

Early and Late Outcome of Stenting in a Consecutive Series of Patients With Coronary Lesions in Vessels Less Than 2.8 mm in Diameter

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SUMMARY

In an attempt to determine the early and late outcomes of small vessel stenting, we retrospectively evaluated our database on 51 consecutive patients (41 males, mean age, 57.1 ± 10.1 years) who underwent stenting of at least one significant lesion in a coronary artery with a reference vessel diameter (RVD) < 2.8 mm between March 1999 and March 2001.

Sixty balloon expandable tubular stents were implanted in 57 lesions (29 Type B2/C, mean RVD: 2.54 ± 0.16 mm) without intravascular ultrasound guidance under a heparin-aspirin-ticlopidine regimen. The mean diameter stenosis (DS) decreased from $75.8 \pm 13.6\%$ to $4.2 \pm 1.9\%$ ($P < 0.0001$) with stenting at a mean deployment pressure of 13.6 ± 1.7 atm and a final balloon to RVD ratio (FB/RVD) of 1.08 ± 0.03 . All stents were deployed successfully. Acute stent thrombosis occurred in 3 patients (6%), one died, and 2 developed non-Q-wave myocardial infarction (procedural success 94%). Clinical follow-up, available in 48 patients, revealed a 29% target lesion revascularization rate, a 2% myocardial infarction rate, and a 71% event-free survival at a mean of 11.6 months. Angiographic follow-up, available in 40 patients, showed a DS of $48.8 \pm 31.3\%$ and a binary restenosis rate of 50% at a mean of 7.7 months. The FB/RVD ratio was significantly lower in the group with restenosis than in the group without (1.06 ± 0.02 vs 1.1 ± 0.05 , $P = 0.04$). Subgroup analysis yielded a significantly greater rate of restenosis in diabetics with complex (Type B2/C) lesion morphology compared to nondiabetics with simple (Type A/B1) lesions (75% vs 21%, $P < 0.05$).

In conclusion, stenting in vessels < 2.8 mm was found to be associated with a high rate of acute stent thrombosis and in-stent restenosis. Further analysis detected a subgroup of patients without diabetes or complex lesions who could be stented with an acceptable in-stent restenosis rate. (Jpn Heart J 2003; 44: 163-177)

Key words: Stenting, Small vessel, Coronary artery

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AVAILABLE data support the superiority of stenting over conventional percutaneous balloon angioplasty (PTCA) in reducing the risk of restenosis in coronary vessels ≥ 3 mm in diameter.^{1,2)} Moreover, acute or threatened vessel closure, which constitute the second major drawback of conventional PTCA, are effectively managed by coronary stents.³⁻⁶⁾ With the emergence of evidence demonstrating a major reduction in stent thrombosis rate by the combination of an optimal stenting technique and potent antithrombotic therapy composed of aspirin-ticlopidine,^{7,8)} the indications of coronary stenting broadened considerably and started to cover complex lesions including small vessels, which once were considered contraindications for stenting. Considering that about one third of interventional procedures are performed on coronary vessels < 3 mm in diameter,⁹⁾ the feasibility of utilizing stents to overcome the problems of acute/threatened vessel closure and restenosis in this lesion subset must be established. Accordingly, the purpose of the current study was to evaluate the acute and long-term outcomes of a consecutive series of patients who received stents in coronary vessels < 2.8 mm in diameter.

METHODS

We retrospectively analyzed all consecutive patients with symptomatic coronary artery disease who underwent coronary stenting of significant ($> 50\%$ diameter stenosis) lesions with a reference vessel diameter < 2.8 mm between March 1999 and March 2001 in our center. By design, the study population involved a group with heterogeneous clinical (stable angina, unstable angina, acute myocardial infarction) and lesional (de novo, restenotic, vein graft) characteristics.

Angiographic analysis: Coronary angiography was performed via the femoral or brachial route by using 6F or 7F diagnostic catheters. Quantitative coronary angiographic (QCA) analysis was performed after intracoronary injection of 200 μg of nitroglycerin in two nearly orthogonal views with the help of commercially available software (Telecardiology System, Version 1.900, Medcon Telemedicine Technology, Israel). The reference vessel diameter (RVD) at the lesion site, minimum lumen diameter (MLD), and percent diameter stenosis (DS) were measured using the dye-filled catheter as the scaling device. All calculations were repeated on the same projections after coronary stenting and at follow-up control angiogram when available. Acute gain was defined as the difference between the MLD immediately after stent implantation and the basal MLD, and late loss was defined as the difference between the MLD immediately after stent implantation and the MLD at follow-up. The lesions were classified angiographically as Type A, B1, B2 and C according to the modified ACC/AHA Classification.¹⁰⁾ They

were further subclassified as complex (Type B2 and C) and non-complex (Type A and B1) for the purpose of this study.

