Eur J Vasc Endovasc Surg 16, 110–119 (1998)

Intravascular Ultrasound Predictors of Restenosis After Balloon Angioplasty of the Femoropopliteal Artery

A. van der Lugt[1], E. J. Gussenhoven*[1], G. Pasterkamp[2], T. Stijnen[1], J. A. Reekers[3], F. G. van den Berg[4], A. V. Tielbeek[5], J. L. Seelen[6] and H. Pieterman[1]

[1]*University Hospital Rotterdam-Dijkzigt, Erasmus University Rotterdam,* [2]*Academic Hospital Utrecht,* [3]*Academic Medical Center Amsterdam,* [4]*Free University Hospital Amsterdam,* [5]*Catharina Hospital Eindhoven,* [6]*Maria Hospital Tilburg, The Netherlands*

Objectives: *To determine intravascular ultrasound parameters related to restenosis following percutaneous transluminal balloon angioplasty (PTA) of the femoropopliteal artery.*
Design: *Prospective study.*
Materials and methods: *Patients were studied with intravascular ultrasound before and after angiographic successful PTA (n = 114). Intravascular ultrasound cross-sections obtained with 1 cm interval in the dilated segment were analysed. A distinction was made between anatomic (duplex scanning) and clinical (Rutherford criteria) restenosis assessed within 1 month and at 6 months after PTA.*
Results: *Intravascular ultrasound predictors of 1 month anatomic outcome were lumen area stenosis after PTA, lumen area increase, plaque area decrease, and area stenosis decrease; predictor of 6 months anatomic outcome was area stenosis after PTA. Multivariate analysis revealed that area stenosis after PTA was the only independent predictor of both 1 and 6 months anatomic outcome.*

Intravascular ultrasound predictors of 1 month clinical outcome were the presence of hard lesion and the mean arc of hard lesion. Multivariate analysis revealed that the mean arc of hard lesion was the only independent predictor of 1 month clinical outcome. No predictors for 6 months clinical outcome were found.
Conclusions: *Intravascular ultrasound can elucidate parameters predictive of restonosis after PTA. The strongest intravascular ultrasound parameter predictive of anatomic restenosis was a larger area stenosis after PTA.*

Key Words: Intravascular ultrasound; Balloon angioplasty; Femoral artery; Restenosis.

Introduction

Percutaneous transluminal angioplasty (PTA) is an accepted technique in the management of patients with obstructive disease of the femoropopliteal artery. Success rates vary considerably among series of reported cases (1-year patency: 47–73%).[1–6] Given the lack of correlation between successful angioplasty assessed angiographically and the outcome, there is a need for better prediction of restenosis following intervention. There is evidence that intravascular ultrasound may reveal parameters related to restenosis following PTA.[7–9]

We conducted a multicentre study named EPISODE (evaluation peripheral intravascular sonography on dotter effect). The main objective of this study was to determine the value of intravascular ultrasound restenosis following PTA of the femoropopliteal artery. Clinical, angiographic and intravascular ultrasound data obtained before and after PTA were evaluated to identify parameters associated with the outcome of PTA.

* Please address all correspondence to: E. J. Gussenhoven, Erasmus University Rotterdam (Ee 2312), Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands.

Materials and Methods

Study group

A total of 137 patients referred for PTA of symptomatic obstructive disease of the femoropopliteal artery ($n = 148$) were enrolled in the study: 11 of these patients underwent bilateral PTA. The investigation was approved by the local committee on human research. Patients were included in the study after informed consent.

Data collected on each patient included age, gender, hypertension (medication dependent), hypercholesterolaemia (medication dependent or serum cholesterol >6.5 mmol/l in fasting blood samples), diabetes, history of smoking and indication for intervention (intermittent claudication, rest pain, ischaemic ulceration). Preoperative assessment included measurements of ankle-brachial blood pressure index (ABI) at rest and after treadmill exercise, and single plane intra-arterial digital subtraction angiography.

Balloon angioplasty

The intervention was preceded and followed by routine single plane angiography and intravascular ultrasound study. The selection of balloon type, diameter, inflation pressure and additional inflations were determined by the radiologist in charge and were based on angiography only. Data collected on each patient included the status of the artery before intervention (stenosis; occlusion), the number of open run-off vessels and the length of the dilated segment. Crural run-off vessels assessed angiographically were categorised in two groups (good: 2 or 3; bad: none or 1). The length of the dilated segment, recorded using a radiopaque ruler, was categorised in four groups ($\leq$5 cm, 6–10 cm, 11 – 15 cm, >15 cm). Angiographic success assessed by the radiologist in charge was defined as a decrease in angiographic diameter stenosis.

