Total (%)</i>	<i>M:F</i>
	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>		
<i>RCA</i> $\geq 50\%$	12	31	0	5	4	1	53 (41)	1:2.3
<i>LMT</i> $\geq 50\%$	21	27	3	8	4	0	63 (50)	1:1.3
<i>Both</i>	1	6	0	1	1	3	12 (9)	1:5
<i>Total</i>	34	64	3	14	9	4	128	1:1.8

M=male; *F*=female; *RCA*=right coronary artery; *LMT*=left main trunk

strual history

Ninety-three (73%) of the 128 patients underwent coronary arteriography because of angina pectoris, while the others (27%) were studied because of atypical chest pain, valvular heart disease, or an abnormal exercise test. All of the patients with primary SOS were studied because of angina pectoris. Female patients with primary SOS tended to be more symptomatic, had fewer coronary risk factors ($p < 0.01$), and were more commonly premenopausal ($p < 0.01$) than those of the atherosclerotic group. Menopause was post-surgical in all 8 of the females with primary SOS.

Location of stenosis

Among the 243 patients, which includes those with total ostial occlusion, 65% had stenosis of the right coronary ostia. However, in the 128 patients without total occlusion, the left coronary ostium was more fre-

quently involved than the right (Table II). Fifty percent of the lesions involved the left ostium, 41% involved the right ostium, and 9% involved both ostia. Ten (89%) of the 12 patients with bilateral ostial lesions were females.

Risk of catheterization and cardiac surgery

Patients with SOS had increased risk associated with cardiac catheterization and bypass surgery. One patient died during catheterization (Table III, Case #1) and another sustained cardiac arrest after contrast injection into the stenotic left coronary ostium. Of the 65 patients with atherosclerotic SOS who were treated with bypass surgery, one (1.5%) died during the immediate postoperative period (Case #2). An acute subendocardial myocardial infarction was seen microscopically at autopsy despite a patent bypass graft. Two (15.4%) patients with primary SOS died on the day of the surgery.

TABLE III CLINICAL FEATURES AND AUTOPSY RESULTS IN SOLITARY OSTIAL STENOSIS

Case	Sex	Age	Site	%	Menopause	Clinical Diagnosis	Cause of Death	Result of Autopsy
1	F	52	L	75	Pre-menopause	ASHD	Sudden onset of hypotension during catheterization	ASHD, Scattered old myocardial infarctions
2	F	59	R	60	Surgical	ASHD	Idioventricular rhythm 3 days postoperatively	ASHD, Stenosis in both ostia, SVG patent
3	F	42	L	75	Surgical	Primary	Sudden onset of hypotension during bypass surgery	ASHD, Hemorrhage into AV node, SVG patent
4	F	46	L	90	Pre-menopause	Primary	Ventricular tachycardia 3 h postoperatively	Focal fibromuscular dysplasia SVG distal obstruction
5	F	60	L	95	Surgical	ASHD	Acute hepatitis 6 years postoperatively	ASHD, SVG patent
6	F	64	L	75	Post-menopause	Secondary	Acute renal failure 2 months postoperatively	ASHD, SVG patent

F=female; L=left coronary ostium; M=Male; R=right coronary ostium; ASHD=atherosclerotic heart disease; SVG=saphenous vein graft; %= % stenosis of coronary ostium

Fig.2. Solitary ostial stenosis secondary to fibromuscular dysplasia, LAO projection (Table III, Case #4). Left coronary ostium has 90% stenosis and the distal coronary artery is normal.

Fig.3. Photomicrograph of fibromuscular dysplasia involving the left coronary ostium. There is marked thickening of the media with luminal stenosis (100X, hematoxylin and eosin).

One patient (Case #3) had a patent graft, but also severe hemorrhage into the AV node. The other patient (Case #4) had complete occlusion of the vein graft at its distal anastomotic site. There were no surgical deaths in patients with secondary SOS.

Pathogenesis

Six patients were studied at autopsy. Two patients with clinically suspected atherosclerotic SOS (Table III, Cases #1 & #2) had severe atheromatous lesions at the coro-

nary ostia. In 2 patients (Cases #3 & #5) with clinically suspected primary SOS, atheroma were detected at the coronary ostia. In another patient with clinically suspected primary SOS, fibromuscular dysplasia (perimedial type) was found at the time of autopsy (Case #4) (Figs. 2 & 3). The autopsy was restricted to the chest and no other lesions secondary to fibromuscular dysplasia were recognized in the branches of the thoracic aorta. This patient's only coronary risk factor was a familial history of a

maternal heart attack. Two patients with primary SOS underwent punch biopsy of the aorta during bypass surgery, which was non-diagnostic in both cases. In secondary SOS, one patient who died of non-cardiac causes had atheroma in the coronary ostium at the time of autopsy (Case #6). Takayasu's aortitis was not observed in any of the patients in this series.

DISCUSSION

Definition and Incidence

In the present study, we defined "solitary ostial stenosis" (SOS) as coronary ostial stenosis narrowing of greater than fifty percent without evidence of obstructive distal vessel disease, and then subclassified patients into three groups (Table I). Primary SOS is identical to "isolated ostial stenosis" which has been defined as "localized ostial stenosis without evidence of any other coronary arterial disease and without evidence of specific or nonspecific aortic disease" by other investigators^{3,16}. SOS was observed in 0.19% of patients who underwent coronary arteriography, including patients with total occlusion, and 0.1% without total occlusion.

