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Outcome of Nonobstructive Residual Dissections Detected by Intravascular Ultrasound Following Percutaneous Coronary Intervention

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The purpose of this study was to assess the outcome of nonobstructive (or non-flow-limiting) residual dissection (RD) after percutaneous coronary intervention. Results of 124 consecutive native coronary lesions with angiographic nonobstructive RD in 97 patients (RD group) were compared with outcomes of 124 lesions without RD in 100 patients (non-RD group), whose characteristics were matched with those of the RD group. RD occurred after stent implantation (81 of 124 lesions, 65%) or balloon angioplasty (43 of 124 lesions, 35%). Angiographic types of RD were type A in 8 lesions (6%), B in 101 (82%), and C in 15 (12%). Stents were implanted in 65% of the lesions in each group. Clinical success (94% in RD group vs 95% in non-RD group, $p = 0.77$) and the in-hospital major adverse cardiac event rates were found to be similar in the 2 groups (6% vs 3%, respectively; $p = 0.33$). The late angiographic and clinical

outcomes were also comparable. By intravascular ultrasound (IVUS) evaluation of the dissections in the RD group, area stenosis correlated with the incidence of in-hospital major adverse cardiac events ($p = 0.023$), whereas the final minimal lumen area correlated inversely with the occurrence of restenosis ($p = 0.011$). An area stenosis $\geq 58\%$ was the best predictor for the incidence of in-hospital major adverse cardiac events (sensitivity 0.68, specificity 0.68). Most nonobstructive RDs are "favorable" and do not need stent implantation. IVUS evaluation identifies "unfavorable" nonobstructive (or non-flow-limiting) dissections that might be prone to acute occlusion. Nonobstructive dissections can be left untreated when final IVUS reveals an area stenosis of $< 60\%$ at the site of a dissection. ©2002 by Excerpta Medica, Inc.

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The purpose of this study was to assess the outcomes of patients who developed a nonobstructive (or non-flow-limiting) residual dissection (RD) after percutaneous coronary intervention (PCI) and compare them with outcomes in patients who did not have RD,¹⁻³ and to assess the usefulness of intravascular ultrasound (IVUS) imaging to identify "unfavorable" nonobstructive (or non-flow-limiting) RDs that might need additional stenting.

METHODS

Selection of study population: We reviewed 2,146 PCI procedures on native coronary arteries performed in 1,197 patients in our institution between June 1997 and May 1999. Patients who had an acute myocardial infarction, who underwent catheter-based radiation therapy, or had in-stent restenosis were excluded from analysis. We identified a total of 297 angiographic dissections (14%) after the procedure. Prespecified criteria for stenting RD were: (1) type C or worse

dissections, (2) residual diameter stenosis $\geq 50\%$, (3) Thrombolysis In Myocardial Infarction (TIMI) flow < 3 , and (4) signs and/or symptoms of myocardial ischemia referable to the index vessel. These 297 dissections were treated as follows: (1) additional stent implantation in case of obstructive and/or flow-limiting dissection: i.e., all type C or worse dissections, dissections with residual diameter stenosis $\geq 50\%$ by angiography, and TIMI flow < 3 ($n = 173$); and (2) angiographic and IVUS observation, without any additional treatment, in case of nonobstructive and/or non-flow-limiting dissections: i.e., all the type A to B dissections, dissections with residual diameter stenosis $< 50\%$, and TIMI flow 3 ($n = 124$) occurring after otherwise optimal or acceptable PCI. The present study deals with the 124 consecutive lesions in 97 patients who had angiographic nonobstructive RDs that were left untreated and were evaluated by IVUS (RD group). IVUS examination was performed to better define the anatomic findings of these dissections but not to guide treatment, because the clinical and the angiographic results were acceptable and did not meet the predefined criteria for stenting.

