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Angioscopic Versus Angiographic Detection of Intimal Dissection and Intracoronary Thrombus

PETER DEN HEIJER, MD, PHD, DAVID P. FOLEY, MD,* JAVIER ESCANED, MD,*
HANS L. HILLEGE, MD, RENÉ B. VAN DIJK, MD, PHD, PATRICK W. SERRUYS, MD, PHD, FACC,*
KONG I. LIE, MD, PHD

Groningen and Rotterdam, The Netherlands

Objectives. This study was undertaken to compare coronary angioscopy with angiography for the detection of intimal dissection and intracoronary thrombus.

Background. It has been demonstrated previously that coronary angioscopy provides more intravascular detail than cineangiography. Both imaging methods have to be compared directly to assess the additional diagnostic value of angioscopy.

Methods. The angiograms and videotapes of 52 patients who had undergone angioscopy were reviewed independently by two observers unaware of other findings. Classic angiographic definitions were used for dissection and thrombus. Angioscopic dissection was defined as visible cracks or fissures on the lumen surface or mobile protruding structures that are contiguous with the vessel wall. Angioscopic thrombus was defined as a red, white or mixed red and white intraluminal mass.

Results. Angiography and angioscopy were in agreement in 40.4% of cases in the absence of thrombus and in 11.5% in the presence of thrombus. No fewer than 25 (48.1%) angioscopically observed thrombi remained undetected at angiography. With angioscopy as the standard, although the specificity of angiography for thrombus was 100%, sensitivity was very low at 19%. Angioscopic dissection was present in 40 patients (76.9%) versus angiographic dissection in 15 patients (28.8%). With regard to dissection, there was no correlation between the two imaging methods ($r_{\phi} = 0.15$, $p = 0.29$).

Conclusions. Coronary angiography underestimates the presence of intracoronary thrombus. Angioscopy and angiography are complementary techniques for detecting and grading intimal dissections.

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Coronary angioscopy is a relatively new technique for imaging the vascular inner surface and intraluminal structures of the coronary arteries (1–3). The recent introduction of a small, flexible, wire-guided, high resolution coronary angioscopy system has led to an increasing acceptance of this imaging method for clinical and investigational purposes (4–8). From the beginning of its clinical application, it has been recognized that angioscopy provides more intravascular detail than can be detected with angiography. The presence of intracoronary thrombus and intimal dissection has been clearly documented in angiographically unremarkable vessels (9–15).

Coronary angiography, by contrast, is accepted as the standard for imaging the coronary arteries and is irreplaceable for routine patient care in diagnostic and interventional cardiology. However, with the increasing availability of angioscopy and its potential for rapid and comprehensive direct visualization of the coronary lumen, the definition of intracoronary thrombus and intimal dissection by angiography must be questioned. The purpose of this study was to compare and contrast imaging information obtained in 52 patients undergoing coronary angioplasty, using a combination of angiography and angioscopy, with specific attention to the detection of intracoronary thrombus and intimal dissection.

Methods

Patients. At the catheterization laboratories of the University Hospital Groningen and the Thoraxcenter, Rotterdam, the Netherlands, 52 patients (mean age 60.5 years, range 40 to 76) underwent coronary angioscopy before (15 patients) or after (37 patients) coronary balloon angioplasty.

Coronary angioscopy. Angioscopy was performed with the ImageCath system (Baxter, Interventional Cardiology Division). Visualization of the coronary lumen is facilitated by low pressure inflation of a proximal cuff (maximal diameter 6 mm) and continuous flushing of prewarmed normal saline solution at 40 ml/min through the irrigation channel of the angioscope. Specific features of the angioscope include a mobile fiber bundle allowing 5-cm longitudinal movement after cuff infla-

From the Department of Cardiology, Thoraxcenter, University Hospital, Groningen and *Erasmus University, Thoraxcenter, Rotterdam, The Netherlands. This study was supported in part by a Biomedical and Health Research (Biomed I) Grant from the Commission of the European Communities, Directorate-General XII for Science, Research and Development, Rotterdam, The Netherlands.

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Address for correspondence: Dr. Peter den Heijer, Department of Cardiology, Thoraxcenter, University Hospital, Oostersingel 59, 9713 EZ Groningen, The Netherlands.

