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Morphologic Changes in Infarct-Related Plaque After Coronary Stent Placement

A Serial Angioscopy Study

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OBJECTIVES The aim of this study was to investigate the morphologic changes in infarct-related lesions after stenting in acute or recent myocardial infarction (MI) with coronary angioscopy.

BACKGROUND There is no information on the serial morphologic changes, which occur after stenting, and the time course of neointimal coverage of stents for disrupted unstable plaques.

METHODS Forty-three patients with MI within seven days of onset were examined. Angioscopy was serially performed for the infarct-related lesions at baseline (n = 43), after balloon angioplasty (n = 35), and after stenting following balloon angioplasty (n = 39) and at one (n = 36) and six months (n = 30) after stenting.

RESULTS At baseline, most of the lesions had complex morphology, yellow plaque color, and protruding thrombus (96%, 96%, and 74%, respectively). Although balloon angioplasty reduced the protruding thrombus, it remained in 37%, and an intimal flap was observed in 89% of the lesions. After stenting, the protruding thrombus and intimal flap disappeared, with an increased luminal size obtained in all lesions. At one-month follow-up, an irregular and yellow surface, along with a lining thrombus, was still observed, with partial neointimal stent coverage in most of the lesions. At six-month follow-up, the neointima was found to have sufficiently formed over the stent. The plaque shape and color were almost all classified as smooth (97%) and white (93%).

CONCLUSIONS These results suggest that a stent not only compressed and covered a disrupted plaque with a protruding thrombus and intimal flap, leading to a wide vessel lumen, but also helped to seal the unstable plaque through neointimal proliferation. (J Am Coll Cardiol 2003;42: 1558–65) © 2003 by the American College of Cardiology Foundation

Coronary angioscopy is a relatively new technique for visualizing the intracoronary surface morphology in detail (1). Recently, angioscopic observations have revealed new insights that: 1) the characteristics of plaque instability presenting complex morphology, yellow color, and thrombus lasted for one month after myocardial infarction (MI), even in patients treated with thrombolysis or percutaneous

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transluminal coronary angioplasty (PTCA) (2,3); and 2) morphologic changes in infarct-related plaque were recognized at one to six months after PTCA, as part of the healing process evoked by angioplasty. A reduction in the yellow color and thrombogenicity of the disrupted plaque was observed through neointimal proliferation, called "angioscopic plaque stabilization" (4,5). However, there is still no information available on the serial morphologic changes in infarct-related lesions treated with coronary stents. Compared with balloon angioplasty, the neointimal response to a stent is more extensive and takes a different form. Little is known, however, regarding the plaque-stabilizing effect of a stent in this setting, despite the fact that it is widely used as one of the most effective revascularization therapies for patients with MI. The objective of the present study with angioscopy was to assess the morphologic changes of the infarct-related lesion occurring in a series of stent placement procedures in the months after stenting in patients with acute or recent MI.

METHODS

Patient selection. From October 1997 to December 1999, 208 patients with either acute or recent MI within seven days of onset were admitted to our institute. The diagnosis for acute or recent MI was satisfied by the following criteria: total creatine kinase (CK) or CK-MB greater than twice the upper limit of our hospital's laboratory normal, with electrocardiographic (ECG) evidence of MI or ischemic symptoms. After examinations, 114 (55%) of the 208 MI patients underwent emergency percutaneous coronary interventions of the infarct-related lesion based on the following criteria: 1) continuing ischemic symptoms associated with persistent

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Abbreviations and Acronyms

ECG = electrocardiogram/electrocardiographic
MI = myocardial infarction
PIA = postinfarction angina
PTCA = percutaneous transluminal coronary angioplasty
TIMI = Thrombolysis In Myocardial Infarction

ST-segment elevation of at least 1 mm or more in the contiguous ECG leads; or 2) evidence of postinfarction angina (PIA), which was defined as recurrent anginal pain at rest presenting >24 h after acute MI. This diagnosis also required the recording of transient ST-segment elevation or depression of ≥1 mm or inverted or normalized T waves on the original ECG leads of the acute MI during an episode of chest pain.