To define a group of lesions for comparison, we selected from the 2,049 lesions (in 1,634 patients) without angiographic dissection, 124 lesions in 100 patients who underwent PCI and final IVUS evaluation (non-RD group). The selection was made to

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TABLE 1 Baseline Angiographic Characteristics			
	RD Group	Non-RD Group	p Value
Number of narrowings	124	124	
Coronary artery			
Anterior descending artery	66 (53%)	66 (53%)	1.00
Circumflex artery	19 (15%)	26 (21%)	0.32
Right	25 (20%)	21 (17%)	0.62
Other branch	14 (11%)	11 (9%)	0.67
Location			
Ostial	7 (6%)	7 (6%)	1.00
Proximal	47 (38%)	44 (35%)	0.79
Mid or distal	70 (56%)	73 (59%)	0.80
Calcium	27 (22%)	27 (22%)	1.00
Thrombus	2 (2%)	4 (3%)	0.68
Occlusion	21 (17%)	21 (17%)	1.00
Restenotic lesion	6 (5%)	6 (5%)	1.00
ACC/AHA class			
A	0	0	—
B1	5 (4%)	3 (2%)	0.72
B2	56 (45%)	64 (52%)	0.37
C	63 (51%)	57 (46%)	0.53
Reference diameter (mm)	2.88 ± 0.52	2.86 ± 0.47	0.77
Minimal lumen diameter (mm)	0.74 ± 0.50	0.78 ± 0.48	0.51
Diameter stenosis (%)	74 ± 16	73 ± 16	0.44
Lesion length (mm)	18.4 ± 10.4	18.0 ± 9.4	0.78
ACC/AHA = American College of Cardiology/American Heart Association.			

TABLE 2 Procedural Characteristics			
	RD Group	Non-RD Group	p Value
Number of narrowings	124	124	
Stent*	81 (65%)	81 (65%)	1.00
Slotted tube or multidesign	78 (63%)	71 (57%)	0.44
Coil	4 (3%)	9 (7%)	0.25
Total deployed stent length (mm)	15 ± 16	15 ± 15	0.92
Balloon angioplasty or cutting balloon alone	36 (29%)	36 (29%)	1.00
Directional coronary atherectomy	6 (5%)	5 (4%)	1.00
Rotational atherectomy	12 (10%)	15 (12%)	0.68
Abciximab	22 (18%)	14 (11%)	0.21
*Some lesions were treated with >1 type of stent.			

match case by case the characteristics of the patients, lesions, and interventional procedures in the non-RD group to those in the RD group. The parameters used for the matching process were age of patient, presence of diabetes mellitus, lesion characteristics, reference vessel diameter, preintervention minimal lumen diameter, lesion length, type of vessel, and implanted stent length. After matching, we identified 124 lesions in 100 patients who represented the non-RD group.

Interventional procedure: All patients were pretreated with aspirin (100 to 325 mg/day) and ticlopidine (250 mg twice daily); aspirin treatment was maintained indefinitely and ticlopidine for 1 month. Heparin was given intravenously at the beginning of the interventional procedure at a dose of 100 U/kg body weight, and the activated clotting time was maintained at >250 seconds throughout the procedure by additional heparin boluses. Stents were implanted

at the discretion of the operator. A final high-pressure inflation was used to achieve an angiographic residual stenosis of <10%.

Angiographic assessment and IVUS study: Quantitative angiography was performed using an off-line semiautomatic, edge-detection system⁴ (QCA-CMS, MEDIS, Leiden, The Netherlands). The immediate lumen gain was defined as the diameter change from before to after the procedure, with the relative immediate lumen gain being calculated as the immediate lumen gain divided by the reference vessel diameter.