Stenting procedure: Systemic anticoagulation was achieved by an intravenous bolus of 10,000 units of heparin at the beginning of the procedure. Additional injections of 2500 units were given to keep the activated clotting time above 250 seconds during the procedure.

Antithrombotic medication comprised aspirin (300 mg daily) plus ticlopidine (250 mg twice daily) which was started at the time of stent implantation and continued for a month. Aspirin was given indefinitely. No glycoprotein IIb/IIIa inhibitors were used.

Three types of premounted stents (Jostent [JOMED International AB, Helsingborg, Sweden], ACS MultiLink [Guidant, Advanced Cardiovascular Systems, Santa Clara, California, USA] and BiodivYsio SV stent [Biocompatibles Ltd., Farnham, UK]) were used. A 2.5 mm stent was chosen for lesions with a RVD ≤ 2.55 mm and a 2.75 mm stent was utilised for lesions with an RVD between 2.56-2.79 mm. Other than RVD, the choice of stent type was determined by availability and lesion length. Stents were deployed at 10 atmospheres of pressure. Additional high-pressure inflation with the same semicompliant balloon at up to 16 atmospheres was performed if deemed necessary by the operator. No high pressure inflations with a larger balloon were applied. One or more stents were deployed to cover the entire lesion or dissection when present. Both direct stenting and stenting with predilatation were performed and the decision to choose among these two strategies was at the discretion of the operator. No intravascular ultrasound (IVUS) guidance was used.

Stenting was performed either electively or in the presence of a suboptimal PTCA result (residual DS > 30% after ballooning), or a bail-out situation (acute or threatened vessel closure). Written informed consent was obtained from the patients before the procedure.

In-hospital follow-up: No additional heparin infusion was given and the patients were followed up for at least 48 hours in the hospital. Cardiac enzymes (total CK and CK-MB) were followed up for 24 hours (3 times daily). The sheaths were removed 3 hours after the procedure in uncomplicated cases.

Long-term follow-up: Follow-up was scheduled at 1, 3 and 6 months, at the end of which a control angiogram was offered regardless of symptomatic status and performed in those patients who did not refuse. Control angiograms were performed earlier in case of symptom recurrence.

Definitions: Angiographic success was defined as a reduction of DS to <20% with stenting in association with a TIMI III flow downstream. In-hospital major adverse cardiac events (MACE) were death, myocardial infarction (MI) and urgent revascularization during hospital stay. Myocardial infarction was defined

as either the appearance of pathologic Q-waves in two or more contiguous leads (Q-wave MI) or an increase in CK-MB to more than twice the upper limit of normal without accompanying Q-waves on ECG (non-Q-wave MI). Urgent revascularization was defined as either angioplasty or coronary bypass of the stented lesion due to acute thrombotic occlusion, defined as thrombotic occlusion of the stented segment within 2 days of the procedure. Procedural success was defined as angiographic success in the absence of in-hospital MACE. Angiographic restenosis was defined as a DS $\geq 50\%$ in or at the edges of the stented lesion at the follow-up angiogram. Target lesion revascularization (TLR) was defined as either repeat angioplasty or bypass surgery of the treated lesion during follow-up. Event-free survival (EFS) was defined as survival in the absence of MI or TLR at follow-up.

Statistical analysis: Data are expressed as mean $\pm$ SD. A commercially available software (SPSS) was used to evaluate differences between continuous (Student's *t*-test) and categorical (chi-square or Fisher's exact test where appropriate) variables. A *P* value below 0.05 was considered significant. Univariate Spearman correlation analysis was performed to evaluate the association of angiographic restenosis rate with clinical, lesional, and procedural factors that may potentially affect the occurrence of restenosis. Categorical variables found to be associated with restenosis with borderline statistical significance (diabetes mellitus and complex lesion morphology) were used to classify patients into 4 subgroups and the restenosis rates in these 4 groups were compared thereafter.