For 114 patients, angioscopy was performed if the following criteria were met: 1) the infarct-related artery was clearly identified from the ECGs, echocardiographic wall motion abnormalities, and coronary angiographic findings; 2) the infarct-related artery was found to be anatomically suitable for angioscopy according to previously described criteria (2); 3) both appropriate angioscopy instruments and sufficiently skilled staff members to perform angioscopy and staff skilled in angioscopy were available at the time; 4) patients did not have cardiogenic shock, left main coronary artery disease, or a history of coronary artery bypass graft surgery; and 5) written, informed consent for angioscopy was obtained from the patient. Angioscopy of the infarct-related lesion was performed in 43 patients with acute or recent ST-segment elevation MI within seven days of onset. Angioscopic observations were serially performed at baseline, immediately after balloon angioplasty with subsequent stenting, immediately after stenting, at one-month follow-up (mean 31 ± 9 days, median 31 days), and at six-month follow-up (mean 224 ± 68 days, median 201 days). This project was approved by the Institutional Review Board of our hospital.

Stent implantation procedures. All patients were treated with aspirin (81 mg/day), ticlopidine (100 mg twice daily), cilostazol (100 mg twice daily for 3 days after admission), and heparin (5,000 IU intravenously) immediately after admission. Cilostazol was administered as an antiplatelet agent, which inhibits platelet aggregation earlier than ticlopidine or aspirin (6). Heparin was administered to maintain an activated clotting time of 250 s or longer. All stent implantations were performed after balloon angioplasty by the femoral approach. Four types of slotted tube or multidesign stents were used in this study: GFX (Applied Vascular Engineering, Santa Rosa, California), Multi-link (Guidant, Advanced Cardiovascular Systems, Santa Clara, California), NIR (Boston Scientific, Galway, Ireland), and Palmaz-Schatz (Cordis, Johnson & Johnson, Warren, New Jersey) stents.

Angioscopic equipment and procedures. Coronary angioscopy was performed with a 4.5F rapid-exchange angioscope (Vecmova, Clinical-Supply Corp., Gifu, Japan), which is compatible with a conventional 0.014-in. angioplasty guide wire and an 8F guiding catheter. This angioscope system consists of an imaging catheter, a light source, a color television camera and monitor, and a videotape recorder. The light source employed is a high-intensity (300 W) xenon light. The angioscope is composed of two elements (image bundle in delivery catheter). The image bundle consists of 3,000 optical fibers with a microlens at the distal tip, which can be independently advanced 6 cm in front of the delivery catheter. A compliant occlusion balloon is located at the distal tip of the delivery catheter, which, when inflated, occludes the anterograde flow during imaging. Warmed physiologic saline was continuously irrigated through the delivery catheter for the displacement of blood at a rate of 0.6 to 0.8 ml/s by a power injector, and the occlusion balloon was gradually hand-inflated until the image was viewed. When the field of view was flushed clear of blood, the inflation of the occlusion balloon was constantly maintained. The light intensity was manually adjusted to illuminate the dark interior and also to prevent halation during angioscopic observation. The guiding catheter pressure, ST-segment changes, cardiac rhythm, and patient comfort were monitored continuously during angioscopy. Each angioscopic image acquisition took from 15 to 25 s, and all sequences were recorded on s-VHS videotape for subsequent analysis. In performing pre-intervention angioscopy, the angioscopic catheter was not passed through the distal site of the infarct-related lesion, in order to avoid either injuring or destroying the plaque and thrombus. The average duration for one angioscopic procedure was 13 min. The average amount of infused saline was 15.6 ml per one angioscopic procedure.

Angiographic analysis. Initial and postprocedural flow in the infarct-related artery was graded according to the Thrombolysis In Myocardial Infarction (TIMI) trial classification. Quantitative angiographic measurements of the lesion were performed by using digital angiograms that were analyzed off-line with an automated edge-detection system (CMS, Medis Medical Imaging System, Nuenen, The Netherlands). The minimum luminal diameter, reference diameter, and percent diameter stenosis were measured from end-diastolic frames and the projection that demonstrated the highest stenotic site. The measurement of the reference vessel diameter was made at the proximal part of the vessel nearest the initial stenotic or occluded lesion. We routinely perform angiography in at least two projections after the intracoronary injection of nitroglycerin (0.1 mg). Total occlusion was defined as TIMI flow grade 0 or 1. Total occlusion was assigned a value of 0 mm for minimum luminal diameter and 100% for percent diameter stenosis. Restenosis was defined as an increase in percent stenosis to ≥50%.