A 3.2Fr monorail system with a 30-MHz transducer-tipped catheter (Ultracross, Boston Scientific-CVIS Corp., Sunnyvale, California) was used; automatic pullback of the IVUS catheter was performed at a speed of 0.5 mm/s. Images were recorded on super-VHS videotape. The lumen area was measured by tracing the leading edge of the circumferential

blood/intima interface, and the vessel area was defined as the area enclosed by the outline of the external elastic lamina.⁵ The plaque area was calculated as the difference between the lumen area and the vessel area. The area stenosis was calculated using the formula: (plaque area/vessel area) × 100. A coronary dissection was defined as a tear parallel to the vessel wall or the pulsatility of an echolucent area within a plaque or between the plaque and the media.^{5,6} At the site of dissection, the incidence of dissections that reached the media was recorded and the minimal lumen and vessel cross-sectional areas were measured. The circumferential extent (arc) of calcium was measured at the site of a dissection. The axial length of a dissecting segment was calculated based on the time interval of the automatic pullback.

Definitions: An obstructive or flow-limiting dissection was defined as dissection with a residual diameter stenosis of ≥50% or with a persistent filling defect inside the lumen. A flow-limiting dissection was defined as any dissection associated with TIMI flow ≤2 (TIMI flow ≤1 for initially occluded lesions). The angiographic appearance of RD was defined as follows⁷: type A, radiolucent area within the lumen with minimal or no persistence of contrast; type B, parallel tracts or double lumen separated by a radiolucent area with minimal or no persistence of contrast; type C, presence of contrast outside the coronary lumen with persistence of contrast after clearance of dye from the coronary lumen; type D, spiral luminal filling defects; type E, new persistent filling defects; type F, those non-A to E types that lead to impaired flow or total occlusion.

A Q-wave myocardial infarction was defined as the development of new Q waves in ≥2 contiguous leads

	Stented Lesion	Non-Stented Lesion	p Value	All lesions
Number of narrowings	81	43		124
Dissection reaching media	52 (64%)	38 (88%)	0.005	90 (73%)
Calcium in dissection site	42 (52%)	33 (77%)	0.007	75 (60%)
Arc of calcium at dissection (degree)	51 ± 67	88 ± 84	0.009	64 ± 75
Axial length of dissection (mm)	7.8 ± 7.8	13 ± 9.7	0.004	9.5 ± 8.8
Minimal lumen area at dissection (mm ²)	6.7 ± 3.5	6.1 ± 2.5	0.28	6.5 ± 3.2
Vessel cross-sectional area at dissection (mm ²)	14 ± 5.5	12 ± 4.3	0.20	13 ± 5.1
Plaque area at dissection (mm ²)	6.9 ± 3.3	6.3 ± 2.8	0.32	6.6 ± 3.2
Area stenosis at dissection (%)	50 ± 14	50 ± 12	0.93	50 ± 13
Dissection proximal to stented segment	39 (48%)	—	—	—
Dissection distal to stented segment	49 (60%)	—	—	—
Dissection both distal and proximal to stent	7 (9%)	—	—	—

	RD Group	Non-RD Group	p Value
Immediate angiographic results			
Number of narrowings	124	124	
Angiographic success	124 (100%)	123 (99%)	1.00
Final minimal lumen area (mm)	2.76 ± 0.67	2.79 ± 0.60	0.67
Final diameter stenosis (%)	13 ± 15	10 ± 14	0.16
Acute gain (mm)	2.02 ± 0.76	2.01 ± 0.75	0.95
Relative gain	0.68 ± 0.29	0.64 ± 0.23	0.38
Late angiographic results			
Number of lesions	98	97	
Follow-up interval (mo)	6.9 ± 5.0	6.4 ± 6.4	0.52
Minimal lumen area (mm)	1.75 ± 0.76	1.75 ± 0.88	0.98
Diameter stenosis (%)	39 ± 23	39 ± 28	0.90
Restenosis	27 (28%)	25 (26%)	0.87
In-hospital outcomes			
Number of patients	97	100	
Clinical success	91 (94%)	95 (95%)	0.77
Global major cardiac events	6 (6%)	3 (3%)	0.33
Death	0	0	—
Coronary bypass	0	0	—
Q-wave myocardial infarction	0	0	—
Non-Q-wave myocardial infarction	5 (5%)	3 (3%)	0.49
Repeat target vessel PCI	3 (3%)	1 (1%)	0.36
Late outcomes			
Number of patients	93	95	
Follow-up interval (mo)	12 ± 7.8	12 ± 8.3	0.82
Global major cardiac events	28 (30%)	24 (25%)	0.52
Death	2 (2%)	3 (3%)	1.00
Coronary bypass	2 (2%)	2 (2%)	1.00
Myocardial infarction	3 (3%)	2 (2%)	0.68
Target lesion PCI	18 (19%)	19 (20%)	1.00
Target vessel PCI	25 (27%)	21 (22%)	0.50