Intravascular ultrasound

The intravascular ultrasound study was performed using mechanical 30 MHz imaging systems. In three hospitals a CVIS "insight" system was used (Sunnyvale, CA, U.S.A.), in five other hospitals a Du-MED "intrasound" system (Rotterdam, The Netherlands) was used. Before intervention the ultrasound catheter was advanced via the sheath over the wire distally beyond the lesion and intravascular ultrasound cross-sections were recorded along the dilation tract during manual pull-back of the catheter. After completion of the intervention, when the procedure was deemed angiographically successful or no additional procedures would be performed to further improve the angiographic result, the intravascular ultrasound study was repeated. Care was taken to image the site with the smallest lumen area (i.e. the bottle-neck) both before and after PTA. In order to match the intravascular ultrasound cross-sections obtained before and after PTA a radiopaque ruler and fluoroscopic control were used.[10] The ultrasound images were stored on an S-VHS recorder. The videotapes were reviewed off-line for analysis. The radiopaque ruler and anatomic markers such as side-branches and calcium deposits were used to match the intravascular cross-sections obtained before and after PTA. The matched cross-sections within the dilated segment (including the bottle-neck) were selected with 1 cm interval for analysis. Qualitative and quantitative analyses of the intravascular ultrasound images were performed by one of the researchers of the participating academic hospitals. The analyses were centrally reviewed by a second observer. Differences between the observers were solved by consensus.

Qualitative analysis

Intravascular ultrasound cross-sections were assessed for lesion topography and morphology before PTA and for vascular damage after PTA. Criteria for evaluating these features with intravascular ultrasound have been described previously.[10,11] The topography of the lesion may be either eccentric or concentric. Lesion topography in cross-sections obtained from occluded segments was based on the position of the ultrasound catheter. Lesion morphology includes the presence or absence of a hard lesion (Figs 1 and 2).

After PTA, the presence or absence of vascular damage (dissection and media rupture) was documented. These morphologic features could be present simultaneously in one cross-section (Figs 1 and 2).

Quantitative analysis

The extent of hard lesion and dissection was graded visually as an arc of the circumference with the centre of the lumen as reference point (arc in steps of 30°; range 0–360°). Measurements of lumen and media-bounded areas before and after PTA were performed using a digital video analyser system.[12] Plaque area was calculated by subtracting lumen area from media-bounded area. The percentage area stenosis was calculated as plaque area divided by media-bounded area × 100. In the absence of a visible media on ultrasound the outer hyperechoic layer representing the adventitia was used as reference. When extensive drop-out due to calcification was encountered (>120° of the circumference), media-bounded area was not calculated (Fig. 2). The difference between the measurements obtained at the smallest lumen area before