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Table 1. Classification System for Angioscopic Thrombus and Dissection

Dissection	
0	Not assessable, not applicable
1	None
2	Small surface disruptions (flaps)
3	Large dissection
Red thrombus	
0	Not assessable, not applicable
1	None
2	One lining thrombus
3	Multiple lining thrombus
4	Protruding thrombus, <⅓ of lumen
5	Protruding thrombus, ⅓–⅔ of lumen
6	Protruding thrombus, ⅔–3/3 of lumen
White thrombus	
0	Not assessable, not applicable
1	None
2	One lining thrombus
3	Multiple lining thrombus
4	Protruding thrombus, <⅓ of lumen
5	Protruding thrombus, ⅓–⅔ of lumen
6	Protruding thrombus, ⅔–3/3 of lumen
Mixed red/white thrombus	
0	Not assessable, not applicable
1	None
2	One lining thrombus
3	Multiple lining thrombus
4	Protruding thrombus, <⅓ of lumen
5	Protruding thrombus, ⅓–⅔ of lumen
6	Protruding thrombus, ⅔–3/3 of lumen

tion. All angioscopic images were recorded on Super-VHS videotape.

Coronary angiography. Coronary angiography was performed according to the normal routine of both catheterization laboratories, with multiple projections of the treated coronary artery segments both before and after angioplasty. The angiograms were recorded at 12.5 to 25 frames/s on cinefilm.

Data acquisition and definitions. The angioscopic videotape recordings were reviewed in a predetermined random order by two interventional cardiologists with ample experience in angioscopy. The presence of dissection and thrombus was scored with the use of a classification system to provide grading scales for these diagnoses (Table 1). Presence of thrombus was subclassified as red, white or mixed red and white. The angioscopic definition for a thrombus was as follows: red, white or mixed red and white, intraluminal, superficial or protruding mass, adherent to the vessel surface but clearly a separate structure. A white thrombus should fulfill the additional criterion of a shaggy, irregular and cotton wool–like appearance. The magnitude of a protruding thrombus, classified as grades 4 to 6, was determined by visual estimation. Angioscopic dissection was defined as visible cracks or fissures on the lumen surface or mobile protruding structures that are contiguous with the vessel wall and of homogeneous appearance with the vessel wall. These definitions and classifications of thrombus and dissection are part of an angioscopic classification system that was developed and evaluated by the European Working Group on Coronary Angioscopy (16). Intraobserver and interobserver agreements of angioscopic recordings, evaluated by this working group, were considered acceptable. Intraobserver and interobserver agreements for the angioscopic presence of red thrombus were found to be 91% and 81%, respectively. For dissection, intraobserver agreement was 87% and 73% for interobserver agreement.

Table 2. Modified National Heart, Lung, and Blood Institute Classification of Angiographic Dissection

No dissection	
Type A	Small radiolucent area within the lumen of the vessel disappearing with the passage of contrast material
Type B	Filling defect parallel to the lumen of the vessel disappearing with the passage of contrast material
Type C	Dissection protruding outside the lumen of the vessel persisting after passage of the contrast material
Type D1	Spiral-shaped filling defect with normal runoff of the contrast material in the anterograde flow
Type D2	Spiral-shaped filling defect with delayed runoff of the contrast material in the anterograde flow
Type E	Persistent lumen filling defect with delayed runoff of the contrast material in the distal vessel
Type F	Filling defect accompanied by total occlusion

The cineangiograms were scored off-line by the same observers in blinded manner in a different random order. Intimal dissection was defined as intraluminal filling defects, extravasation of contrast material or linear lumen density staining and was categorized according to modified National Heart, Lung, and Blood Institute criteria (Table 2) (17–20). Angiographic evidence of intracoronary thrombus was defined as the presence of an intraluminal central filling defect or lucency surrounded by contrast material, seen in multiple projections and with absence of calcifications within the defect (21).

Statistical analysis. The angioscopic and angiographic absence, presence or degree of dissection and thrombus was scored by consensus of the two observers. If they differed in their judgment, consensus was reached by the opinion of a third, independent observer. The observers were uninformed of all patient data to allow for independent, unbiased review of angioscopic images and angiograms.