PCI = percutaneous coronary intervention.

stenosis with a TIMI flow 3 in non-occlusive lesions or with a TIMI flow of ≥ 2 in initially occluded lesions. Restenosis was defined as $\geq 50\%$ diameter stenosis at follow-up angiography. Target lesion revascularization was regarded as a revascularization procedure on the original treated lesion either by percutaneous intervention or by coronary artery bypass surgery. Death was defined as any mortality regardless of the cause. In-hospital major adverse cardiac events included death, myocardial infarction (Q-wave and non-Q-wave) or target lesion revascularization during hospital stay. Clinical success was defined as achievement of angiographic success with the absence of in-hospital major adverse cardiac events. Major adverse cardiac events during follow-up refer to any death, coronary artery bypass surgery, myocardial infarction, repeat target PCI, or target vessel revascularization that occurred during hospital stay and the follow-up period.

Statistical analysis: Continuous variables are expressed as mean $\pm$ SD, and were compared by either the unpaired Student's *t* test or the Mann-Whitney U test. Discrete variables were expressed as counts and percentages and the Fisher's exact test was used to compare proportions. All statistical analyses were 2-tailed. The best threshold for diagnostic accuracy was considered to be the cutoff point where sensitivity equals specificity.⁸ Receiver-operating characteristic (ROC) curves were drawn, and the area under the curve, which indicates the diagnostic accuracy of the threshold, was then reported.⁹ Statistical significance was accepted at a *p* level < 0.05 . All statistical analyses were performed using SPSS for Windows 10.0 (SPSS Inc., Chicago, Illinois).

RESULTS

Baseline clinical characteristics: Mean age of patients was 59 ± 10 years in the RD group versus 60 ± 10 years

in the non-RD group (*p* = 0.80); 93% were men and 92% were women (*p* = 1.00), respectively. Left ventricular ejection fraction was $60 \pm 10\%$ in the RD group versus $59 \pm 12\%$ in non-RD group (*p* = 0.42). Systemic hypertension was present in 50 patients (52%) in the RD group and in 54 patients (54%) in the non-RD group (*p* = 0.78); diabetes mellitus was

accompanied by increases in creatine kinase and creatine kinase-MB levels of more than twice the normal upper limit. A Non-Q-wave myocardial infarction was defined as elevation in creatine kinase and creatine kinase-MB levels to more than twice the normal upper limit without the development of new Q waves. Angiographic success was defined as $< 50\%$ residual

FIGURE 1. *Left*, correlates of the occurrence of in-hospital major adverse cardiac events (MACE). The area stenosis at the dissection site correlates with the incidence of in-hospital major adverse cardiac events in the RD group. The mean area stenosis at the dissection site was $62 \pm 8.6\%$ in patients who had in-hospital major adverse cardiac events ($n = 6$) and $50 \pm 13\%$ in the remaining patients ($n = 91$) who did not. *Right*, correlates of the incidence of restenosis. The lumen cross-sectional area (CSA) at the dissection site negatively correlates with the incidence of angiographic restenosis in the RD group. The mean lumen cross-sectional area at the dissection was $5.2 \pm 2.3 \text{ mm}^2$ in lesions with restenosis ($n = 27$) at follow-up angiography and $6.8 \pm 3.4 \text{ mm}^2$ in the remaining lesions without restenosis ($n = 71$).