Angioscopic analysis. Angioscopic definitions were based on an angioscopic classification system developed by the European Working Group on Coronary Angioscopy (7), as

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Table 1. Clinical Characteristics

	Total (n = 43)	Acute MI (n = 28)	PIA (n = 15)	p Value
Age (yrs)	61 ± 11	61 ± 11	62 ± 9	0.95
Men	32 (74%)	21 (75%)	11 (73%)	0.91
Hypertension	15 (35%)	9 (32%)	6 (40%)	0.61
Diabetes mellitus	18 (42%)	11 (39%)	7 (47%)	0.64
Hyperlipidemia	29 (67%)	17 (61%)	12 (80%)	0.20
Current smokers	29 (67%)	17 (61%)	12 (80%)	0.20
Previous MI	3 (7%)	3 (11%)	0	0.19
Killip class I/II on admission	26 (93%)/2 (7%)	26 (93%)/2 (7%)	11 (73%)/4 (27%)	0.08
Previous thrombolysis (t-PA)	19 (44%)	13 (46%)	6 (40%)	0.69
Non–Q-wave MI	1 (2%)	1 (4%)	0	—
Interval from acute MI onset to catheterization (h)				
Median	17	15	77	< 0.0001
<6	8 (19%)	8 (29%)	—	
6 ≤< 12	4 (9%)	4 (14%)	—	
12 ≤< 24	12 (28%)	12 (43%)	—	
24 ≤< 48	6 (14%)	4 (14%)	2 (13%)	
48 ≤< 72	3 (7%)	—	3 (20%)	
≥72	10 (23%)	—	10 (67%)	
Medications				
Beta-blockers	15 (35%)	10 (36%)	5 (33%)	0.88
ACE inhibitors	19 (44%)	11 (39%)	8 (53%)	0.38
Nitrate	10 (23%)	7 (25%)	3 (20%)	0.71
Calcium blockers	10 (23%)	6 (21%)	4 (27%)	0.70
Antiplatelet drugs	43 (100%)	28 (100%)	15 (100%)	1.00
Lipid-lowering drugs	29 (67%)	19 (68%)	10 (67%)	0.94

Data are presented as the mean value ± SD or number (%) of subjects. 6 ≤<12 means more than or equal to 6 h, and less than 12 h; 12 ≤<24 means more than or equal to 12 h, and less than 24 h; 24 ≤<48 means more than or equal to 24 h, and less than 48 h; 48 ≤<72 means more than or equal to 48 h, and less than 72 h.

ACE = angiotensin-converting enzyme; MI = myocardial infarction; PIA = postinfarction angina; t-PA = tissue-type plasminogen activator.

well as our previous studies (8,9). A thrombus was defined as: 1) a coalescent red, white, or mixed color; and 2) a superficial (lining) or protruding mass adhering to the vessel wall. The shape of the plaque was classified as smooth plaque if a segment of a normal-appearing wall was visualized; complex plaque was defined when the surface had a rough, ulcerated, or irregular appearance with ragged, cracked, and fissured edges. An intimal flap was defined as visible cracks or fissures on the luminal surface or large and thick structures protruding into the lumen (large surface disruptions), except for small, thin, and free fronds of tissue. The predominant color of the plaque was classified as white or yellow. The extent of neointimal stent coverage was semiquantitatively evaluated using a 5-point scoring system: 0 = complete exposure of stent struts; 1 = exposure of stent struts with partial coverage; 2 = >50% coverage; 3 = almost complete coverage with slightly visible stent struts; and 4 = complete coverage.

The angioscopic results were separately reviewed by two experienced angioscopists who were unaware of either the angiographic or clinical findings. In case of any disagreement, a third observer evaluated the angioscopic images, and consensus was obtained by discussion. Intra-observer agreement was measured by having an observer repeat the assessment of 20 angioscopic images (presented in random order) after one week. The inter-observer agreement was measured by comparing the assessment of 20 angioscopic images by two observers. The rate of intra- and inter-observer agreements for the evaluated angioscopic items (protruding thrombus, intimal flap, complex plaque, and yellow plaque) were both 95%. The kappa values for intra-observer agreement of a protruding thrombus, intimal flap, complex plaque, and yellow plaque were 1.00, 0.78, 0.90, and 0.90, respectively. In addition, the kappa values for inter-observer agreement of those items were 1.00, 0.74, 0.90, and 0.89, respectively.

Statistical analysis. The data are presented as the mean value ± SD. Differences between proportions were assessed by chi-square analysis. Continuous variables were compared using the unpaired Student *t* test and one-way analysis of variance with concomitant Fischer protected least significant difference and Scheffé F tests. Statistical significance was accepted at $p < 0.05$. The baseline clinical and angiographic characteristics and procedural details are described in Tables 1 and 2.