RESULTS

The baseline clinical characteristics of the study population are given in Table I. The mean age was 57.1 ± 10.1 years. Eighty percent were males. Diabetes mellitus (DM) was present in 16 (31%). Stable angina was the presenting symptom in 45% of cases. There were 14 (27%) cases with unstable angina, 1 (2%) with acute MI (primary PTCA), and 13 patients (26%) were in the early (first week) post MI period. A history of prior revascularization was present in 9 (5 PTCA, 4 coronary by-pass) and a history of prior MI was present in 20 (39%) cases. The left ventricular ejection fraction was $58.7 \pm 10.6\%$. Single vessel coronary artery disease was present in 19 (37%) and multivessel disease in 32 (63%) cases. Additional dilatation on a larger coronary artery at the same session was performed in 17 (33%) cases.

A total of 57 lesions were treated in these 51 patients. Fifty-five (96%) were de novo lesions. There were 11 total occlusions (19%). Twelve (21%) were located on the infarct related artery. The vessel involved was the left anterior descending (LAD) artery in 8 (14%), circumflex artery in 20 (35%), right coro-

nary artery (RCA) in 19 (33%), diagonal artery in 9 (16%), and saphenous vein graft in 1 (2%) lesion. Of the 57 lesions treated, 29 (51%) were complex (type B2 and C). Thirty-five (61%) of the lesions were located in the proximal segment of the involved artery. The lesion characteristics are shown in Table II.

Table I. Baseline Characteristics of the Study Population

Characteristic	Number
Age	57.1±10.1 years (range:25-77)
Ejection fraction	58.7±10.6 % (range:34-74)
Male : Female	41:10 (80%:20%)
Clinical presentation	
Stable angina	23 (45%)
Unstable angina	14 (27%)
Post MI	13 (26%)
Acute MI	1 (2%)
Coronary risk factors	
Diabetes mellitus	16 (31%)
Hypertension	24 (47%)
Smoking	30 (59%)
Hyperlipidemia	33 (65%)
Family history	20 (39%)
History of prior MI	20 (39%)
History of prior revascularization	
PTCA	5 (10%)
By-pass	4 (8%)
Extent of coronary artery disease	
Single vessel	19 (37%)
Two-vessel	17 (33%)
Three-vessel	15 (30%)
Additional dilatation	
None	34 (67%)
One-vessel	15 (29%)
Two-vessel	2 (4%)

Table II. Lesion Characteristics

Characteristic	Number
Number of lesions	57
Lesion type	
De novo	55 (96%)
Restenotic lesion	2 (4%)
Infarct related artery	12 (21%)
Total occlusion	11 (19%)
Vessel involved	
LAD	8 (14%)
Circumflex	20 (35%)
Right coronary artery	19 (33%)
Diagonal	9 (16%)
Saphenous vein graft	1 (2%)
Lesion morphology	
Type A	12 (21%)
Type B1	16 (28%)
Type B2	14 (25%)
Type C	15 (26%)
Lesion location	
Mid/distal	22 (39%)
Proximal	35 (61%)

LAD=left anterior descending coronary artery.

Table III summarizes the procedural characteristics. A total of 60 stents were used to stent 57 lesions. Two overlapping stents were used to treat 3 lesions. This led to a stent/lesion ratio of 1.05. Twenty-seven (45%) of the 60 stents were deployed directly, while the remaining 33 (55%) were deployed after balloon predilatation. Thirty-two (53%) stents were placed with elective indications, 24 (40%) due to a suboptimal PTCA result, and 4 (7%) in bailout situations (2 acute and 2 threatened vessel closures). The stent type used was Jostent in 18 (30%), ACS MultiLink in 39 (65%), and BiodivYsio SV in 3 (5%). Twenty-seven (45%) of the stents were 2.5 mm, while the remaining 33 (55%) were 2.75 mm in diameter. The implanted stent length ranged between 8 to 19 mm and had a mean value of 12.6 ± 4 mm. The stents were deployed at a mean deployment pressure of 13.6 ± 1.7 atm (range, 10-16).

Both the pre-and postprocedural QCA findings are shown in Table IV. The mean lesion length was 9.4 ± 3.6 mm (range, 4.2-15.8) and the mean RVD was 2.54 ± 0.16 mm (range, 2.16-2.76) before stenting. Angiographic success was achieved in all lesions and stenting resulted in a decrease in DS from $75.8 \pm 13.6\%$ to $4.2 \pm 1.9\%$ ($P < 0.0001$) and an increase in MLD from 0.62 ± 0.35 mm to 2.64 ± 0.18 mm ($P < 0.0001$), resulting in an acute gain of 2.04 ± 0.35 mm. These results were achieved at a final balloon diameter of 2.73 ± 0.1 mm and a resulting final balloon diameter to RVD ratio (FB/RVD) of 1.08 ± 0.03 . A residual non-flow limiting distal dissection was present in 2 lesions at the completion of the procedure.