FIGURE 2. The best cutoff point for the incidence of in-hospital major adverse cardiac events. An area stenosis of 60% was the cutoff point where sensitivity equals specificity.

present in 7 patients (7%) versus 6 patients (6%), respectively ($p = 0.78$). Hypercholesterolemia was present in 60 patients (62%) in the RD group versus 56 patients (56%) in the non-RD group ($p = 0.47$). Sixty patients (62%) had multivessel coronary artery disease in the RD group and 72 patients had it (72%) in the non-RD group ($p = 0.17$).

Baseline angiographic and procedural characteristics (Tables 1 and 2): The 124 nonobstructive RDs occurred after stent implantation in 81 cases (65%) and balloon angioplasty in 43 cases (45%). Angiographic types of RD in the RD group were type A in 8 lesions (6%), type B in 101 lesions, and type C in 15 lesions (12%). Because of the design of the case-matching

lesion selection, there were no differences in the angiographic or procedural characteristics between the 2 groups.

IVUS study of RD in RD group: Table 3 lists IVUS findings at the site of RD occurring with (stented lesions) or without (nonstented lesions) stent implantation in the RD group. The minimal lumen cross-sectional area and area stenosis were found to be similar between stented and nonstented lesions.

Angiographic and early clinical outcomes (Table 4): Angiographic and early clinical outcome in the RD and non-RD groups were similar. There was no significant statistical difference in the incidence of acute occlusion between the RD and non-RD groups. Acute occlusions during hospital stay occurred in 2 patients in the RD group (1.6%); both lesions had a type B dissection. In these instances, IVUS evaluation revealed an area stenosis of 68% and 71%, respectively, despite an acceptable angiographic result. Both patients underwent repeat PCI during their hospital stay. One of the 2 acute occlusions occurred after balloon angioplasty and caused an in-hospital non-Q-wave myocardial infarction; the other occlusion was caused by stent thrombosis. No acute occlusions or subacute stent thrombosis occurred in the non-RD group.

Usefulness of IVUS examination to identify unfavorable nonobstructive RD: All IVUS parameters presented in Table 3 were analyzed to find correlation with the occurrence of major adverse cardiac events. The final area stenosis at the dissection site was found to correlate significantly with the occurrence of in-hospital major adverse cardiac events (Figure 1). By

	MACE (n = 34)	No MACE (n = 63)	p Value
Angiographic variable			
Reference diameter (mm)	2.87 ± 0.57	2.93 ± 0.50	0.62
Pre-minimal lumen diameter (mm)	0.69 ± 0.45	0.77 ± 0.50	0.45
Pre-diameter stenosis (%)	75 ± 16	74 ± 16	0.73
Pre-lesion length (mm)	17.2 ± 8.7	19.5 ± 11.8	0.36
Post-minimal lumen diameter (mm)	2.73 ± 0.64	2.90 ± 0.68	0.25
Post-diameter stenosis (%)	14 ± 14	10.0 ± 15	0.27
Type A or B dissection	29 (85%)	56 (89%)	0.75
Type C dissection	5 (15%)	7 (11%)	0.75
Final IVUS variable			
Residual dissection reaching media	27 (79%)	41 (65%)	0.17
Calcium in residual dissection site	23 (68%)	32 (51%)	0.14
Arc of calcification at residual dissection (degree)	65 ± 70	63 ± 82	0.90
Axial length of residual dissection (mm)	7.9 ± 6.4	10.1 ± 9.3	0.23
Minimal lumen area at residual dissection (mm ²)	6.4 ± 3.9	7.0 ± 3.2	0.45
Vessel cross-sectional area at residual dissection (mm ²)	13 ± 5.8	14 ± 5.1	0.80
Plaque area at residual dissection (mm ²)	6.9 ± 3.5	6.7 ± 2.9	0.68
Area stenosis at residual dissection (%)	52 ± 15	49 ± 12	0.34

