Tohoku J. Exp. Med., 1991, **163**, 167-174

Silent Obstruction of the Coronary Stenosis between Diagnostic Angiography and Later Percutaneous Transluminal Coronary Angioplasty without Myocardial Infarction

TOMOYUKI YAMBE, SHIN-ICHI NITTA, SHIGEKI CHIBA, YOSHIFUMI SAIJOH, SHIGERU NAGANUMA, HIROSHI AKIHO, YOSHITO KAKINUMA, KENJI IZUTSU, YUH-ICHI KIKUCHI, TOHRU NAGANUMA, SHIGEO SUGAWARA, MOTONAO TANAKA, TAI-ICHIROH MEGURO,* HIDEHIKO SASAKI,* MIKIO MITSUOKA,* YOSHIO TERASAWA,* KEIKO NITTA,† YOSHIAKI KATAHIRA,† TATSUSHI OHTOMO,† NORIO ENDOH,† HISANAO TAKEDA,‡ TAROH SONOBE,‡ KAZUHIKO TAKAHASHI,‡ MAKOTO MIURA,§ NAOSHI SATO§ and HITOSHI MOHRI§

*Department of Medical Engineering and Cardiology, the Research Institute for Tuberculosis and Cancer, Tohoku University, Sendai 980, *Department of Cardiology, Sendai Shakaihoken Hospital, Sendai 980, † Department of Cardiology, Tohoku Kousei-Nenkin Hospital, Sendai 983, ‡Department of Cardiology, Miyagi Prefectural Semine Hospital, Miyagi 989-45, and §Department of Thoracic and Cardiovascular Surgery, School of Medicine, Tohoku University, Sendai 980*

YAMBE, T., NITTA, S., CHIBA, S., SAIJOH, Y., NAGANUMA, S., AKIHO, H., KAKINUMA, Y., IZUTSU, K., KIKUCHI, Y., NAGANUMA, T., SUGAWARA, S., TANAKA, M., MEGURO, T., SASAKI, H., MITSUOKA, M., TERASAWA, Y., NITTA, K., KATAHIRA, Y., OHTOMO, T., ENDOH, N., TAKEDA, H., SONOBE, T., TAKAHASHI, K., MIURA, M., SATO, N. and MOHRI, H. *Silent Obstruction of the Coronary Stenosis between Diagnostic Angiography and Later Percutaneous Transluminal Coronary Angioplasty without Myocardial Infarction.* Tohoku J. Exp. Med., 1991, **163** (3), 167-174 —— Among 204 patients with severe coronary artery stenosis amenable to percutaneous transluminal coronary angioplasty (PTCA), 5 (2.5%) developed new silent total coronary occlusion of the vessel to be dilated without any chest symptom during the period between diagnostic coronary angiography and repeat

Received November 6, 1990; revision accepted for publication February 5, 1991.

Reprint requests: Tomoyuki Yambe, M.D., D.M.Sci., Department of Medical Engineering and Cardiology, the Research Institute for Tuberculosis and Cancer, Tohoku University, 4-1 Seiryo-machi, Aoba-ku 980, Sendai, Japan.

coronary angiography at the time of the operation. We evaluated the clinical and angiographical characteristics of the patients with silent obstruction of the coronary artery in a short time, compared with the patients with unstable angina pectoris, who is considered to be suffering from acute myocardial infarction with severe chest symptom. None of the clinical variables studied showed a significant difference between the two groups. Among the angiographic variables, the degree of collateral was higher and impaired coronary perfusion distal to the lesion was more frequently found in unstable angina group. These results suggest that unstable angina is in a later stage of the ischemic heart disease compared with the time of the diagnostic angiography in patients with silent obstruction. Silent obstruction of high degree coronary stenosis is presumably due to the development of collateral circulation. ———— silent obstruction; percutaneous transluminal coronary angioplasty; acute myocardial infarction; unstable angina pectoris; coronary stenosis

Percutaneous transluminal coronary angioplasty (PTCA) has become a commonly performed therapeutic procedure in patients with coronary artery disease since Gruentzig et al. performed the first coronary angioplasty in 1977 (Gruentzig et al. 1979). The development of this procedure made it possible to study the short-time course of coronary stenosis (Kimbiris et al. 1984), because patients undergoing coronary angioplasty are subjected to two consecutive coronary arteriograms within a short time (Danchin et al. 1989). Rapid progression of the coronary artery stenosis was reported by the previous investigators (Bemis et al. 1973), however, silent obstruction of the coronary artery stenosis in a short time without myocardial infarction has not been studied yet.