RESULTS

Angioscopy procedures (Fig. 1). In 4 (9%) of 43 patients, angioscopy could not be successfully performed at baseline. It was impossible to deliver the angioscopy catheter in one of four patients or to visualize the entire circumference of

Table 2. Baseline Angiographic Characteristics and Stent Implantation Procedures

	Total (n = 43)	Acute MI (n = 28)	PIA (n = 15)	p Value
Infarct-related artery				0.42
RCA	16 (37%)	9 (32%)	7 (47%)	
LAD	23 (54%)	17 (61%)	6 (40%)	
LCx	4 (9%)	2 (7%)	2 (13%)	
TIMI flow grade				0.40
0/1	17 (40%)/2 (4%)	13 (46%)/1 (4%)	4 (27%)/1 (7%)	
2/3	5 (12%)/19 (44%)	4 (14%)/10 (36%)	1 (7%)/9 (60%)	
Quantitative angiographic measurements				
Reference diameter (mm)	3.37 ± 0.77	3.39 ± 0.45	3.31 ± 0.45	0.86
Minimal luminal diameter (mm)	0.43 ± 0.57	0.43 ± 0.56	0.43 ± 0.66	0.99
Percent stenosis	83 ± 22	83 ± 23	83 ± 22	0.96
Balloon angioplasty				
Maximum balloon size (mm)	2.88 ± 0.31	2.87 ± 0.32	2.90 ± 0.28	0.73
Maximum pressure (atm)	9.0 ± 1.5	9.1 ± 1.4	8.7 ± 1.4	0.41
Stent implantation				
Reason for stenting				0.58
Planned	31 (72%)	17 (61%)	14 (93%)	
Suboptimal result	7 (16%)	7 (25%)	0	
Bail-out use	5 (12%)	4 (14%)	1 (7%)	
Type of implanted stent				
Palmaz-Schatz	6 (14%)	3 (11%)	3 (20%)	
Multi-link	12 (28%)	10 (36%)	2 (13%)	
NIR	10 (23%)	7 (25%)	3 (20%)	
GFX	15 (35%)	8 (29%)	7 (47%)	
Stent length (mm)	17.6 ± 3.8	16.9 ± 3.5	18.8 ± 4.1	0.11
Maximum balloon size postdilation (mm)	3.56 ± 0.42	3.55 ± 0.43	3.57 ± 0.42	0.92
Maximum pressure postdilation (atm)	13.1 ± 2.6	12.9 ± 2.8	13.4 ± 2.3	0.58

Data are presented as the number (%) of patients or mean value ± SD.
LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

the target lesion in the other three patients, because of tortuous or angular vessels. For 39 patients, angioscopic observations were obtained for 39 lesions at baseline, for 35 lesions immediately after balloon angioplasty, for 39 lesions immediately after stenting, for 36 lesions at one-month follow-up, and for 30 lesions at six-month follow-up.

Angiographic findings. Improvement in TIMI flow grade 3 after balloon angioplasty and stenting was achieved in 38 (88%) and 41 (95%) of 43 patients, respectively. In two patients, "no reflow" was observed immediately after stenting. The percent diameter stenosis was significantly reduced from 83 ± 22% at baseline to 55 ± 28% after balloon angioplasty ($p < 0.01$) and to 7 ± 7% after stenting ($p < 0.01$). The percent diameter stenosis at one- and six-month follow-up were 12 ± 9% and 25 ± 23%, respectively ($p < 0.01$). Restenosis at the six-month follow-up was noted in 6 (20%) of 30 patients.

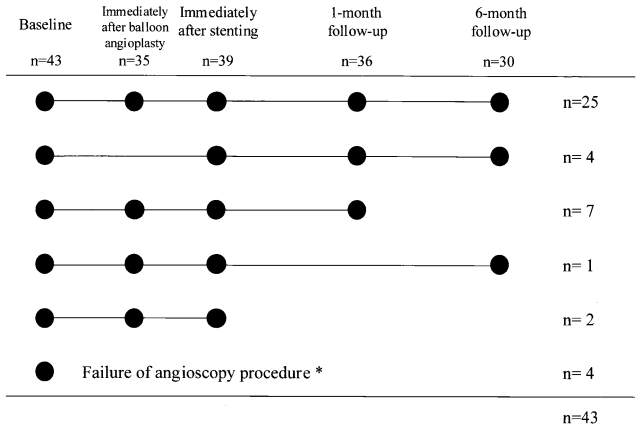

Figure 1. Coronary angioscopy procedures. *Failure of the angioscopy procedure was defined as when the angioscope could not visualize the entire circumference of the target lesion in order for it to be adequately evaluated or if it could not reach to the target lesion because of a tortuous proximal vessel.

