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Percutaneous Coronary Angioscopy in Patients With Restenosis After Coronary Angioplasty

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Percutaneous transluminal coronary angioscopy with a flexible steerable microangioscope was performed in five patients undergoing repeat angioplasty. Recurrent lesions were assessed by angioscopy before and after the angioplasty procedure. The most common surface morphology observed in these restenosis lesions was that of white unpigmented lesions consistent with the proliferation of fibrous tissue. Also noted during angioscopy was the presence or absence of thrombus or dissection in association with the lesions either before or after angioplasty. Filmy wisps of tissue, presumably intimal flaps, were commonly visualized after angioplasty. There were no complications related to angioscopy or angioplasty in these patients.

The surface morphology of restenosis lesions appears to be different from that of primary atherosclerotic lesions. The lesions in these five patients with restenosis were generally white and fibrotic in appearance, as opposed to the pigmented yellow to yellow-brown lesions commonly seen in undilated atherosclerotic lesions. It was also noted that the presence of intracoronary thrombus was strongly associated with the clinical syndrome of unstable angina. These findings support the hypothesis that restenosis lesions are the result of a reparative process consisting of smooth muscle cell proliferation and fibrosis.

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Restenosis after coronary balloon angioplasty remains a major limitation of this technique. Attempts to lessen the incidence of restenosis by pharmacologic interventions or procedural techniques have been either unsuccessful or equivocal. To better understand the mechanism by which restenosis occurs and thereby develop a rational approach to the reduction of restenosis, investigators have studied animal models and a relatively small number of human specimens at autopsy after angioplasty. Animal models of atherosclerosis are capable of producing lesions that in some respects resemble human lesions, but none of these experimentally induced lesions reproduce the full spectrum of the atherosclerotic lesion as it occurs in human patients. Morphologic studies of autopsy material are hindered by the possibility of artifacts induced in the preparation of the tissue and are biased in that the majority of specimens studied to date reflect the unsuccessful outcome of the procedure resulting in the patient's death.

The advent of a steerable microangioscope has allowed us to examine the intravascular morphology of selected lesions during percutaneous coronary artery catheterization. This device permits the in vivo surface morphology of human coronary artery lesions to be studied in detail. In this study we report our angioscopic observations in five patients undergoing repeat coronary balloon angioplasty for symptomatic restenosis.

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Methods

Study patients. Five patients with clinical evidence of restenosis after percutaneous coronary balloon angioplasty underwent repeat dilation in conjunction with coronary angioscopy. Patient demographic characteristics are listed in Table 1. This protocol was approved by our Clinical Investigation Committee. Informed consent was obtained from each patient.

Angioscopy. The coronary angioscopy system (Advanced Cardiovascular Systems [ACS]) consists of the angioscope catheter, a guide wire and a video chain. The video chain includes a video camera, a character generator, a high resolution video monitor, a high intensity xenon light source and a ¾ in. (1.91 cm) videotape recorder. The angioscope catheter (Fig. 1) is 1.4 mm in diameter and has similar performance characteristics as coronary angioplasty balloon catheters. The angioscope catheter contains channels for the inflation and deflation of the distal occlusion balloon, a lumen that will accommodate a 0.014 in. (0.036 cm) guide wire and allow the infusion of clear flush solution to clear the lumen of blood, one channel for 11 illumination fibers and a channel to accommodate 2,000 imaging fibers. The distal occlusion balloon is not a dilating balloon, but rather a low

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Table 1. Characteristics of Five Patients

Pt. No.	Age (yr)/ Gender	Artery	Clinical Status	Prior PTCA (weeks)	PTCA No.
1	40/M	LCx	SA	69	2
2	78/M	RCA	UA	8	2
3	48/M	RCA	UA	34	3
4	53/F	LAD	UA	6	2
5	60/M	RCA	UA	31	2

F = female; LAD = left anterior descending artery; LCx = left circumflex artery; M = male; Pt. = patient; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery; SA = stable angina; UA = unstable angina.

pressure polyethylene balloon (2.5 to 4 mm inflated diameter) designed to occlude anterograde flow when inflated to ≤3 atm in an appropriately sized artery. The specially designed angioscope guide wire is configured with preformed curves at its distal end to allow the operator to manually direct the tip of the angioscope by rotating or withdrawing the guide wire.