Cross-tables were made to compare angioscopic and angiographic scores. Correlations were calculated using the Spearman rank-order correlation coefficient r_s and the phi coefficient for 2 × 2 tables (r_ϕ). These correlations were computed using the SPSS statistical package, version 5.01. Statistical significance was set at the 5% level ($p < 0.05$).

Results

There were no major complications caused by angioscopy in this patient cohort. There was one case of ventricular fibrillation, which was easily cardiovertable, resulting from an excessively long period of ischemia during our learning curve. Severe coronary spasm, air embolism, angiographic evidence of dissection caused by angioscopy, balloon or wire entrapment

Table 3. Angioscopic Thrombus Grade Versus Angiographic Thrombus Presence

Angiographic Thrombus	Angioscopic Thrombus Grade					
	1	2	3	4	5	6
Absent	21 (40.4%)	7 (13.5%)	11 (21.2%)	4 (7.7%)	2 (3.8%)	1 (1.9%)
Present	—	1 (1.9%)	3 (5.8%)	1 (1.9%)	—	1 (1.9%)

Data presented are number (%) of patients.

or trauma caused by the occlusion cuff did not occur in this patient group.

Coronary angioscopy revealed both intracoronary thrombus and dissection in many angiographically unremarkable vessels.

Intracoronary thrombus. All intraluminal filling defects fulfilling the criteria for thrombus that were observed with angiography were confirmed by angioscopy as representing intracoronary thrombus. The angioscopic score of thrombus versus the absence or presence of thrombus at angiography is presented in Table 3. Angiographic evidence of thrombus was reported in only six cases. Angioscopy, by contrast, revealed 31 (59.6%) cases of intracoronary thrombus, varying from a single lining thrombus to large occluding thrombi. The distribution of the colors of the thrombi that were detected was as follows: 24 cases of red thrombus, 6 cases of mixed thrombus and 1 purely white thrombus.

Table 4 shows the presence or absence (angioscopy grade >2) of thrombus in a 2 × 2 cross-table. There is agreement between angiography and angioscopy in 21 cases (40.4%) with regard to the absence of thrombus and in 6 cases (11.5%) with regard to the presence of thrombus. However, no fewer than 25 (48.1%) angioscopically observed thrombi remained undetected at angiography. This underdetection was independent of the thrombus color; in other words, white or mixed thrombus was missed by angiography as often as red thrombus. Compared with angioscopy, there were no false negative angiographic thrombus observations. There was a weak but significant correlation between angiographic and angioscopic presence or absence of thrombus (r_{ϕ} = 0.30, p = 0.03). A typical example of intracoronary thrombus formation detected by angioscopy but obscured by angiography is presented in Figure 1.

Sensitivity and specificity. On the basis of these findings, as well as on previous publications (9,14,22–24), angioscopy can be regarded as the most reliable means of in vivo detection of

Table 4. Angioscopic Versus Angiographic Thrombus

Angiographic Thrombus	Angioscopic Thrombus (≥grade 2)	
	Absent	Present
Absent	21 (40.4%)	25 (48.1%)
Present	—	6 (11.5%)

Data presented are number (%) of patients.

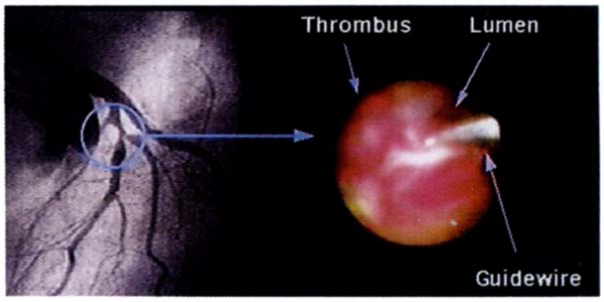

Figure 1. Coronary angiogram (left anterior oblique view with cranial angulation) showing a significant stenosis in the left anterior descending coronary artery. The lesion has a smooth angiographic appearance, without filling defects suggestive of intracoronary thrombus. Coronary angioscopy reveals two fairly **large red thrombi** located on the proximal side of the eccentric narrowing.