Comparison of baseline angioscopic characteristics between acute MI and PIA (Table 3). There was no difference in the color of thrombus between acute MI and PIA. However, a higher frequency of protruding thrombus was observed in patients with acute MI (85% in acute MI vs. 54% in PIA, $p = 0.038$). The plaque shape and color did not differ between acute MI and PIA.

Angioscopic morphologic changes before and after stenting. THROMBUS AND INTIMAL FLAP (FIG. 2). At baseline, thrombus was seen in all lesions. The thrombus was classified as a protruding thrombus in 29 (74%) and a lining thrombus in 10 lesions (26%). The color of the thrombus was red in seven (18%), mixed in 28 (72%), and white in four (10%) (Table 3). After balloon angioplasty, the protruding thrombus significantly decreased compared with baseline (37% vs. 74%, $p < 0.01$). Immediately after stenting, the protruding thrombus was completely resolved

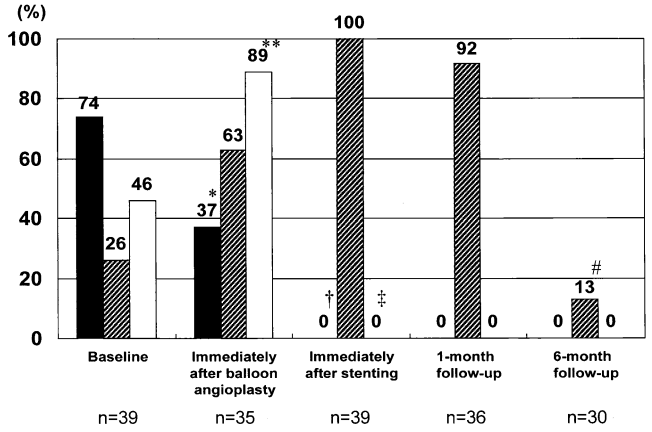

Figure 2. Changes in the incidence of thrombus and intimal flap. The intimal flap was assessable in 28 of 39 lesions at baseline. In the 11 remaining lesions, the intimal flap could not be seen because it occupied the lumen due to occlusive thrombus. *$p < 0.01$ vs. protruding thrombus at baseline. †$p < 0.01$ vs. protruding thrombus immediately after balloon angioplasty. #$p < 0.01$ vs. lining thrombus immediately after stenting. ‡$p < 0.01$ vs. intimal flap immediately after balloon angioplasty. **Solid bars** = protruding thrombus; **hatched bars** = lining thrombus; **open bars** = intimal flap.

($p < 0.01$), and a lining thrombus was seen in all lesions. At one-month follow-up, a lining thrombus was observed in 33 (92%) of 36 lesions, whereas it was seen in 4 (13%) of 30 lesions at six-month follow-up ($p < 0.01$).

The plaque shape and color were assessable in 28 of the 39 lesions at baseline. In the 11 remaining lesions, it was impossible to assess the plaque because an occlusive thrombus was occupying the lumen.

At baseline, complex and yellow plaque was observed in 27 lesions (96%) and an intimal flap was seen in 13 (46%) of 28 assessable lesions. After balloon angioplasty, an intimal flap was observed in 31 (89%) of 35 lesions and was more frequently observed after balloon angioplasty than at baseline (89% vs. 46%, $p < 0.01$). After stenting, the flap disappeared in all lesions.

Table 3. Baseline Angioscopic Findings

	Total (n = 39)	Acute MI (n = 26)	PIA (n = 13)	p Value
Thrombus	39 (100%)	26 (100%)	13 (100%)	
Size				
Lining	10 (26%)	4 (15%)	6 (46%)	0.038
Protruding	29 (74%)	22 (85%)	7 (54%)	
Color				0.42
Red	7 (18%)	6 (23%)	1 (8%)	
Mixed	28 (72%)	18 (70%)	10 (77%)	
White	4 (10%)	2 (8%)	2 (15%)	
Plaque*				
Shape				
Smooth	1 (2.5%)	1 (4%)	0	0.65
Complex	27 (69%)	17 (65%)	10 (77%)	
Color				
White	1 (2.5%)	1 (4%)	0	0.65
Yellow	27 (69%)	17 (65%)	10 (77%)	

*Plaque surface and color were assessable in 28 of the 39 lesions at baseline. In the 11 remaining lesions, it was impossible to assess the plaque because the thrombus occupied the lumen. Data are presented as the number (%) of subjects.