In this study, we evaluated the clinical and angiographical morphologic characteristics of the patients with silent obstruction of the coronary artery without myocardial infarction in a short time, compared with the patients with unstable angina pectoris, who are considered to become an acute myocardial infarction with severe chest symptom (Raffiendeul et al. 1979).

Material and Methods

Patients

From January 1986 to June 1989, 204 consecutive patients who underwent their initial coronary angiography at our institutions were found to have coronary artery disease suitable for PTCA and were referred for this procedure (Yambe et al. 1989, 1990a, b). Criteria for selection of patients for PTCA were those originally suggested by Gruentzig (Gruentzig et al. 1979) and the National Institute of Health Registry for coronary angioplasty (Levy et al. 1979). All lesions to be dilated were located on the proximal segments of the coronary arteries and were judged "high grade" ($>70\%$ reduction of intraluminal diameter) by 3 independent observers.

Patients with restenosis after previous PTCA, those referred for angioplasty of a saphenous bypass graft or of a totally occluded artery and those having undergone the initial coronary angiogram at another center were excluded.

Baseline clinical and angiographical characteristics of the patients were studied. Clinical data at the time of initial characterization comprised age, gender, duration of the anginal symptoms before the catheterization. Coronary angiography were performed using

the Judkins technique with 5 Fr catherters. At least 5 views of the left coronary artery and 3 views of the right coronary artery were firmed (KXO-2050; Toshiba Co., Tokyo). Bi-plane left ventriculography was performed in the 30° right anterior oblique projection and 60° left anterior oblique projection (KXO-2050, Toshiba Co.). All coronary angiograms were reviewed by 3 independent observers who were unaware of the subsequent clinical course of the patients. Coronary perfusion distal to the lesion to be dilated was graded according to the Thrombolysis in Myocardial Infarction (TIMI) classification (Sheeman et al. 1987). Collaterals were graded according to the criteria of Rentrop (Rentrop et al. 1985).

Two groups of patients were reviewed. Group 1 comprised patients who developed complete coronary obstruction (absence of antegrade filling of the coronary artery beyond the lesion) or functional coronary obstruction (faint and late antegrade filling with no discernible lumen continuity) at the time of the PTCA, without myocardial infarction between diagnostic angiography and repeat coronary angiography at the time of the operation. Group 2 included patients who were suffering from unstable angina pectoris selected for coronary angioplasty at the time of the diagnostic angiography. Unstable angina pectoris was defined as angina of recent onset, chronic angina with a recent change of pattern, or recent onset of angina at rest.

Statistical analysis

Values were expressed in terms of mean $\pm$ S.D. Comparisons between two groups were made using Student's unpaired t tests for continuous variables and χ-square tests for discrete variables. Differences between means were considered significant for p values <0.05.

Results

Incidence of new silent total occlusion

Silent obstruction of the coronary stenosis between the diagnostic angiography and later PTCA without myocardial infarction was found in 5 patients (2.5% of the entire study group). These 5 patients shows normal left ventriculograms. Of these, 4 had complete occlusion and 1 had functional occlusion (Fig. 1).

Clinical presentation and angiographic findings

All group 1 patients were men (mean age 62.5 ± 9.7 years). At the time of diagnostic catheterization, 1 patient (20%) had angina pectoris and 1 patient (20%) had a history of previous myocardial infarction. But they had not any chest symptom between diagnostic angiography and later PTCA. The coronary artery to be dilated was the left anterior descending artery in 2 patients (40%). The mean degree of stenosis was 72.7 ± 11.3. All patients had short (<10 mm) stenosis (eccentric in 4 and concentric in 1). Intracoronary filling defects suggesting possible thrombus were seen in 1. Collateral vessels were not seen in these patients (collateral grade 0) and no patient had impaired coronary perfusion distal to the lesion to be dilated (TIMI grade 0) at the time of diagnostic angiography.