Table III. Procedural Characteristics

Characteristic	Number
Number of stents	60
Stent/lesion	1.05
Type of procedure	
Direct stenting	27 (45%)
Stenting with predilatation	33 (55%)
Indication for stent placement	
Elective	32 (53%)
Suboptimal PTCA result	24 (40%)
Bailout	
Acute closure	2 (3.5%)
Threatened closure	2 (3.5%)
Type of stent	
Jostent	18 (30%)
ACS Multi Link	39 (65%)
BiodivYsio SV	3 (5%)
Stent size	
2.5 mm	27 (45%)
2.75 mm	33 (55%)
Mean stent deployment pressure	13.6 ± 1.7 atm (range:10-16)
Mean stent length	12.6 ± 4 mm (range:8-19)

Table IV. Procedural QCA Findings

Characteristic	Value
Lesion length	9.4±3.6 mm (range: 4.2-15.8)
RVD	
Prestent	2.54±0.16 mm (range: 2.16-2.76)
Poststent	2.76±0.16 mm
MLD	
Prestent	0.62±0.35 mm (*)
Poststent	2.64±0.18
DS	
Prestent	75.8±13.6% (*)
Poststent	4.2±1.9%
Acute gain	2.04±0.35
Final balloon diameter	2.73±0.1 mm
FB/RVD ratio	1.08±0.03
Residual dissection	2 (3%)

RVD = reference vessel diameter; MLD = minimum lumen diameter; DS = percent diameter stenosis; FB/RVD ratio = final balloon size to reference vessel diameter ratio (*) $P < 0.0001$ vs poststent.

Procedural success was achieved in 48 cases (94%). Acute stent thrombosis occurred in 3 patients. One was a diabetic female who underwent stenting of a Type C lesion in the RCA together with another 2.5 mm stent in her left circumflex artery. She developed chest pain and ST elevation in the inferior leads 2 hours after the initial procedure and was found to have a thrombosed stent in the RCA. The left circumflex was patent. Despite opening the thrombosed RCA by repeat PTCA and intraaortic balloon counterpulsation, she developed electromechanical dissociation and died. The second patient was a diabetic male with a long type C lesion in the mid LAD who received two overlapping 2.75 mm stents in the initial procedure. He developed chest pain and ST elevation in the anterior leads an hour after the initial procedure and was found to have acute stent thrombosis. He underwent repeat PTCA with balloon angioplasty and the vessel was opened with relief of chest pain and ECG findings, but he subsequently experienced a significant rise of CK-MB and was diagnosed as non-Q-wave MI. The last patient was a male with an osteal and moderately calcific type C lesion in a diagonal artery. He developed chest pain and ST elevation in lateral leads 2 hours after the initial procedure. The acutely thrombosed diagonal artery was successfully recanalized by balloon angioplasty, but like the second patient he developed non-Q-wave MI. Accordingly, death occurred in 1 (2%), urgent revascularization in 2 (4%), acute stent thrombosis in 3 (6%), and non-Q-wave MI in 2 (4%) cases (Table V). The rest of the hospital stay was uneventful in these 2 and all of the remaining patients.

Of the 50 eligible patients, clinical follow-up was available in 48 (96%). Two patients were lost to follow-up and could not be contacted. There were no deaths. One patient developed acute MI 5 months after the procedure. Seventeen patients underwent a second revascularization procedure during this period. Three of these were performed on nontarget lesions at a mean of 12 ± 7 months. A total of 15 target lesions in 14 patients were revascularized (12 repeat PTCA, 3 coronary bypass) during follow-up at a mean of 5.6 ± 2.9 months. Accordingly, the event-free survival of patients available for follow-up was 71% (34/48) at a mean of 11.6 ± 5.9 months (Table VI).