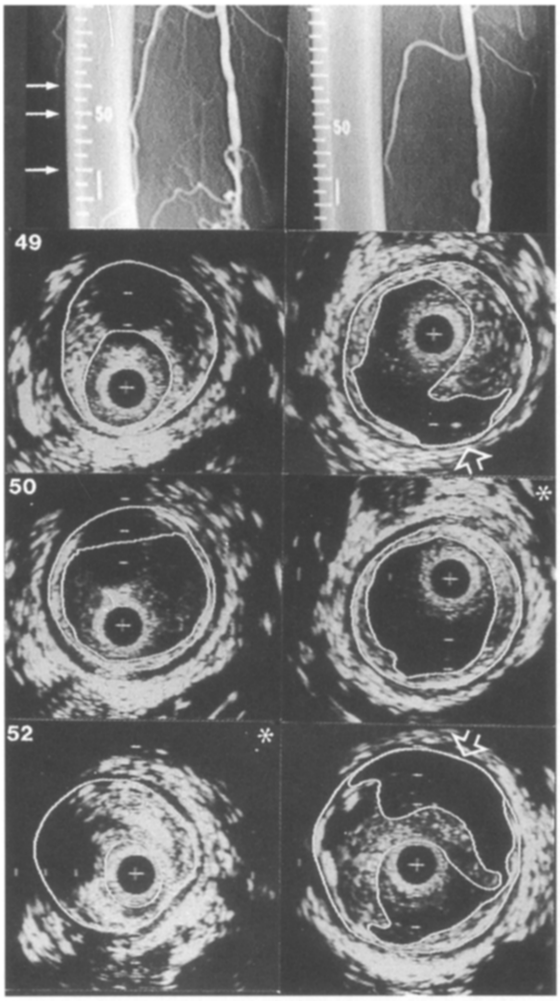

Fig. 1. Angiograms and corresponding intravascular ultrasound cross-sections obtained before (left) and after (right) balloon angioplasty (PTA) of the femoropopliteal artery display the variety of anatomic features involved. The intravascular ultrasound cross-sections are contour traced off-line facilitating the recognition of lumen area (inner contour) and media-bounded area (outer contour). Before PTA: soft eccentric lesions were seen. After PTA: no effect (level 50), dissection and media rupture (open arrow) were seen (levels 49 and 52). At 6 months follow-up no restenosis was evidenced anatomically and clinically. Asterisk indicates the narrowest site. + = catheter; calibration = 1 mm.

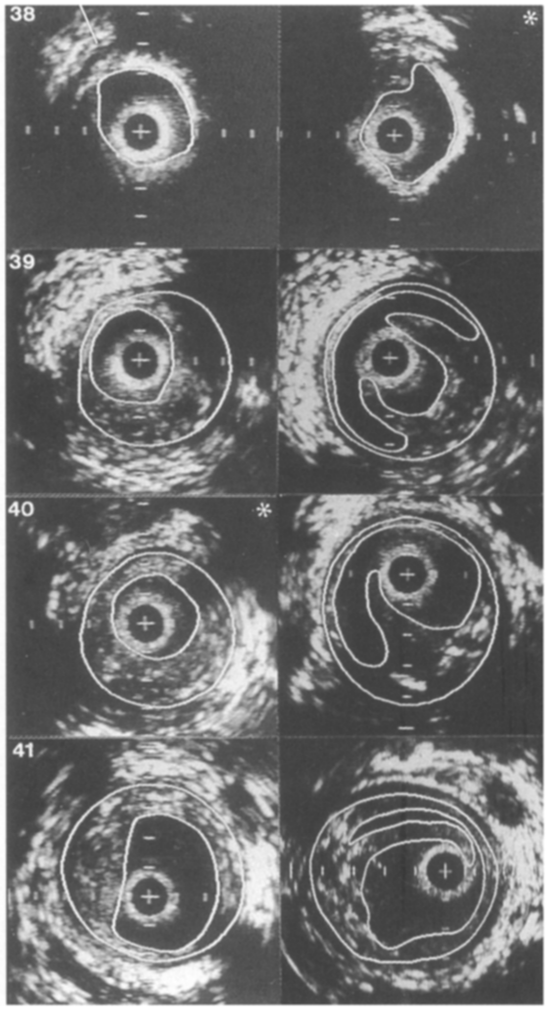

Fig. 2. Corresponding intravascular ultrasound cross-sections obtained before (left) and after (right) balloon angioplasty (PTA) of the femoropopliteal artery. The intravascular ultrasound cross-sections are contour-traced off-line facilitating the recognition of lumen area (inner contour) and media-bounded area (MBA; outer contour). In the first corresponding cross-sections (level 38) the presence of a hard lesion prevented measurement of the MBA. Distally the lesion was classified as soft. Asterisk indicates the narrowest site. After PTA, dissections were seen + = catheter; calibration = 1 mm.

PTA and its matched site after PTA was calculated. In the occluded segments seen angiographically the most proximal intravascular ultrasound cross-section obtained was considered as the location with the smallest lumen area. In order to rule out a Dotter effect of the wire and/or ultrasound catheter at this site, lumen area of the occluded lumen on intravascular ultrasound was considered as 0.0 mm^2 and the area stenosis as 100%.

Intravascular ultrasound parameters selected for the analysis are listed in Table 1. They included: (1) qualitative and quantitative data obtained at the smallest lumen area before PTA and its matched site after PTA and those obtained at the smallest lumen area after PTA; (2) the mean arc of hard lesions and the mean and maximum arc of dissection encountered in the dilated segment; and (3) the presence of dissection and media rupture encountered in the dilated segment.

Follow-up

The follow-up protocol included clinical assessment, ABI pressure measurements at rest and after treadmill exercise, and colour-flow duplex examination within 1 and at 6 months after intervention.

Table 1. Intravascular ultrasound parameters selected for analysis at different locations.