Twenty-three of the 204 patients had unstable angina pectoris. 18 in group 2 patients were men (mean age 60.9 ± 9.6 years). At the time of diagnostic characterization, 4 patients (17.4%) had a history of previous myocardial infarction. The coronary artery to be dilated was the left anterior descending artery in

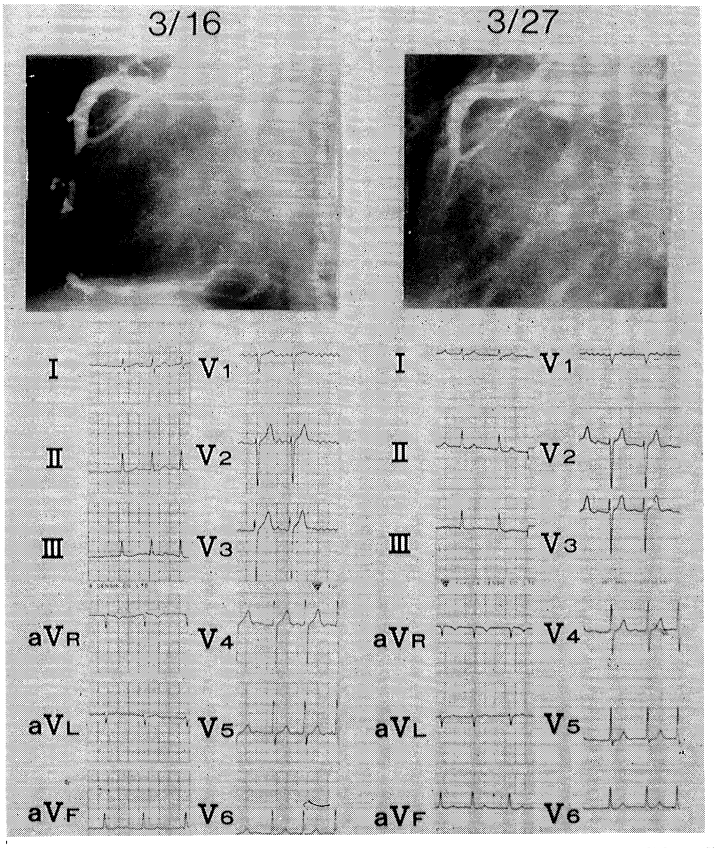

Fig. 1. Left side: RCA arteriogram in the LAO projection, and ECG. Severe proxismal stenosis. Right side: Total occlusion of the stenosis 11 days after without myocardial infarction.

4 patients (17.4%). The mean degree of stenosis was 83.3±13.3. All patients had short (<10 mm) stenosis (eccentric in 4 and concentric in 1). Intracoronary filling defects suggesting possible thrombus were seen in 1. Collateral vessels were seen in 2 patients (0.26±0.44), and 6 patient had impaired coronary perfusion distal to the lesion to be dilated (TIMI grade 2.73±0.44) at the time of diagnostic angiography.

Factors related to development of new silent total occlusion or unstable angina pectoris

None of the clinical variables studied showed a significant difference between the two groups (Table 1). Among the angiographic variables, the degree of collateral was higher in group 2 and impaired coronary perfusion distal to the lesion was more frequently found (Tables 2 and 3).

TABLE 1. *Baseline characteristics and clinical course of patients with unstable angina pectoris and silent total coronary obstruction*

Factors	Spontaneous obstruction ($n=6$)	Unstable angina ($n=23$)
Age (years)	62.5± 9.7	60.9± 9.6
Sex (male %)	83.3	82.6
Duration (months)	14.0±15.6	16.3±27.8
Risk factors		
Smoking (pack-years)	13.5±20.9	31.7±32.0
Hypertension (%)	33.3	78.2
Hyperlipidemia (%)	16.6	21.7
Diabetes mellites (%)	16.6	21.7
Obesity (%)	83.3	47.8
Family history (%)	83.3	21.7
Hyperuricemia (%)	0	8.6

Values are means±S.D.

TABLE 2. *Angiographic morphology of the coronary artery in patients with unstable angina pectoris and silent total coronary obstruction*

Angiographic morphology	Spontaneous obstruction ($n=6$)	Unstable angina ($n=23$)	
Percent stenosis	72.3±11.3	83.3±13.3	N.S.
Irregular or smooth (irregular %)	16.6	17.4	N.S.
Concentric or excentric (concentric %)	16.6	34.8	N.S.
Discrete or diffuse (discrete %)	100	100	N.S.
Dissection (%)	0	4.3	N.S.
Haziness (%)	33.3	0	N.S.
Overhang (%)	0	17.4	N.S.