Abbreviations as in Table 1.

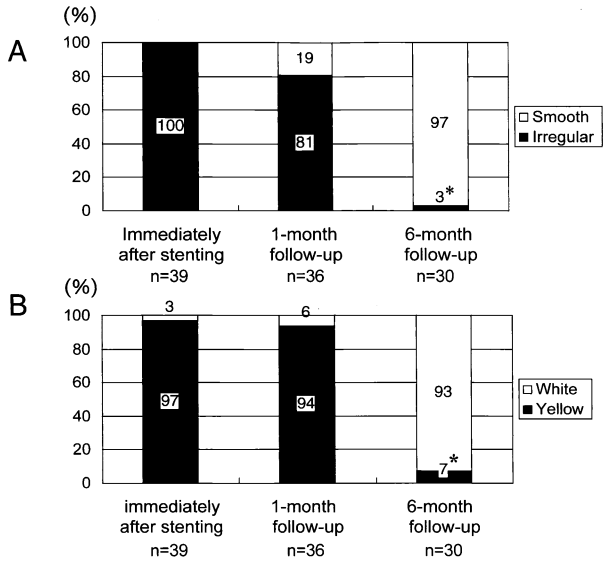

Figure 3. Changes in the plaque surface **(A)** and color **(B)** after stenting. *$p < 0.01$ vs. immediately after stenting and one-month follow-up.

PLAQUE SURFACE AND COLOR (FIG. 3). The plaque surface was defined as irregular in all and as yellow in 38 (97%) of 39 lesions immediately after stenting. At the one-month follow-up, an irregular surface and yellow color were still observed through the stent struts in 29 (81%) and 34 (94%) of 36 lesions, respectively. At six-month follow-up, the plaque surface was classified as smooth in 29 (97%) and the plaque color as white in 28 (93%) of 30 lesions. An irregular shape and yellow color were observed in only one (3%) and two (7%) lesions.

Stent coverage (Fig. 4). In 36 assessed lesions at one-month follow-up, a coverage score of 0 was observed in one lesion (3%), whereas a score of 1 was observed in 25 (69%), a score of 2 in eight (22%), and a score of 3 in two (6%) lesions. In 30 assessed lesions at six-month follow-up, a coverage score of 4 was observed in 24 lesions (80%), a score of 3 in 5 lesions (17%), and a score of 2 in 1 lesion (3%). The

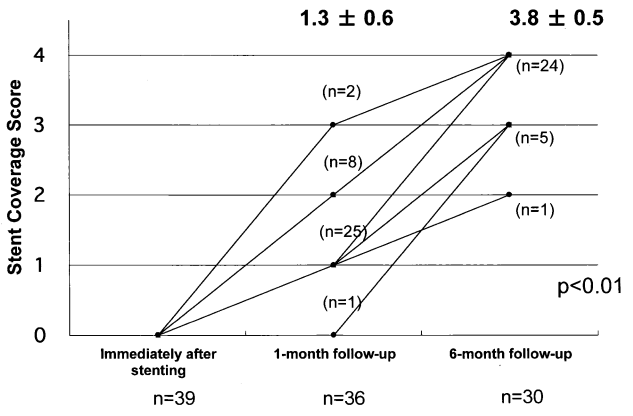

Figure 4. Changes in the stent coverage score after stenting. Data are presented as the mean value ± SD.