	Location		
	Smallest LA before and matched site after PTA	Smallest LA after PTA	All cross-sections matches
Eccentric lesion	+/−		
Hard lesion	+/−		extent (mean)
Dissection	+/− extent	+/− extent	+/− extent (mean; maximum)
Media rupture	+/−	+/−	+/−
LA, MBA, PLA %S	before, after, difference	after	

PTA = percutaneous transluminal angioplasty; +/− = present/absent; LA = lumen area; MBA = media-bounded area; PLA = plaque area; %S = area stenosis.

Anatomic outcome was determined by colour-flow duplex scanning of the femoropopliteal artery with special emphasis on the dilated segment. A ruler was used to determine the site of a stenosis. Stenotic segments were identified by a locally increased velocity and poststenotic turbulence characterised by colour changes. The peak systolic velocity at the site of a stenosis (PSV stenosis) was compared with the peak systolic velocity of a nearby normal proximal arterial segment (PSV artery). The peak systolic velocity ratio was calculated as PSV stenosis/PSV artery. A ratio ≥2.5 was considered a stenosis of ≥50%.[13–15] An occlusion was characterised by the absence of detectable arterial flow. Early (within 1 month) and late (at 6 months) anatomic restenosis were defined as a stenosis ≥50%.

Clinical outcome was classified according to the Society for Vascular Surgeons/International Society for Cardiovascular Surgery criteria on a scale from −1 to −3 for deterioration of symptoms and ABI; 0 for unchanged symptoms; +1 for either a categorical improvement of clinical classification or increase of ABI >0.10; +2 for at least a single category improvement combined with ABP increase of >0.10; and +3 for markedly improved or absence of clinical symptoms combined with an ABI >0.90.[16,17] Early restenosis (within 1 month) was defined as unchanged or deterioration of symptoms (score < +1), late restenosis was defined as each deterioration evidenced at 6 months.

Study endpoints and statistical analysis

The relationship between clinical, angiographic and intravascular ultrasound variables (Tables 1 and 2) and the outcome of intervention was studied. Predictors of both 1 month outcome (early success versus early restenosis) and 6 months outcome (late success versus early and late restenosis) were assessed. The early success group comprised all procedures with 1 month success and included all procedures with subsequent late success, late restenosis and those without further follow-up. In addition, procedures with late success and late restenosis were compared to determine whether different predictors were found for early and late restenosis.

Table 2. Clinical and angiographic data obtained in 109 patients with 114 treated femoropopliteal arteries.

Clinical data		
Age (median, range), (years)		67 (39–93)
Male		68 (62%)
Hypertension		36 (33%)
Hypercholesterolaemia		22 (20%)
Diabetes		34 (31%)
History of smoking		75 (69%)
Angiography		
Stenosis		86 (75%)
Occlusion		28 (25%)
Run-off:	good (2, 3 arteries)	76 (67%)
	bad (0, 1 artery)	33 (29%)
	unknown	5 (4%)
Length of PTA:	≤5 cm	39 (34%)
	6–10 cm	27 (24%)
	11–15 cm	20 (18%)
	>15 cm	28 (25%)
Rutherford category before PTA		
1 (mild claudication)		14 (12%)
2 (moderate claudication)		48 (42%)
3 (severe claudication)		16 (14%)
4 (restpain)		16 (14%)
5 (minor tissue loss)		18 (16%)
6 (major tissue loss)		2 (2%)
Clinical outcome 1 month after PTA		
+3		40 (36%)
+2		39 (35%)
+1		15 (13%)
0		13 (12%)
−1		4 (4%)
ABI		
Before PTA		66 ± 18 mmHg
1 month after PTA		91 ± 16 mmHg

PTA = percutaneous transluminal angioplasty.

Table 3. Anatomic and clinical outcome ($n = 114$) evidenced at 1 and 6 months.

	Interval (month)	No. at risk	No. of failures	Died	No. lost to follow-up	Interval patency rate (%)	Cumulative patency rate (%)	Standard error (%)
Anatomic outcome	0–1	114	18	3	15	81	81	3.3
	1–6	78	18	2	8	74	60	4.4
Clinical outcome	0–1	114	17	3	0	85	85	3.1
	1–6	94	32	2	4	64	54	3.8

n = number of procedures; No. = number.

Results were expressed as mean value ±S.D. For univariate analysis the Chi-squared test or Fisher's exact test was used to assess differences in dichotomous variables. The Mantel–Haenszel Chi-squared trend test was used to assess differences in ordinal categorical variables. Differences in continuous variables were compared using Student's two sample t-test. Clinical, angiographic and intravascular ultrasound variables with $p \leq 0.1$ univariately were entered into a stepwise forward logistic regression analysis (SPSS, SPSS Inc, Chicago, U.S.A.) to detect variables that were independently significantly related to the anatomic and clinical outcome of the intervention, respectively. The statistical significance level was set at $p \leq 0.05$.