Angiographic follow-up was available for 44 lesions in 40 patients (83%) at a mean of 7.7 ± 5.5 months. The 8 patients who refused a control angiogram were all asymptomatic and had no evidence of ischemia on stress testing. The control angiogram revealed a mean DS of $48.8 \pm 31.3\%$ and restenosis in 22 of the 44 lesions, which yielded a binary restenosis rate of 50%. Of the restenotic lesions, 5 (23%) were totally occluded, 2 (9%) were focal, and 15 (68%) were diffuse type in-stent stenoses (Table VII).

Table V. Early Outcome

Event	Number
Angiographic success	51/51 (100%)
Procedural success	48/51 (94%)
In-hospital MACE	
Death	1 (2%)
MI	
Q-wave	0
Non-Q-wave	2 (4%)
Urgent revascularization	
PTCA	2 (4%)
Coronary by-pass	0
Acute stent thrombosis	3 (6%)
Any event	3 (6%)

Table VI. Clinical Follow-up

Finding	Number
Eligible for follow-up	50
Follow-up data available	48 (96%)
Duration of follow-up	11.6 ± 5.9 months (range: 6-24)
Events	
Death	0
MI	1 (2%)
Non TLR	3 (6%)
PTCA	1 (2%)
Coronary by-pass	2 (4%)
TLR	14 (29%)
RePTCA	11 (23%)
Coronary by-pass	3 (6%)
Event-free survival	34 (71%)

TLR = target lesion revascularization.

Table VII. Angiographic Follow-up

Finding	Number
Eligible	48
Available	40 (83%)
Duration of follow-up	7.7±5.5 months (range: 2-24)
RVD	2.54±0.19 mm
MLD	1.33±0.85 mm
DS	48.8±31.3%
Late loss	1.3±0.8 mm
Restenosis (per lesion)	22/44 (50%)
Type of restenosis	
Focal	2 (9%)
Diffuse	15 (68%)
Total occlusion	5 (3%)

Table VIII. Comparison of Lesions With and Without Restenosis

Characteristic	No Restenosis (n = 22)	Restenosis (+) (n = 22)	P
Age	55.6±7.6	57.8±11.3	NS
Sex (M/F)	19/3	16/6	NS
Hypertension	12	13	NS
Diabetes mellitus	4	10	NS
Smoking	14	11	NS
Family history	7	8	NS
Hyperlipidemia	14	14	NS
Multivessel disease	16	13	NS
Infarction related artery	6	3	NS
Lesion in proximal segment	11	16	NS
Restenotic lesion	0	2	NS
Total occlusion	4	5	NS
Complex lesion	9	15	NS
Multiple stents	0	2	NS
Direct stenting	12	11	NS
Elective stenting	13	14	NS
2.5 mm stent	10	11	NS
2.75 mm stent	12	13	NS
Residual dissection	1	1	NS
Stent length (mm)	12.4±3.9	12.9±4.2	NS
Deployment pressure (atm)	13.4±1.9	13.9±1.4	NS
RVD _{pre} (mm)	2.51±0.17	2.56±0.14	NS
RVD _{post} (mm)	2.73±0.11	2.74±0.1	NS
MLD _{pre} (mm)	0.56±0.32	0.64±0.38	NS
MLD _{post} (mm)	2.6±0.18	2.67±0.16	NS
DS _{pre} (%)	77.4±12.8	75.3±14.6	NS
DS _{post} (%)	4.9±1.9	3.8±2	NS
Acute gain	2.04±0.4	2.03±0.4	NS
Late loss	0.52±0.2	2.01±0.4	<0.0001
Final balloon diameter	2.73±0.11	2.74±0.1	NS
FB/RVD ratio	1.1±0.05	1.06±0.02	0.041

RVD = reference vessel diameter; MLD = minimum lumen diameter; DS = per cent diameter stenosis; pre = prestenting; post = poststenting; FB/RVD ratio = final balloon to reference vessel diameter ratio.

Table IX. Restenosis Rates in Lesion Subgroups

Subgroup	Restenosis rate
DM+complex lesion (*)	75% (*)
DM+non-complex lesion	67%
Non DM+complex lesion	56%
Non DM+non-complex lesion	21%

DM = diabetes mellitus; (*) $P < 0.05$ vs Non DM + non-complex lesion.