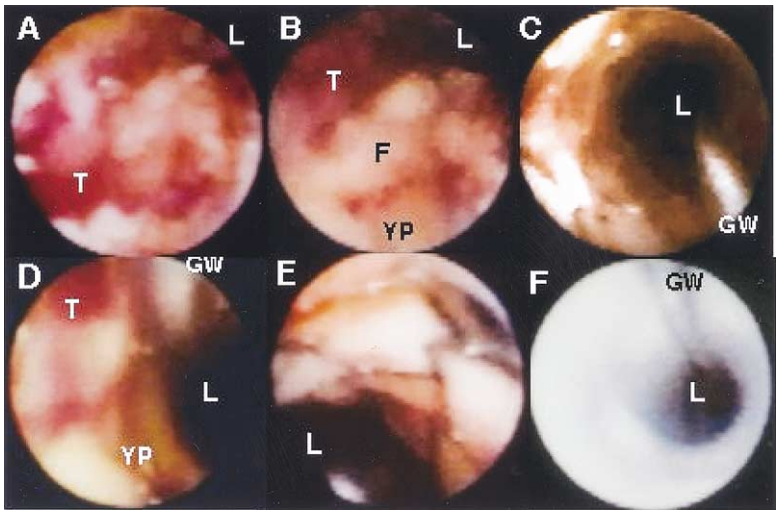

Figure 5. Serial angioscopic images. **(A)** At baseline, a protruding mixed thrombus was seen. **(B)** Immediately after balloon angioplasty, a protruding thrombus and intimal flap were seen. **(C)** Immediately after stenting, a wide vessel lumen was obtained by the stent. **(D)** At one-month follow-up, a lining thrombus was seen. **(E)** At one-month follow-up, there was partial neointimal coverage (coverage score = 1). **(F)** At six-month follow-up, there was smooth and white plaque (coverage score = 4) without thrombus. F = intimal flap; GW = guide wire; L = lumen; YP = yellow plaque; T = thrombus.

stent coverage score significantly increased at six-month follow-up compared with one-month follow-up (1.3 ± 0.6 vs. 3.8 ± 0.5, $p < 0.01$).

Clinical outcome. In our series, no major cardiac events (death, reinfarction, and urgent revascularization for recurrent ischemia) occurred during follow-up. At one-month follow-up, no reocclusion or restenosis were recognized in any cases. At six-month follow-up, no patient presented with an unstable coronary syndrome. However, restenosis was observed in 6 (16%) of 30 eligible patients for angiographic and angioscopic follow-up, and target lesion revascularization was performed for 2 patients (6%) with asymptomatic restenosis A representative example case is shown in Figure 5.

DISCUSSION

This study represented the first serial assessment by coronary angioscopy to evaluate the short- and inter-mediate-term results of stent implantation for unstable plaque.

Baseline characteristics of infarct-related lesion. Despite the fact that our population was composed of a heterogeneous group of MI patients at the time of angioscopic observation at baseline, the morphologic aspect of infarct-related lesions showed plaque instability demonstrating a complex morphology, yellow color, and thrombus in the majority of patients. In addition, patients with PIA, as well as those with acute MI, had a high prevalence of massive thrombus. Shapiro et al. (10) reported that thrombolysis effectively restored the flow on angiography, accompanied with a resolution of angina in some patients with PIA. Based on our data, it might be reasonable that thrombolysis in patients with PIA was effective to improve the flow of the infarct-related artery.

Early morphologic changes after stenting. Despite the fact that balloon angioplasty resulted in a significant reduction in thrombus size, a protruding thrombus was still present in 37% of the lesions. Furthermore, the vessel surfaces were found to have evidence of extensive intimal damage, with a flap at the angioplasty site in almost all lesions. The extent of the damage was distinctly higher after balloon angioplasty than at baseline. These intra-luminal structures may contribute to high rates of an early adverse outcome after balloon angioplasty for unstable coronary disease (11). In fact, some investigators reported that angioscopic thrombus was strongly associated with PTCA complications (12,13); in particular, a protruding thrombus was a high risk factor for reocclusion and restenosis (14). However, the majority of abrupt occlusions after PTCA were due to dissections and flaps (15). In our series, however, no adverse outcome was observed in any patients, despite the fact that a lining thrombus was seen in almost all patients immediately after stenting. This difference might be due to differences in the coronary intervention method. All of our patients underwent stent implantation. On the other hand, a non-stent coronary intervention was performed in the previous studies. Our angioscopic study demonstrated that a subsequent stent placement completely compressed and covered a protruding thrombus and intimal flap, potentially causing an adverse outcome and resulting in an increased size of the vessel lumen. This finding may be one of the favorable effects of stenting.

Angioscopic follow-up after stenting. At one-month follow-up, a thrombus, irregular surface, and yellow color were still observed at the stented lesions. This finding suggested that the plaque instability seen on angioscopy lasted for at least one month, even after stenting. Neointimal stent coverage was nearly completed by about six months after stenting. Surprisingly, a thrombus was still presented in some cases, even at six-month follow-up. Several possible explanations can be offered for the presence

of a residual thrombus. Sakatani et al. (16) reported an interesting case in which the implanted stent was completely exposed, along with a thrombus, even at 16 months after stenting. They speculated that the development of neointimal proliferation might be retarded because of a poor stent apposition to the vessel wall. Similarly, an inadequate stent apposition might cause incomplete neointimal coverage with thrombus in some of our patients. Second, some of these lesions could also have had a wall hemorrhage rather than a thrombus. Third, the tissue factor contained in the neointima may be responsible for luminal surface thrombogenicity, when neointimal proliferation was the most active at six months after stenting.