Values are means±S.D.

N.S., not significant.

TABLE 3. *Coronary perfusion distal to the lesion*

Angiographic evaluation	Spontaneous obstruction ($n=6$)	Unstable angina ($n=23$)	
Collateral score	0±0	0.26±0.44	$p<0.05$
TIMI grade	3±0	2.73±0.44	$p<0.05$

Values are means±S.D.

Discussion

Previous studies with repeated coronary arteriograms have demonstrated that coronary stenosis in patients with angina pectoris is progressive in more than half of the patients over an interval of 2 or 3 years (Bemis et al. 1973). However, studies with arteriographic evidence of the natural course of coronary artery stenosis were limited. PTCA offers a unique opportunity to study the progression of coronary artery disease over a short period of time in patients who undergo 2 coronary angiograms, 1 for diagnostic and the other for therapeutic purposes, independently of their clinical symptoms between the 2 examinations.

Silent obstruction of severe coronary artery stenosis amenable to PTCA is not uncommon and was observed in 2.5% of our patients. This rate is comparable with that reported in a previous study of spontaneous obstruction, and the phenomenon is time dependent (Wijns et al. 1983).

Cohen et al. reported that collateral circulation limits myocardial ischemia as assessed by the extent of new ventricular asynergy and electrocardiographic changes during coronary occlusion in patients (Cohen and Rentrop 1986). This study suggested that the presence of collateral circulation was associated with occurrence of the acute myocardial infarction. Malinow et al. have shown that coronary stenosis progressed to complete obstruction in almost half of the patients on whose stenotic arteries a bypass graft had been placed (Malinow et al. 1973). This study suggested that sufficient flow to the stenosed coronary artery from the other vessels might be promotive factor of the stenosis. These reports show the importance of the coronary collateral circulation in myocardial infarction.

Determination of subsequent silent obstruction or unstable angina pectoris seems impossible on an individual basis. Moise et al. showed that progression to complete occlusion was more frequent in men (Moise et al. 1984). However, in this study, few factors have been related to subsequent silent coronary occlusion. Our only predictive variables between 2 groups were impaired coronary perfusion distal to the lesion and higher degree of collateral scores. These results suggest that unstable angina is in a later stage of the ischemic heart disease compared with the time of the diagnostic angiography in patients with silent obstruction.

The most plausible explanation is that longstanding high degree stenosis would stimulate collateral circulation, but abrupt closure of coronary stenosis would not leave time for collateral vessels to develop. Unstable angina pectoris is possibly at the stage of abrupt closure of the coronary artery, so they have little but not sufficient collateral vessels, yet. Silent obstruction is probably caused by gradual development of coronary stenosis, and they have enough time to wait the development of good collateral vessels, though there is no collateral circulation at the time of the diagnostic angiography. Such hypothesis might also explain the low rate of myocardial infarction in the medically treated patients in the Randomised Coronary Artery Surgery Study, who had severe coronary stenosis (C.A.

S.S. investigators, et al. 1984). These results suggest that the generally accepted reasoning, "high degree coronary stenosis implies high risk of coronary occlusion and high risk of myocardial infarction or other adverse cardiac event" is probably not warranted.

Acknowledgment

We thank Mrs. Hisako Iijima and Miss Taeko Ishiyama for the assistance and the excellent cooperation.