Location of solitary ostial stenosis

In typical coronary arterial atherosclerosis, the right coronary ostium is more susceptible to narrowing than the left^{1,19}. This phenomenon may be related to the hemodynamic and mechanical effects of turbulent blood flow toward the right coronary ostium, or to the anatomic and structural characteristics of the vessel^{19,20}. However, the left main ostium was more susceptible in this study, even in atherosclerotic SOS. The left ostium was involved about twice as frequently in primary SOS as was the right. This finding is supported by Miller et al.¹⁶ who observed lesions in the left ostia of all 5 of their patients with "isolated ostial stenosis". The cause of left coronary ostial dominance in primary SOS is entirely unknown.

Etiology

Hypoplasia or atresia of the coronary artery ostium¹ or congenital membrane of the coronary artery^{21,22} are causes of ostial stenosis in children. However, such causes are extremely rare in adults. In the litera-

ture, only two adults have been studied histopathologically^{3,4}. Two female patients, ages 31 and 54 years, with type II diabetes mellitus and unstable angina pectoris, died during cardiac catheterization. The angiographic appearance in both patients was consistent with primary SOS. At autopsy, the underlying lesions were atherosclerotic. Of the six patients examined at autopsy in this series, five had atherosclerosis of the ostia. Using angiographic criteria, two were diagnosed as atherosclerotic SOS, two as primary SOS, and one as secondary SOS. These results support the contention of Pritchard et al. that "premature atherosclerosis" is the most likely and frequent pathogenetic cause of ostial stenosis².

Clinical atherosclerotic coronary artery disease is more common in males than in females. The male/female ratio has been reported to range from 5:1 to 20:1²³⁻²⁵. The gender differences have been explained by the protective effect of estrogens in women. However, females predominate in SOS. Because sexual hormonal effects on the cardiovascular system are so exceedingly complex, the mechanism of such premature atherosclerosis in the coronary ostium in females is unclear. However, it is speculated that an abrupt decrease of estrogen secretion as a result of surgical menopause may play a role in the pathogenesis of premature atherosclerosis. The prevalence of surgical menopause in patients with atherosclerotic SOS and primary SOS was 59% and 100%, respectively, compared with 27% of females in the Framingham study²⁶.

Fibromuscular dysplasia is another common cause of primary SOS. It is characterized by nonatherosclerotic segmental stenosis, and tends to predominate in young or middle-aged females²⁷. Although fibromuscular dysplasia is a well known cause of renovascular hypertension, and is sometimes identified in carotid or vertebral arteries²⁸, it is rarely found in the coronary arteries²⁹⁻³¹, especially at the coronary ostia. The etiology of fibromuscular dysplasia is unknown. However, dominant inheritance with incomplete penetrance^{28,31}, abnormalities of the vasa vasorum with physical strain to the artery^{32,33}, or effects of the sympathetic nervous system³⁴ have been suspected.

Clinical implications

SOS is a rare cause of angina pectoris, myocardial infarction, syncope, or fatal arrhythmia. It is more common in young or middle-aged premenopausal females with few coronary risk factors. Some of these patients who present with atypical chest pain could be misdiagnosed as having noncardiac symptoms. Stress testing in young female patients has not been reliable in screening for coronary artery disease and cardiac catheterization is not commonly performed in this age group. The cardiac angiographer should be alert to the possibility of coronary ostial stenosis, since the catheter tip is frequently positioned beyond the ostial narrowing, resulting in misdiagnosis. Thus, catheterization studies should begin with a non-selective injection into the aortic sinus in the shallow left or right anterior oblique projection. An abrupt damping of blood pressure when the catheter is engaged in the coronary artery is an important clue to the presence of ostial narrowing^{2,18}. Prolonged pressure damping may result in cardiac arrest or serious cardiac arrhythmia. The Sones catheter is probably safer than the Judkins catheter because of side holes. Cohen et al. reported that among 5 patients with left main trunk disease who died during the catheterization procedure, 3 were studied with Judkins catheters, and 2 with a Sones catheter.³⁵ It is possible that cannulation may produce coronary spasm resulting in complete occlusion of the vessel. Therefore, these patients should be monitored carefully during and after coronary arteriography.

Coronary ostial stenosis is not an indication for angioplasty. Therefore, surgical revascularization is the treatment of choice. Since female patients have a higher surgical mortality rate and lower graft patency,³⁶ those patients with SOS should be considered as higher-risk patients for cardiac surgery.

CONCLUSIONS

- 1) The angiographic incidence of SOS including total occlusion is 0.19%. SOS is twice as common in females than in males.
- 2) In SOS without total occlusion, 50% involved the left coronary ostium, 41% in-

volved the right ostium, and 9% involved both ostia.

- 3) Primary SOS is commonly found in middle-aged premenopausal females or patients with surgical menopause who have few coronary risk factors.
- 4) SOS patients have an increased risk in cardiac catheterization and surgery.
- 5) Punch biopsy of the ascending aorta is not helpful for determining the pathogenesis of primary SOS.
- 6) The etiology of primary SOS has been shown pathologically to be atherosclerosis or fibromuscular dysplasia.

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