Reproducibility of qualitative and quantitative IVUS parameters in cross-sections obtained before and after PTA has been previously reported.[18]

Results

Intravascular ultrasound study was completed in 129 of the 148 interventions. Complications related to intravascular ultrasound were not encountered. In 19 procedures, intravascular ultrasound images were not available for the following reasons: ultrasound equipment failure ($n = 6$), inability to advance the wire and the ultrasound catheter along the PTA tract ($n = 6$), inability of the ultrasound catheter to pass the aortic bifurcation in cases of contralateral entry of the artery ($n = 4$), and intervention was not performed ($n = 3$). Angiographically, the interventions ($n = 129$) were classified as successful in 114 procedures and as initial failure in 15 procedures (thrombosis of the dilated segment was seen in seven, a stent was placed in five, and an additional PTA was performed in three procedures; for technical reasons no additional intravascular ultrasound examination was performed in the last three procedures). These 15 procedures were excluded from the analysis. This group ($n = 15$) had significantly more occlusions and a longer PTA length than the group with an angiographically successful procedure ($n = 114$).

For the present study, data of the 114 angiographically successful procedures obtained from 109 patients were included in the analysis (Table 2).

Intravascular ultrasound data were available before and after intervention in 102 of the 114 procedures. In 12 procedures, intravascular ultrasound data were not available prior to intervention because the wire or the ultrasound catheter could not be advanced across the lesion (11 occlusions and one stenosis). In total, 920 cross-sections before (102 procedures) and 1171 cross-sections after PTA (114 procedures) were subjected to analysis. Lumen area and media-bounded area could be assessed in 97% and 81% of the cross-sections available, respectively. Poor image quality and presence of a hard lesion were the main reasons preventing adequate identification of the media-bounded area.

It was found that the smallest lumen area site seen on intravascular ultrasound before PTA did not necessarily correspond to the smallest lumen area site seen after PTA: in 73 procedures the distance between the smallest lumen area before and after PTA was ≤ 2 cm, in 19 procedures between 2 and 5 cm and in 10 procedures >5 cm (Figs 1 and 2).

Anatomic and clinical outcome evidenced at 1 and 6 months are summarised in Table 3.

Predictor variables of anatomic outcome

Intravascular ultrasound parameters ($p \leq 0.10$) in the procedures with early restenosis, late restenosis and late success are listed in Table 4.

Predictors of 1-month outcome (early success versus early restenosis). Neither clinical nor angiographic variables were related to anatomic outcome. Intravascular ultrasound predictors of early restenosis were a smaller lumen area and a larger area stenosis after PTA, a smaller lumen area increase, a smaller plaque area

Table 4. Intravascular ultrasound parameters ($p \leq 0.10$) in procedures with early anatomic restenosis, late anatomic restenosis and late anatomic success.

	Early restenosis ($n=18$)	Late restenosis ($n=18$)	Late success ($n=50$)	* p	† p	‡ p
Smallest LA before and its matched site after PTA						
Hard lesion	9 (56%)	3 (19%)	15 (35%)	0.10	0.82	0.34
MBA before PTA (mm^2)	30.6±11.9	22.9±8.5	26.8±10.1	0.10	0.90	0.19
LA after PTA (mm^2)	11.8±4.8	14.5±4.5	15.0±4.7	**0.019**	0.11	0.74
Area stenosis after PTA (%)	66±11	54±9	53±8	**0.001**	**0.009**	0.76
LA increase (mm^2)	7.3±4.6	10.8±6.1	10.3±4.5	**0.21**	0.28	0.73
PLA decrease (mm^2)	1.8±2.3	3.9±5.2	4.0±6.1	**0.035**	0.39	0.94
Area stenosis decrease (%)	18±12	32±13	29±15	**0.006**	0.25	0.56
Smallest LA after PTA						
LA after PTA (mm^2)	10.0±4.2	11.2±3.0	12.3±4.2	0.054	0.051	0.32
Area stenosis after PTA (%)	67±10	57±11	57±9	**0.002**	0.063	0.95
All cross-sections in the dilated segment						
Maximum arc of dissection (°)	122±91	143±90	107±67	0.83	0.13	0.076
Media rupture	4 (22%)	9 (50%)	23 (46%)	0.063	0.36	0.77

* = Comparison of early success versus early restenosis; † = comparison of late success versus early and late restenosis; ‡ = comparison of late success versus late restenosis; PTA = percutaneous transluminal angioplasty; LA = lumen area; MBA = media-bounded area; PLA = plaque area; significant values are shown in bold.

decrease and a smaller area stenosis decrease at the smallest lumen area before and its matched site after PTA. Moreover, a larger area stenosis at the smallest lumen area after PTA was found predictive for early restenosis.