Procedure. After routine preoperative sedation and sterile preparation of the right femoral access site, an 8F vascular sheath (Cordis) was inserted percutaneously into the right femoral artery with a modified Seldinger technique and 10,000 U of heparin was administered. An 8F angioplasty guiding catheter (ACS) was advanced under fluoroscopic guidance to the coronary ostium of interest. Baseline angiography of the target lesion was then performed in two or more views. The angioscope and angioscope guide wire were advanced through the guiding catheter to the coronary ostium. The angioscope guide wire was then advanced across the target lesion and the angioscope catheter advanced up to but not through the lesion. Imaging was then performed with inflation of the distal occlusion balloon to ≤3 atm, distal infusion of 2 to 10 ml of warmed Ringer's lactate solution and manual manipulation of the angioscope guide wire to deflect the tip of the angioscope catheter toward the lesion. The duration of each imaging attempt was approximately 30 s. After adequate images had been obtained, the angioscope was withdrawn and exchanged over a guide wire for a dilating balloon and angioplasty was then performed.

After angioplasty, immediate angiography was performed with the guide wire across the lesion. The angioplasty balloon was exchanged for the angioscope catheter and postangioplasty angioscopy was performed. After angioplasty, it was possible to advance the angioscope through the lesion and a much more complete examination of the dilated lesion was possible. After completion of the angioscopic examination, the catheter and guide wire were withdrawn and final angiography was performed.

During angioscopic viewing, patients experienced chest pain and electrocardiographic changes consistent with ischemia that were transitory and resolved with balloon deflation. All patients received routine postangioplasty care.

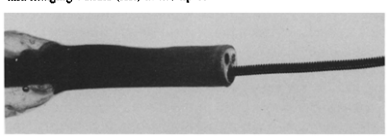
Lesion assessment. Angiography of the lesions before and after angioplasty was reviewed on 35 mm cine film. The presence of intracoronary thrombus was defined as evidence of an intravascular filling defect. Arterial dissection was defined as a linear stain of contrast medium associated with the lesion. Angioscopic images were reviewed on ¾ inch videotape and evaluated for the presence or absence of thrombus or dissection. Thrombus was defined as a red or red-brown collection of material that persisted despite adequate flushing to clear the lumen of blood. Dissection or tear in the wall of the artery was defined as either an intimal flap or deeper medial dissection. Intimal flaps were identified as thin fronds of white tissue that appeared to be loosely adherent to the wall. Deeper dissections appeared as crevices in the wall of the artery and were linear in configuration. One other morphologic feature noted included pigmentation of the lesion. Nonpigmented lesions appeared white compared with pigmented lesions, which contained yellow to yellow-brown coloration.

Case Reports

Case 1. This patient is a 40 year old man who underwent angioplasty of a left circumflex coronary artery lesion 18 months before the recurrence of exertional angina pectoris 1 year later and 6 months before this hospitalization. Cardiac catheterization revealed inferior hypokinesia of the left ventricle, total occlusion of the right coronary artery (documented at catheterization 18 months previously) and a recurrent 95% focal stenosis of the mid circumflex artery. Angiographically, the stenosis was concentric and after angioplasty it was reduced from 95% to 20% without evidence of thrombus, dissection or ulceration of the plaque. Angioscopy before angioplasty showed the lesion to be white and nodular without thrombus or dissection. After angioplasty, marked improvement in the lumen and several very delicate fronds of intimal tissue that had been disrupted after angioplasty were noted on angiography and angioscopy.

Case 2. This patient is a 78 year old man who initially underwent angioplasty of a posterior descending coronary artery lesion for symptoms of unstable angina. Two months later, he experienced recurrent symptoms of angina pectoris at rest. Cardiac catheterization revealed a recurrent 99% stenosis at the origin of the posterior descending artery.

Figure 1. Angioscope (Advanced Cardiovascular Systems) showing a guide wire (right) through the distal flush lumen, illumination fibers and imaging bundle (left) at the tip of the 1.4 mm diameter catheter.



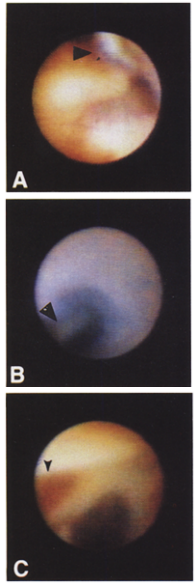


Figure 2. A, Case 2. Preangioplasty view of a complex lesion showing a healed dissection from the prior angioplasty (**arrow**). Thrombus is present at the 7 o'clock position. B, Case 4. Preangioplasty image of a white nonpigmented restenosis lesion. The guide wire (**arrow**) is in view within the lumen of the artery. C, Postangioplasty view of a primary lesion. The lesion is heavily pigmented. The guide wire can be seen within the dilated lumen (**arrow**).

Angiography before and after angioplasty did not reveal evidence of thrombus or dissection associated with the lesion. Angioscopy before angioplasty did show the presence of several mural thrombi at the site of the lesion. The lesion also showed evidence of a healed dissection, with the irregular edges of the initial medial dissection still protruding into the lumen of the artery (Fig. 2A). The restenosis lesion was white and had a nodular consistency, with mounds of heaped-up tissue seen on its surface.