Table VIII summarizes the comparison of various clinical and procedural characteristics of lesions with and without restenosis on the control angiogram. Late loss was obviously greater in the group with restenosis. The final balloon to reference vessel diameter ratio was the only parameter that significantly differed between the two groups and it was higher in the group without restenosis (1.1 ± 0.05 vs 1.06 ± 0.02 , $P = 0.041$). The categorical variables that may potentially affect the occurrence of restenosis were subjected to a Spearman univariate correlation analysis. Diabetes mellitus ($P = 0.054$) and complex lesion morphology ($P = 0.072$) were found to be correlated with the occurrence of restenosis with borderline significance. They were used to subgroup the population into four as shown in Table IX. Accordingly, restenosis rates differed significantly between diabetics with complex lesion morphology and nondiabetics with noncomplex lesion morphology (75% vs 21%, $P < 0.05$).

DISCUSSION

With the available technology, it is technically possible to stent lesions in vessels < 3.0 mm in diameter with a more than 95% success rate.¹¹⁻²¹⁾ However, the incidence of acute or subacute stent thrombosis in this lesion subset still creates a point of controversy even with the current antithrombotic regimens. Although most authors report a stent thrombosis rate below 5% in small vessel stenting,¹¹⁻²⁴⁾ the Coronary Stenting without Coumadin French Registry, which is a prospective registry of 2900 patients being stented for suboptimal PTCA results or bailout conditions with the antithrombotic regimen of aspirin-ticlopidine, reports a $> 10\%$ subacute thrombosis rate for stents implanted with a balloon < 3.0 mm and a rate below 1% with a balloon ≥ 3.5 mm.²⁵⁾ Similarly, earlier studies demonstrate a higher stent thrombosis rate with small stents²⁶⁻³¹⁾ and also with bailout stenting,²⁶⁻²⁹⁾ but most of these data belong to the warfarin era. On the other hand, recent large series reveal no effect of vessel size on stent thrombosis rates,^{18,32)} except a very recent report by Hsieh, *et al*²¹⁾ which demonstrated a sig-

nificantly higher subacute thrombosis rate in <2.5 mm vessels compared to larger ones (0.9% vs 0%, $P < 0.05$). The 6% rate of acute thrombotic occlusion in our series may be explained by the absence of ticlopidine pretreatment resulting in inadequate antithrombotic activity during and early after the procedure, at which time all the thrombotic events were seen. All 3 lesions that ended up with thrombosis were Type C and 2 of the 3 patients were diabetic. But the association of diabetes mellitus with an increased risk of stent thrombosis in small vessel stenting has not been shown and very favorable subacute occlusion rates have been reported for small vessel stenting in complex lesions.^{14,24} Another factor that may contribute to this high stent thrombosis rate in our series may be related to the stent implantation technique. Although we used a mean deployment pressure of about 13 atmospheres, we ended up having a mean FB/RVD ratio of 1.08. Moreover, we did not use IVUS to optimize our stenting procedures, so stent underexpansion may be a likely explanation for our high stent thrombosis rate. Akiyama, *et al*¹⁸) with a mean FB/RVD ratio of 1.29, achieved a 1.5% subacute thrombosis rate, which was considerably better than the 3.6% rate reported in a retrospective analysis of the STRESS trial¹⁹) where a less aggressive dilatation strategy was used. Studies have shown stent underexpansion^{33,34}) and residual dissection after stenting^{28,35}) to be closely related with the occurrence of subacute stent thrombosis. None of the 2 residual dissections in our series led to stent thrombosis and none of the patients who experienced stent thrombosis had residual dissections. Considering that stent overexpansion, in an attempt to improve the stent deployment technique, may create distal dissections especially in small tapering coronary arteries, one has to be careful to balance these two factors to optimize the early outcome.

Although restenosis rates range between 26%²¹) to 66%²⁹) in small vessel stenting, most series report a rate of 30-40%.^{11,12,14-16,18-20,23,24,32}) The highest rate of restenosis comes from an earlier report of small vessel stenting with coil stents for acute or threatened closure in the warfarin era.²⁹) The lowest number comes from a very recent report by Hsieh *et al*²¹) where the restenosis rate was found to be 26% for lesions in <2.5 mm arteries, 22% for lesions in 2.5-3.0 mm arteries, and 14% for those in >3.0 mm arteries ($P < 0.05$). A similar finding is provided by Elezi, *et al*³²) such that with decreasing vessel size from >3.2 mm to <2.8 mm in diameter, the rate of restenosis increases progressively from 20.4% to 38.6%. Lau, *et al*¹⁶) have reported a lower restenosis rate for stented vessels with a RVD >2.6 mm than those with a RVD ≤ 2.6 mm (22.7% vs 40.9%, $P < 0.05$). In general, a small RVD has been shown to be an independent predictor of in-stent restenosis.^{21,36-38}) In-stent restenosis is almost entirely due to intimal proliferation^{39,40}) and the amount of intimal hyperplasia and thus late loss is relatively constant and