intracoronary thrombus. Accordingly, to enhance the interpretation of our data, we used angioscopy as the standard to calculate the sensitivity and specificity of angiography for thrombus. Although the specificity of angiography for thrombus was 100%, sensitivity was very low at 19.4%. The positive predictive value was 100%; the negative predictive value 45.7%. It can be argued that the angiographic criteria for thrombus (intraluminal filling defect surrounded by contrast in multiple projections) allow detection of only larger, lumen space-occupying thrombi (25). Furthermore, although the angioscopic presence of red thrombus has been validated in a postmortem study by Siegel et al. (14), it can be argued that wall hemorrhage after angioplasty may be misinterpreted as lining red thrombus. Therefore, we recalculated these variables counting only protruding thrombi (grade 4 or more) as positive angioscopic thrombus observations, disregarding mural, lining thrombi. This had only a minor influence on the outcome: Sensitivity of angiography for thrombus using angioscopy as the standard was 22.2%, specificity 90.7%, positive predictive value 33.3% and negative predictive value 84.8%.

Dissection. Table 5 represents the comparison of angiographic and angioscopic dissection. Type A, B and D1 dissections were seen with angiography in these patients. There appeared to be no relation to angioscopic intimal dissection grade (Spearman correlation coefficient 0.21, p = 0.14). The variables were dichotomized to test whether the angioscopic

Table 5. Angioscopic Dissection Grade Versus Angiographic Dissection Type

Angiography	Angioscopic Dissection Grade		
	1 (no dissection)	2 (small disruptions)	3 (large dissection)
No dissection	10 (19.2%)	9 (17.3%)	18 (34.6%)
Type A dissection	—	1 (1.9%)	2 (3.8%)
Type B dissection	2 (3.8%)	—	9 (17.3%)
Type D1 dissection	—	1 (1.9%)	—

Data presented are number (%) of patients.

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Table 6. Angioscopic Versus Angiographic Dissection

Angiographic Dissection	Angioscopic Dissection (≥grade 2)	
	Absent	Present
Absent	10 (19.2%)	27 (51.9%)
Present	2 (3.8%)	13 (25.0%)

Data presented are number (%) of patients.

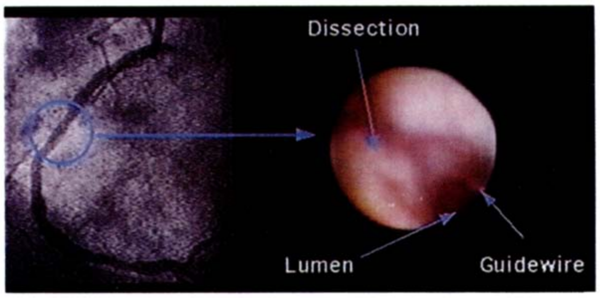

Figure 2. Postangioplasty coronary angiogram (left anterior oblique view) of the right coronary artery with an angiographically optimal result, without evidence of dissection. At angioscopy, a large intimal dissection with **white mobile flaps** is observed.

presence or absence of dissection had a relation to any type of angiographic dissection (Table 6). These data show angioscopic dissection in 40 patients (76.9%) versus angiographic dissection in 15 patients (28.8%), again without any correlation ($r_\phi = 0.15$, $p = 0.29$). There were two cases of angiographic dissection that were not detected by angioscopy. Surface disruptions are typically seen with angioscopy after balloon angioplasty (4,12), as was the case in all postangioplasty observations in this study. Small surface disruptions, like small thrombi, may easily be missed with angiography and may not have clinical consequences. These small flaps may even be regarded as the "normal" aspect of the vascular wall after balloon angioplasty. For this reason the analysis was repeated, comparing only large angioscopic dissections with all types of angiographic dissections, but, again, it did not yield a significant correlation between the two imaging methods ($r_\phi = 0.23$, $p = 0.10$). Figure 2 shows an example of a dissection found with angioscopy that was not visible on the angiogram.

Discussion

Contrast cineangiography is accepted as the standard imaging method for the coronary arteries. Although angiography provides indispensable anatomic information and has set the standard for quantifying stenotic lesions (26) both before and after angioplasty (27), it can be questioned if it still should be regarded as a sufficient means of imaging for studies that require a reliable detection of intracoronary thrombus and intimal dissection. The value of such angiographic studies must be open to question, particularly if they address the sequelae of intracoronary thrombus (28–32).