Case 3. This patient is a 40 year old man who underwent angioplasty of a single vessel right coronary artery lesion in March 1989. Restenosis of this lesion occurred 3 months later and the lesion was successfully redilated. Approximately 8 months after his second angioplasty, he presented with recurrence of angina pectoris at rest that was relieved with sublingual nitroglycerin. Diagnostic coronary angiography revealed that restenosis had occurred and was now a 95% stenosis. Angioplasty and angioscopy were performed at the time of the diagnostic catheterization. Angiography before and after angioplasty revealed no evidence of thrombus or dissection associated with the lesion. Angioscopy before angioplasty showed that the surface of the lesion was white. After angioplasty, linear dissection was evident at the site of the dilated lesion and thrombus within the lesion, firmly adherent to the arterial wall, was plainly visible. Angioplasty reduced the lesion to a 30% residual stenosis by angiography and angioscopy confirmed that the luminal diameter was significantly increased.

Case 4. This patient is a 53 year old woman who presented with a non-Q wave lateral myocardial infarction. Diagnostic angiography revealed a subtotal occlusion of the mid left anterior descending artery that was successfully dilated with a residual stenosis of <5%. She reported recurrent angina in an accelerated crescendo pattern 6 weeks later. Angiography revealed a concentric recurrent 90% stenosis at the site of the prior angioplasty. There was no evidence of thrombus, dissection or ulceration of the plaque on the angiogram. Angioscopy revealed the lesion to be white with a smooth texture (Fig. 2B). The lesion appeared to be concentric within the lumen of the artery. Angioscopy before and after angioplasty showed a dissection involving the lesion and intracoronary thrombi were visualized. After successful angioplasty, the stenosis was reduced to 30%, which was consistent with the increased luminal diameter seen on angioscopy.

Case 5. This patient is a 60 year old man who underwent angioplasty of a right coronary artery lesion 7 months before this presentation in the setting of an acute inferior infarction. Two days before admission, he experienced crescendo angina and angina at rest. Angiography showed a 95% discrete concentric stenosis of the mid right coronary artery without evidence of dissection, thrombus or ulceration of the lesion. Preangioplasty angioscopy showed the lesion to be white with a smooth glistening surface. After angioplasty, there was evidence of small intimal flaps and coronary thrombi associated with the dilated lesion. The lumen after angioplasty appeared to be significantly enlarged and was consistent with the angiographic assessment.

Discussion

Surface morphology of the restenosis lesion: a white fibrotic scar. Restenosis after balloon angioplasty is a complex process that is incompletely understood. However, there appears to be a consistent theme suggesting that restenosis lesions are, in fact, a distinct process separate from the primary lesion. Angiographic findings in patients with restenosis after balloon angioplasty indicate that the restenosis lesion is morphologically dissimilar to the original lesion in the majority of cases (1). The surface morphology before and after angioplasty observed in these five cases of restenosis after balloon angioplasty is distinctly different from the

lesion morphology we have observed in primary lesions. Whereas restenosis lesions often appear to be white, primary lesions commonly contain yellow or brown pigmentation (Fig. 2C).

Evidence from animal models and human autopsy specimens (2) suggests that the restenosis lesion is composed of a fractured atheromatous plaque with superimposed smooth muscle cell proliferation and fibrointimal hyperplasia. Atherectomy specimens removed from restenosis lesions after primary atherectomy or balloon angioplasty reveal hypercellularity and intimal hyperplasia in every case (3). These findings are in agreement with our finding that these restenosis lesions have the appearance of a white fibrotic scar. However, one lesion was associated with yellow pigment. This patient had a relatively early return of symptoms (8 weeks) that was associated with a very prominent healing dissection. Perhaps the restenosis in this case was due to a poor initial angioplasty result rather than to proliferation of smooth muscle cells.

Intracoronary thrombus. The presence of intracoronary thrombus is strongly linked to the clinical syndrome of unstable angina pectoris (4). In four of the five patients, restenosis was manifested clinically as unstable angina. Intracoronary thrombus was seen in association with the recurrent lesion in all four of the patients with unstable angina and was not seen in the patient with stable angina. None of the patients had evidence of intracoronary thrombus by angiography. The intracoronary thrombi seen by angioscopy did not appear to be occlusive. Rather they appeared to be mural thrombi that were firmly attached to the wall of the artery and could not be flushed away. The fact that the thrombi are mural and not protruding into the lumen of the artery may explain the lack of sensitivity of angiography in identifying thrombus. These cases also point to the superior sensitivity of angioscopy in detecting intracoronary thrombus not seen on angiography.

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