The presence and extent of vascular damage were not predictive of early restenosis. Media rupture in the dilated segment was less frequently seen in procedures with early restenosis than early success, but this difference did not reach a significant level (22% versus 46%; $p=0.063$).

By multiple logistic regression analysis the only independent predictor of early restenosis was a larger area stenosis at the location corresponding to the smallest lumen area before PTA (odds ratio = 1.16 (95% CI: 1.07–1.26); $p=0.0001$) (Fig. 3).

Predictors of 6 months outcome (late success versus early and late restenosis). Diabetes and a larger length of dilated segment were more frequently seen in procedures with (early and late) restenosis than late success (diabetes: 36% versus 16%; $p=0.032$; length of dilated segment $p=0.043$). Intravascular ultrasound parameter found predictive of 6 months outcome was area stenosis at the location with the smallest lumen area before PTA. The presence and extent of vascular damage were not predictive of 6 months' outcome.

By multiple logistic regression analysis the independent predictor of (early and late) restenosis was a larger area stenosis at the location with the smallest lumen area before PTA (odds ratio = 1.08 (95% CI: 1.02–1.15); $p=0.017$).

Predictors of late restenosis (late success versus late restenosis). There were no significant differences in the qualitative and quantitative intravascular ultrasound parameters in procedures with late restenosis compared with those with late success; the maximum arc of the dissection seen in the dilated segments was the most significant variable (143±90° and 107±67°, respectively; $p=0.076$).

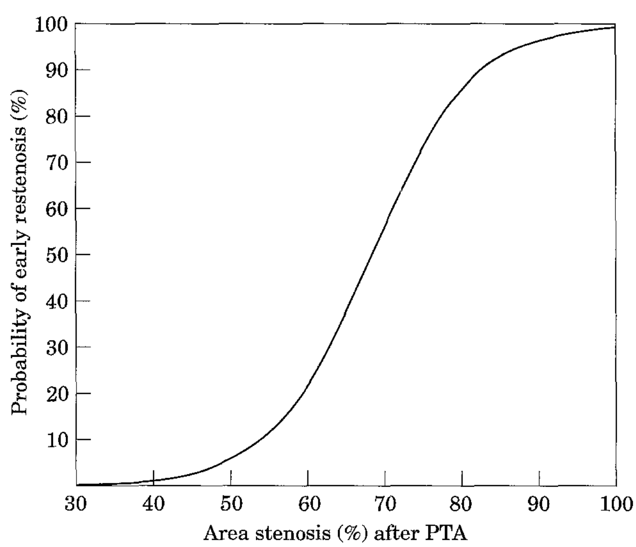

Fig. 3. Predictive model of the probability of early anatomic restenosis based on the area stenosis measured with intravascular ultrasound after balloon angioplasty at the site matched with the smallest lumen area before intervention.

Table 5. Intravascular ultrasound parameters ($p \leq 0.10$) in procedures with early clinical restenosis, late clinical restenosis and late clinical success.

	Early restenosis ($n=17$)	Late restenosis ($n=32$)	Late success ($n=56$)	* p	† p	‡ p
Smallest LA before and its matched site after PTA						
Hard lesion	10 (71%)	7 (24%)	19 (40%)	**0.008**	0.93	0.15
Arc of hard lesion (°)	79±96	20±38	35±59	0.078	0.77	0.21
Area stenosis after PTA (%)	60±9.7	55±10	54±10	0.073	0.19	0.52
Area stenosis decrease (%)	20±14	30±13	28±16	0.089	0.91	0.56
Smallest LA after PTA						
Dissection	8 (47%)	21 (66%)	26 (46%)	0.82	0.19	0.082
Arc of dissection (°)	46±69	71±71	39±60	0.94	0.068	**0.033**
MBA after PTA (mm^2)	31.1±11.0	33.0±11.0	29.1±8.6	0.75	0.13	0.097
All cross-sections in the dilated segment						
Mean arc of hard lesion (°)	68±68	22±33	26±35	**0.028**	0.20	0.63

* = Comparison of early success versus early restenosis; † = comparison of late success versus early and late restenosis; ‡ = comparison of late success versus late restenosis; PTA = percutaneous transluminal angioplasty; LA = lumen area; MBA = media-bounded area; significant values are shown in bold.