References

1) Bemis, C.E., Gorlin, R., Kemp, H.G. & Herma, M.V. (1973) Progression of coronary artery disease: A clinical arteriographic study. *Circulation*, **47**, 455-464.
2) C.A.S.S. principal investigators and their associates (1984) Myocardial infarction and mortality in the coronary artery surgery study (CASS) randomized trial. *N. Engl. J. Med.*, **310**, 750-758.
3) Cohen, M. & Rentrop, K.P. (1986) Limitation of myocardial ischemia by collateral circulation during sudden controlled coronary artery occlusion in human subjects: A prospective study. *Circulation*, **74**, 469-476.
4) Danchin, N., Oswald, T., Voiriot P., Juilliere, Y. & Cherrier, F. (1989) Significance of spontaneous obstruction of high degree coronary artery stenosis between diagnostic angiography and later percutaneous transluminal coronary angioplasty. *Am. J. Cardiol.*, **63**, 660-662.
5) Gruentzig, A.R., Senning, A. & Siegenthaler, W.E. (1979) Nonoperative dilatation of coronary stenosis: Percutaneous transluminal coronary angioplasty. *N. Engl. J. Med.*, **301**, 61-68.
6) Kimbiris, D., Iskandrian, A., Saras, H., Goel, I., Bemis, C.E., Segal, B.L. & Mundth, E. (1984) Rapid progression of coronary stenosis in patients with unstable angina pectoris selected for coronary angioplasty. *Cathet. Cardiovasc. Diagn.*, **10**, 101-114.
7) Levy, R.I., Mock, M.B., Willman, V.L. & Frommer, P.L. (1979) Percutaneous transluminal coronary angioplasty. *N. Engl. J. Med.*, **301**, 101-103.
8) Malinow, M.R., Kremkau, E.L., Kloster, F.E., Bonchek, L.I. & Roshe, J. (1973) Occlusion of coronary arteries after vein bypass. *Circulation*, **47**, 1211-1216.
9) Moise, A., Lesperence, J., Theroux, P., Taeymans, Y., Goulet, C. & Bourassa, M.G. (1984) Clinical and angiographic predictors of new total coronary occlusion in coronary artery disease: Analysis of 313 nonoperated patients. *Am. J. Candiol.*, **54**, 1176-1181
10) Raffiendeul, W., Smith, L.R., Rogers, W.J., Mantle, J.A., Rackley, C.E. & Russel, R.O. (1979) Quantitative coronary arteriography: Coronary anatomy of patients with unstable angina pectoris re-examined 1 year after optimal medical therapy. *Am. J. Cardiol.*, **43**, 699-707.
11) Rentrop, K.P., Cohen, M., Blanke, H. & Phillips, R.A. (1985) Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J. Am. Coll. Cardiol.*, **5**, 587.
12) Sheeman, F.H., Braunwald, E., Canner, P., Dodge, H.T., Gore, J., Natta, P.V., Passamani, E.R., Williams, D.O. & Zaret, B. (1987) The effect of intravenous thrombolytic therapy on left ventricular function: A report on tissue-type plasminogen activator and streptokinase from the thrombolysis in myocardial infarction (TIMI Phase 1) trial. *Circulation*, **75**, 817-829.
13) Wijns, W., Serruys, P.W., van den Brand, M., Suryapramata, H., Kooijman, C.W., Reiber, J.H.C. & Hugenholtz, P.G. (1983) Progression to complete coronary obstruc-

tion without myocardial infarction in patients who are candidates for percutaneous transluminal angioplasty: A 90-day angiographic follow-up. In: *Prognosis of Coronary Heart Disease. Progression of Coronany Atherosclerosis*, edited by H. Roskmann, Springer-Verlag, Tokyo, pp. 190-195.

14) Yambe, T., Nitta, K., Katahira, Y., Meguro, T., Terasawa, Y., Endoh, N., Takeda, H., Sonobe, T., Saijoh, Y., Takahashi, K., Akiho, H., Naganuma, S., Nitta, S. & Tanaka, M. (1989) Clinical efficiency of the long time inflation of the PTCA balloon. *Coronary*, **6**, 403-409.

15) Yambe, T., Nitta, S., Saijoh, Y., Naganuma, S., Akiho, H., Tanaka, M., Yoshioka, S., Nitta, K., Endoh, N., Sugiyama, K., Katahira, Y., Oikawa, Y., Hoshi, A., Meguro, T., Terasawa, Y., Mitsuoka, M., Takeda, H., Sonobe, T., Takahashi, K., Murata, Y., Shimanuki, Y. & Itoh, H. (1990a) Reverse redistribution phenomenon in dipyridamole loading thallium-201 images using single photon emission computed tomography. *Coronary*, **7**, 188-194.

16) Yambe, T., Nitta, K., Katahira, Y., Hoshi, A., Meguro T., Terasawa, Y., Endoh, N., Takeda, H., Shimanuki, Y., Itoh, H., Yoshioka, S., Nitta, S., Saijoh, Y., Takahashi, K., Akiho, H., Naganuma, S., Sonobe, T., Kakinuma, Y. & Tanaka, M. (1990b) Differentiation of the transiently ischemic from infarcted myocardium by thallium-201 exercise scintigram after ergometer rehabilitation. *Coronary*, **7**, 307-312.