Implications. Adequate angioscopic evaluation of intracoronary thrombus can have an impact on routine patient care as well, for instance, in the determination of the optimal management in cases of suboptimal angioplasty result or abrupt reclosure. All nine patients in this study with protruding thrombi (≥grade 4) at angioscopy were treated with adjunctive intracoronary thrombolysis. Intracoronary thrombus was present in 8 of the 15 patients who underwent angioscopy before angioplasty (six cases grade 3, and two cases grade 4 thrombus). All of these eight patients had unstable angina, as opposed to two of seven patients without intracoronary thrombus before angioplasty. This higher incidence of thrombus in patients with unstable angina is in accord with other angioscopic studies (5,6,24). Sassower et al. (33) and Knopf et al. (8) have identified the clinical relevance of reliable angioscopic thrombus detection during coronary angioplasty in cases of abrupt closure, unstable angina and acute myocardial infarction. We previously reported two cases of subacute stent occlusion where angioscopy helped to distinguish dissection from thrombosis as the primary cause (34).

The high sensitivity of angioscopy for the detection of thrombus potentially has clinically relevant implications. Used before the intervention, angioscopy may predict a high incidence of acute or abrupt closure if intracoronary thrombus is detected. Another potentially useful application of angioscopy is in the emergency situation: when an acute occlusion occurs or threatens to occur after angioplasty, it is of utmost importance to be able to differentiate between thrombus and dissection as the primary cause for this adverse outcome. The selection of the optimal emergency strategy, such as stent implantation, prolonged inflation of autoperfusion balloon catheters or intracoronary thrombolysis, could be facilitated by angioscopy.

This study was undertaken to compare objectively the usefulness of angioscopy and conventional angiography for detection of intracoronary thrombus and intimal dissection. Contrasting conclusions may be drawn from the findings with respect to these respective diagnoses. The sensitivity and specificity of angiography for thrombus detection clearly indicate that angiography underestimates the presence of thrombus. The vast majority of angioscopically observed thrombi remain obscured at angiography. For dissection, however, angiography and angioscopy appear to be complementary imaging techniques. There were two cases in which angioscopy missed the dissection although it was evident on the angiogram. Both were type B dissections, with a filling defect parallel to the lumen that must have remained hidden from angioscopic view. Dissection was not seen on angiography in the 15 patients who were studied before angioplasty. With angioscopy, dissection was scored in nine of these patients (six cases grade 2 and three cases grade 3 dissection). It is likely that angioscopically observed dissections in this preangioplasty situation represent spontaneous dissections or ruptured plaques.

Study limitations. Our study has the limitations of a retrospective investigation. Not all types of dissection were present in this group, which included patients with both preangioplasty and postangioplasty lesions. As a result, a positive correlation between angiographic dissection type and angioscopic dissection grade may not be excluded but may merely not have been confirmed with this limited number of 52 paired observations.

We found a considerable angiographic underestimation of thrombus. This may result in part from the strict angiographic criteria for thrombus. More liberal criteria undoubtedly would result in increased sensitivity at the cost of a much lower specificity. Another problem, which may result in inaccurate estimation of angiographic sensitivity and specificity for thrombus and dissection, arises from the difficult angiographic distinction between these two diagnoses. Thrombi may have been misinterpreted as dissections, and vice versa. In five of six cases of angiographic thrombus, dissection was present as well. There were four cases of angiographic thrombus that correlated with angioscopic lining thrombus. By contrast, because lining mural thrombus is not very bulky, in general it would not be detected by angiography (25), so it is highly probable that the lumen filling defects that were observed in these cases were caused by concomitant dissection. In fact, there proved to be a large angioscopic dissection (grade 3) in three of these four cases, and small surface disruptions (grade 2) in one case. Thus, an even lower angiographic sensitivity for thrombus may have been found if a different patient group, with intracoronary thrombus but without dissection, had been studied.

Intravascular ultrasound imaging is another new imaging tool for intraluminal structures (as well as for vascular wall properties). Although it does not have ideal properties for thrombus detection, intraluminal ultrasound imaging has the potential for superior imaging of intimal dissection (35–38), with the ability to discern plaque fracture from more extensive disruption that includes the internal elastic lamina. Future studies should address the combined use of all available coronary imaging techniques.

Conclusions. Coronary angiography considerably underestimates the presence of intracoronary thrombus. In studies that require reliable detection of thrombus, coronary angioscopy is the imaging tool of choice. Angioscopy and angiography are complementary techniques for detection and grading of intimal dissections.

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