Predictor variables of clinical outcome

Intravascular ultrasound parameters ($p \leq 0.10$) in the procedures with early restenosis, late restenosis and late successs are listed in Table 5.

Predictors of 1 month outcome (early success versus early restenosis). Diabetes and rest pain or ulceration were more frequently seen in procedures with early restenosis than early success (both 53% versus 25%; $p = 0.023$). Intravascular ultrasound predictors of early restenosis were the presence of hard lesion at the smallest lumen area and a larger arc of hard lesion. The presence and extent of vascular damage were not predictive of early restenosis.

By multiple logistic regression analysis the only independent predictor of early restenosis was a larger mean arc of hard lesion (odds ratio = 1.69 (95% CI: 1.21–2.36) per increase of 30° $p = 0.007$).

Predictors of 6 months' outcome (late success versus early and late restenosis). No variables were significantly related to 6 months' outcome. The arc of dissection at the smallest lumen area after PTA was the most significant variable related to 6 months outcome: (early and late) restenosis and late success 62±71° and 39±60°, respectively ($p = 0.068$).

Predictors of late restenosis (late success versus late restenosis). The arc of dissection at the smallest lumen area after PTA was significantly larger in procedures with late restenosis than in procedures with late success.

Discussion

The present study shows that the independent intravascular ultrasound predictors of outcome were the extent of hard lesion before (clinical outcome) and area stenosis after PTA (anatomic outcome). Other parameters such as lesion topography (eccentric versus concentric) before, and presence and extent of vascular damage (dissection and media rupture) after intervention, were not predictive for 1 and 6 months outcome.

To compare the present study to intracoronary ultrasound studies the following issues should be addressed.

First, it is common that the outcome of coronary balloon angioplasty is assessed angiographically at 6 months.[19–21] Conversely, the outcome of peripheral PTA is commonly assessed with the use of clinical data and objective vascular laboratory findings. Based on these findings a distinction was made in the present study between anatomic and clinical outcome.

Secondly, in the present study a distinction was made between early and late restenosis. This distinction, based on the large number of failures occurring in the first month of intervention, enabled the assessment of different parameters related to 1 and 6 months outcome. Most of the significant intravascular ultrasound predictors were related to 1 month outcome, while the predictive power of intravascular ultrasound parameters for outcome at 6 months was limited.

Thirdly, intracoronary ultrasound studies usually present data on one single cross-section obtained at the target lesion following intervention. In the present study, intravascular ultrasound images were obtained both before and after PTA and a sequence of cross-sections was collected in the dilated segment. As a consequence the number of intravascular ultrasound parameters studied was larger than in coronary studies.

Comparison with other intravascular ultrasound studies

Lesion morphology. Intravascular ultrasound studies performed in coronary arteries did not demonstrate a relation between hard lesion and outcome of intervention.[8,9,19,20] In the present study, the presence and extent of hard lesion were found to be predictors of early clinical restenosis but not for late restenosis. This observation suggests that lesion morphology has a different effect on early and late restenosis. Thus, hard lesion (i.e. calcified lesion) – a sign of more advanced atherosclerotic disease[22] – may preclude early success of intervention. This is in agreement with the report of Potkin and Roberts, who found that initial angiographic success was most often seen in non-calcified fibrous arteries.[23]

Vascular damage. Tenaglia *et al.* found both a higher incidence and greater severity of dissection on intravascular ultrasound in patients with adverse events after coronary interventions.[8] Similarly, Jain *et al.* observed that an extensive dissection was more frequently found in a lesion that subsequently developed restenosis.[9] Such a relation was not established in other intracoronary ultrasound studies.[19,20] In the present study no significant relation was found between vascular damage and outcome. The results showed a trend which seemed in part contradictory. Media ruptures were less frequently seen in procedures with early anatomic restenosis than with early anatomic success ($p=0.063$). Conversely, comparing the procedures with late restenosis and late success revealed that the maximum arc of dissection was larger in procedures with late anatomic restenosis ($p=0.076$). Similarly, the presence and extent of dissection at the smallest lumen area after PTA was larger in procedures with late clinical restenosis than in procedures with early clinical restenosis ($p=0.082$ and $p=0.033$, respectively). In other words, the presence of vascular damage was related to success at 1-month and to late restenosis at 6 months. An explanation for this may be the difference in mechanism of early and late restenosis. Vascular damage following balloon angioplasty, a prerequisite necessary to allow the adventitia and media to stretch,[24,25] resulted in better initial clinical results;[23] however, extensive dissection, which has first led to a successful lumen enlargement, may be a stimulus for a sequence of events leading to smooth muscle cell proliferation and migration resulting in restenosis during follow-up.[26,27]