Late morphologic changes after stenting. Stable plaque has a thick fibrous cap consisting of smooth muscle cells overlying the lipid core. Although these lesions may be clinically silent or cause angina, they rarely rupture or precipitate life-threatening events. In contrast, a fibrous cap in unstable plaque is thin and contains a few smooth muscle cells. This plaque is prone to rupture, thus leading to the development of life-threatening acute coronary syndrome. Concerning the relationship between plaque color and histologic assessment of plaque, yellow plaque is considered to be atheromatous plaque, which consists of a large lipid pool with a thin fibrous cap. White plaque, in contrast, is fibrous plaque with a thick fibrous cap (17,18). An experimental study showed that the yellow of the plaque color on angioscopy was dependent on the cap thickness overlying the lipid core (19). Indeed, yellow plaques were very common in acute coronary syndromes, and many sites of disrupted plaques were observed in yellow plaques (2,3,9,20). Therefore, yellow plaque can be considered as unstable plaque, whereas white plaque is stable.

In this study, although most of patients had angioscopic characteristics of plaque instability before stenting, the appearance at six months after stenting was almost completely stable plaque, which was observed as smooth white plaque without thrombus, whether restenosis was present or not. And no patient presented with an acute coronary syndrome during follow-up. This change (angioscopic plaque stabilization) is due to the fact that the stent, which sealed off the disrupted plaque, was covered completely by neointimal proliferation. Angioscopic plaque stabilization may be supportive of the finding and speculation of Ruygrok et al. (21), that one of the predictors of asymptomatic restenosis at six-month follow-up after stenting was unstable angina at the initial presentation, and that stents might possibly have a plaque-stabilizing effect in acute coronary syndromes, respectively. Such a stent may also have a plaque-healing effect similar to balloon angioplasty (4,5). This may support the proposal of smooth muscle cell proliferation as a therapy for plaque stabilization (22,23). Due to this fact, it is not surprising that some randomized studies comparing stenting with balloon angioplasty in patients with acute MI have failed to show a reduction in the rate of reinfarction or death, even though stenting had a lower incidence of restenosis and revascularization than balloon angioplasty (24,25). However, it remains unclear as to whether such angioscopic plaque stabilization is directly linked to clinical stabilization or not. Indeed, pathologic studies have demonstrated that neointimal growth after stenting is associated with a high degree of arterial injury and inflammation (26).

Study limitations. Several limitations of this study should be considered. First, our study population consisted of selected patients. Our inclusion criteria limited the number of patients who could be studied. The small number of patients may not be representative of all patients with acute or recent MI. However, it is noteworthy that the serial angioscopic observations have disclosed the macromorphologic changes of stenting for unstable plaque. Second, this study lacked of a contemporary group of patients treated with balloon angioplasty for a comparison purpose. Based on our institutional policy, more than 85% of patients with acute or recent MI in whom percutaneous coronary interventions were performed were treated with stenting in our hospital. Therefore, the impact of stenting could only be inferred by a comparison with the findings of previous reports. Ueda et al. (5) reported that ~80% of infarct-related plaques still had a yellow color, even at six months after PTCA. The angioscopic plaque-stabilizing effect of stenting may appear more rapidly than that of PTCA. Finally, we could not confirm whether or not angioscopic plaque stabilization (smooth and white appearance without thrombus) was linked to clinical stabilization in the present study. Further study is needed to prove that angioscopic plaque stabilization correlates to clinical stabilization.

Conclusions. This angioscopic study demonstrated that the morphologic changes after stenting for unstable plaque were the following: 1) a stent compressed and covered a disrupted yellow plaque, with a protruding thrombus and intimal flap, leading to a wide vessel lumen; and 2) the stent induced angioscopic plaque stabilization (smooth and white and without thrombus) through neointimal proliferation, and the sealing was achieved at about six months after stenting, accompanied with complete neointimal stent coverage. Thus, a stent is like "a bandage on a wound." We suggest that mechanical plaque sealing by stenting may therefore be a potentially effective therapeutic strategy for achieving plaque stabilization.

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