ROC analysis, we identified an area stenosis of 60% at the site of dissection to be the best threshold for distinguishing patients who did or did not have in-hospital major adverse cardiac events (sensitivity 0.68, specificity 0.68; Figure 2). The area under the ROC curve for this cutoff point was 78% ($p = 0.022$, 95% confidence interval 65% to 91%).

Influence of angiographic and IVUS parameters on late outcome in the RD group: The correlation between the incidence of major adverse cardiac events during follow-up and angiographic and IVUS parameters are listed in Table 5. The final minimal lumen cross-sectional area at the dissection site correlated with the incidence of angiographic restenosis (Figure 1). In contrast, no angiographic and IVUS parameters were found to have a significant correlation with the occurrence of late major adverse cardiac events during follow-up.

DISCUSSION

Nonobstructive RD and acute outcome: The major findings of this study are that (1) most nonobstructive (or non-flow-limiting) RDs occurring after successful PCI are acceptable and do not need stenting; and (2) IVUS examination identifies “unacceptable” nonobstructive RDs (that might be more prone to acute occlusion) occurring after an otherwise successful PCI. The area stenosis, as assessed by IVUS at the site of a dissection, correlated with the incidence of in-hospital major adverse cardiac events. The area stenosis may be difficult to measure in a dissection because the torn tissue distorts the usual lines of boundary identification. The prolapsed tissue has been reported to impede blood flow^{3–10} and may predispose to thrombus formation. In our population we had a

1.6% rate (2 of 124 cases) of acute vessel occlusion. Although there was no significant statistical difference in the incidence of acute occlusion between the RD and non-RD groups, the 2 cases of acute occlusion occurred only in the RD group. In these instances, IVUS evaluation revealed an area stenosis of 68% and 71%, respectively, despite an acceptable angiographic result.

This finding contrasts with a recent report suggesting that non-flow-limiting dissections can be left untreated in most instances,¹¹ and that IVUS evaluation does not add information to the decision making process regarding the need for additional stenting. The findings from the present study provide an additional tool for evaluating a dissection and helping to decide if the dissection can be left without further treatment. This concept forms the basis of “spot stenting,” a technique that integrates balloon angioplasty and stenting for the treatment of long lesions. In this

strategy, a RD is left without stenting when the residual lumen evaluated by IVUS is sufficiently large.¹² This concept may be useful to guide and to limit stenting during PCIs performed in patients treated with catheter-based radiation therapy. The possibility of avoiding stent implantation after intracoronary radiation therapy is becoming recognized as an important goal.¹³

Nonobstructive RD and late outcome: The incidence of late major adverse cardiac events in the RD group was comparable to that in the non-RD group. This finding is consistent with results from a recent report in which coronary dissections after balloon angioplasty were evaluated using a Doppler guidewire.¹⁰ In this report, the presence of an angiographic dissection was only found to influence the short-term outcome. Patients having a type C or D dissection associated with an impaired coronary flow velocity reserve had a comparable incidence in restenosis or recurrence of symptoms at 6-month follow-up compared with patients having a lower grade of dissection (type A or B) or the absence of a dissection. In our study, occurrence of angiographic restenosis was correlated with final minimal lumen cross-sectional area as assessed by IVUS, but not with the presence of a nonobstructive RD (Figure 1, right).

Study limitations: Because of the small number of cases, the results from balloon alone and stent cases were combined. Furthermore, because large plaque could hide the presence of thrombus (thrombus vs echolucent plaque), we cannot rule out that thrombosis played a role in the occurrence of in-hospital occlusion rather than a large plaque burden with high residual stenosis.

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