Area measurements. Thus far, intracoronary ultrasound studies presented conflicting results on the predictive value of quantitative intravascular ultrasound parameters on outcome. In some studies no quantitative parameters were found to be predictive of outcome,[7,8,20] whereas others established a relation between area measurements and outcome of intervention.[9,19,21] Jain *et al.* found differences in area stenosis after intervention between the success group (34%) and the restenosis (50%) group.[9] The report of the GUIDE trial revealed that area stenosis after intervention was a predictor of both angiographic and clinical restenosis.[24] Mintz *et al.* found that lumen area, minimum lumen diameter and area stenosis at the lesion site both before and after intervention were predictors of angiographic restenosis.[19]

In the present study a number of intravascular ultrasound parameters found to be predictive for outcome were detected by comparison of the measurements before and after PTA. However, in the multivariate analysis only area stenosis seen after PTA at the site corresponding to the smallest lumen area before PTA was an independent predictor of anatomic outcome. The interrelationship between the quantitative parameters may explain that just one quantitative intravascular ultrasound parameter is an independent predictor.[28,29]

Although in the present study area stenosis after PTA is calculated by the (residual) plaque area divided by the stretched media-bounded area, it is the independent quantitative predictor of outcome rather than lumen area after PTA as is also the case in two of the above-mentioned studies.[19,21] This is in agreement with the histopathologic study conducted by Farb *et al.*, who concluded that the creation of a larger lumen and a larger lumen as a percentage of vessel size were associated with an improved long-term histologic patency.[30]

Clinical implications

Lesion morphology. The presence and extent of hard lesion were predictors of clinical outcome. If severe calcification is present in the diseased segment, other treatment modalities may be considered. The influence of lesion morphology assessed with intravascular ultrasound on decision making has been reported.[31,32] However, there is still no evidence that the outcome of intervention is improved due to decisions based on intravascular ultrasound assessed lesion morphology.

Vascular damage. It seems that the presence of a media rupture is beneficial for 1 month outcome. The absence of vascular damage, especially in the presence of a small lumen area or small luminal gain after PTA, may be an indication of an inadequate dilation and may require a repeat PTA. However, producing extensive vascular damage, such as a large dissection, creates a dilemma because this may result in an increased probability for late restenosis. Large dissections may, therefore, necessitate the placement of stents to prevent the late restenotic process.

Area measurements. Maximising lumen area, and thus minimising area stenosis, may reduce restenosis. In the presence of a large area stenosis after PTA several measures are available to optimise the result: repeat PTA, atherectomy or stent placement.

Limitations

Absence of quantitative angiography prevents the comparison between intravascular ultrasound and angiographic parameters (such as mean lumen diameter and % diameter stenosis) in the prediction of outcome. The present study is also limited by the absence of angiographic follow-up at 6 months. Instead, anatomic (duplex scanning) and clinical parameters (Rutherford criteria) were used to assess restenosis. Duplex follow-up was not available at 1 month in 15 patients and at 6 months in eight patients. Inadequate image quality on ultrasound and the presence of calcification preventing measurements of media-bounded area in 19% of the cross-sections should be acknowledged. Finally, as the number of patients studied is limited, caution is required when drawing conclusions about the non-significant parameters.

Conclusions

This study revealed intravascular ultrasound parameters predictive of anatomic and clinical outcome. The parameters for 1 and 6 months' outcome were different. Whether interventional management based on the intravascular ultrasound parameters found will result in better outcome should be investigated in further studies. These studies will define the true clinical utility of intravascular ultrasound.

Acknowledgements

This study was supported by the Interuniversity Cardiology Institute of The Netherlands and The Netherlands Heart Foundation (grants 900.574.002; 91.016).

We would like to thank N. Bom, R. J. G. Peters and C. Borst for their constructive advice. We appreciate the database management of CADANS and the data analysis provided by D. J. Posthuma.

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Accepted 2 February 1998