independent of stent size,⁴¹⁾ and this has been held responsible for the increased rate of restenosis in stented small vessels by Elezi, *et al*³²⁾ who, in a large series of 2602 stented patients, found small vessel size, DM, previous PTCA, complex lesion morphology, multiple stents, DS before intervention, and a lower balloon-to-vessel ratio to be independent predictors of in-stent restenosis. In an analysis by Akiyama, *et al*¹⁸⁾ baseline RVD, lesion length, and final intrastent cross-sectional area irrespective of vessel size were demonstrated to be independent predictors of in-stent restenosis. Moreover, in series of small vessel stenting, independent predictors of in-stent restenosis were shown to be DM, RVD, and final stent size by Lau, *et al*¹⁶⁾ and lesion type and lesion length by Hsieh, *et al*.²¹⁾

We detected a fairly high rate of 50% restenosis in our series of small vessel stenting. The only significant difference between lesions associated with in-stent restenosis and those without was a lower FB/RVD in the restenosed group. This has been shown by Elezi, *et al*³²⁾ to be an independent predictor of in-stent restenosis. The mean FB/RVD ratio, which is 1.08 in our study, is smaller than the FB/RVD ratios of 1.12 and 1.29 reported by Elezi³²⁾ and Akiyama,¹⁸⁾ respectively, who found considerably lower rates of in-stent restenosis (38.6% and 35.7%, respectively) compared to ours. Considering that late loss is independent of stent size,⁴¹⁾ one would expect to have a lower rate of subsequent in-stent restenosis in small vessels by an initial greater acute gain with a greater FB/RVD ratio. Further support to this idea is provided by Akiyama, *et al*¹⁸⁾ who demonstrated that a small final stent cross-sectional area regardless of vessel size is an independent predictor of a high rate of in-stent restenosis. On the other hand, it has been clearly shown that the amount of neointimal proliferation is closely related to the extent of vessel wall injury after stent placement,^{42,43)} therefore, a high FB/RVD ratio or stent overexpansion may lead, in addition to distal residual dissections that increase the risk of stent thrombosis, to a higher restenosis rate due to an exaggerated amount of intimal hyperplasia. Although stent underexpansion, as expressed by a low FB/RVD ratio, seems to be a likely explanation for the increased rate of in-stent restenosis in small vessel stenting, there is considerable controversy against advising a strategy of using oversized balloons and thus stent overexpansion to overcome the problem of subsequent in-stent restenosis in this lesion subset. Therefore, we believe, stenting techniques in small coronary arteries need to be established more precisely with further work.

None of the clinical and lesional factors were found to be significantly associated with angiographic restenosis by univariate analysis in our study. Diabetes mellitus and complex lesion morphology, two factors previously shown to be independent predictors of in-stent restenosis in small vessels,^{16,21)} were associated with in-stent restenosis with borderline statistical significance only. When we subgrouped our population into 4 by using these two factors, we found a signifi-

cantly greater rate of in-stent restenosis in diabetics with complex lesions when compared to nondiabetics with simple lesions; a similar finding was reported by Elezi, *et al.*³²⁾ Therefore, we could detect a subgroup of patients in whom small vessel stenting resulted in an acceptable 21% rate of in-stent restenosis.

Despite a restenosis rate higher than that reported in the literature, the 1-year event-free survival rate (71%) in our series was not different from other series.^{16,18-21,32)} This can be explained by the low rate of TLR (29%) in our series, which was due to the fact that asymptomatic patients were reluctant to undergo a second interventional procedure although the control angiogram revealed in-stent restenosis.

Study limitations: Being a retrospective and uncontrolled analysis, the current data does not provide an insight into the optimum therapeutic approach to patients with small vessel disease. Similarly, the study is not powered enough to highlight the factors underlying both stent thrombosis and in-stent restenosis in small vessels although there are clues as to the association of in-stent restenosis with DM, complex lesion morphology, and a low FB/RVD ratio.

Conclusion: In conclusion, stenting in vessels <2.8 mm was found to be associated with a fairly high rate of acute stent thrombosis and in-stent restenosis. Further analysis detected a subgroup of patients without diabetes or complex lesions who could be safely stented with an acceptable in-stent restenosis rate.

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