

# Ultrasound-assisted stent implantation in small size coronary arteries: a pilot study

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**Key words:**  
Coronary artery disease; Intravascular ultrasound; Restenosis; Stent.

**Background.** Many studies have indicated that a small lumen size is one of the most important predictors of acute events and of late restenosis after balloon angioplasty or stent implantation. In the last few years many studies have shown that intravascular ultrasound (IVUS) guidance makes it possible to optimize stent implantation. The aim of this pilot study was to evaluate the feasibility and safety of IVUS imaging of small vessels. Secondary endpoints were the immediate and long-term results of IVUS-guided elective BeStent implantation in small vessels.

**Methods.** Fourteen symptomatic patients with small coronary vessel (mean angiographic reference diameter  $2.3 \pm 0.2$  mm) disease underwent IVUS-guided BeStent implantation. IVUS success was defined as the achievement of a final minimal intrastent cross-sectional area (CSA)  $> 90\%$  of the smaller reference lumen CSA.

**Results.** IVUS evaluation was feasible in all patients without any clinical or angiographic adverse events. Procedural success was achieved in all patients with implantation of a BeStent 15 mm. No major complication (death, myocardial infarction, stent acute or subacute thrombosis, coronary artery bypass, re-coronary angioplasty) occurred during the in-hospital phase. Two non-flow-limiting, asymptomatic coronary dissections were detected after stent expansion. The post-stenting lesion stenosis rate decreased from  $72.9 \pm 12.9\%$  to  $0.75 \pm 11.7\%$  with an acute gain of  $1.8 \pm 0.4$  mm. The final IVUS minimal stent CSA was  $5.6 \pm 1.1$  mm<sup>2</sup>. The IVUS criteria of adequate stent expansion were reached in 11 (78.6%) patients. At 6 months of follow-up, the rate of angiographically diagnosed in-stent restenosis was 30.7%; the 6-month late loss in stent diameter was  $1.1 \pm 0.6$  mm. No patient died or presented with a myocardial infarction. The target lesion revascularization rate was 30.7%.

**Conclusions.** Coronary IVUS-guided stenting can be performed in small vessels with a high success rate and low incidence of in-hospital complications. However, despite these encouraging short-term results, the long-term clinical and angiographic outcome is less favorable. Further larger and randomized IVUS studies, probably employing more aggressive IVUS criteria, are needed to clarify the true role of IVUS guidance in this particular field.

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## Introduction

Many studies have indicated that a small lumen size is one of the most important predictors of acute events and of late restenosis after balloon angioplasty, and that the restenosis rate after small vessel coronary angioplasty (PTCA) varies between 41 and 55%<sup>1-5</sup>. Another important disadvantage regarding small vessel angioplasty is the higher association of small vessels with other well-known co-morbid states at increased risk for percutaneous procedures and the presence of extensive lesions or diabetes<sup>6</sup>.

As documented in the randomized studies BENESTENT and STRESS, stent im-

plantation in coronary arteries with a reference diameter  $< 3$  mm is also associated with a higher rate of acute complications and of late restenosis<sup>3</sup>.

More recently, the use of intravascular ultrasound (IVUS) has become more widespread. This technique is now an important tool for the guidance of coronary interventions. In fact, several reports have shown that the most important predictor of long-term success after coronary interventions is the final cross-sectional area (CSA) not only after balloon angioplasty but also and especially after coronary stenting<sup>7</sup>. In case of small vessel angioplasty, IVUS appears to be a very attractive tool. It can provide information on

whether the vessel is a true small vessel or a pseudo-small vessel, on the characteristics of the plaque, and finally it makes it possible to optimize the procedure in order to obtain the largest possible final lesion or stent CSA.

The purpose of this pilot study was to assess the feasibility and safety of IVUS assessment of small vessels. Secondary endpoints were the immediate and long-term results of IVUS-guided elective BeStent implantation in small vessels.

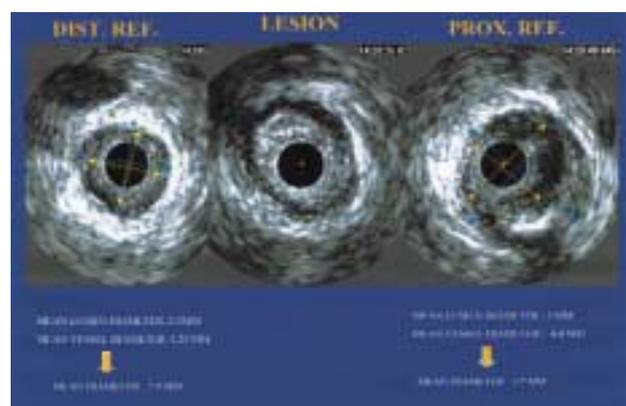
## Methods

**Patient population.** The study population comprised 14 consecutive patients from the Institute of Cardiology of the University of Bologna enrolled between March 1999 and March 2000. All patients had a significant angiographically diagnosed stenosis (> 50% diameter stenosis at quantitative coronary angiography-QCA) of a coronary vessel with a reference diameter between 2.0-2.75 mm associated with clinical or objective evidence of myocardial ischemia. The angiographic vessel diameter was the only inclusion criteria. The exclusion criteria were: 1) a recent myocardial infarction (< 15 days), 2) left main stem stenosis < 50%, 3) saphenous vein graft stenosis, 4) a history including treatment of chronic total occlusion, 5) a coronary lesion > 20 mm in length, 6) treatment of coronary restenosis, 7) a history including treatment of one vessel with multiple lesions, 8) a history including treatment of a lesion located in the distal part of the coronary vessel, 9) contraindications to antiplatelet therapy (aspirin or ticlopidine).

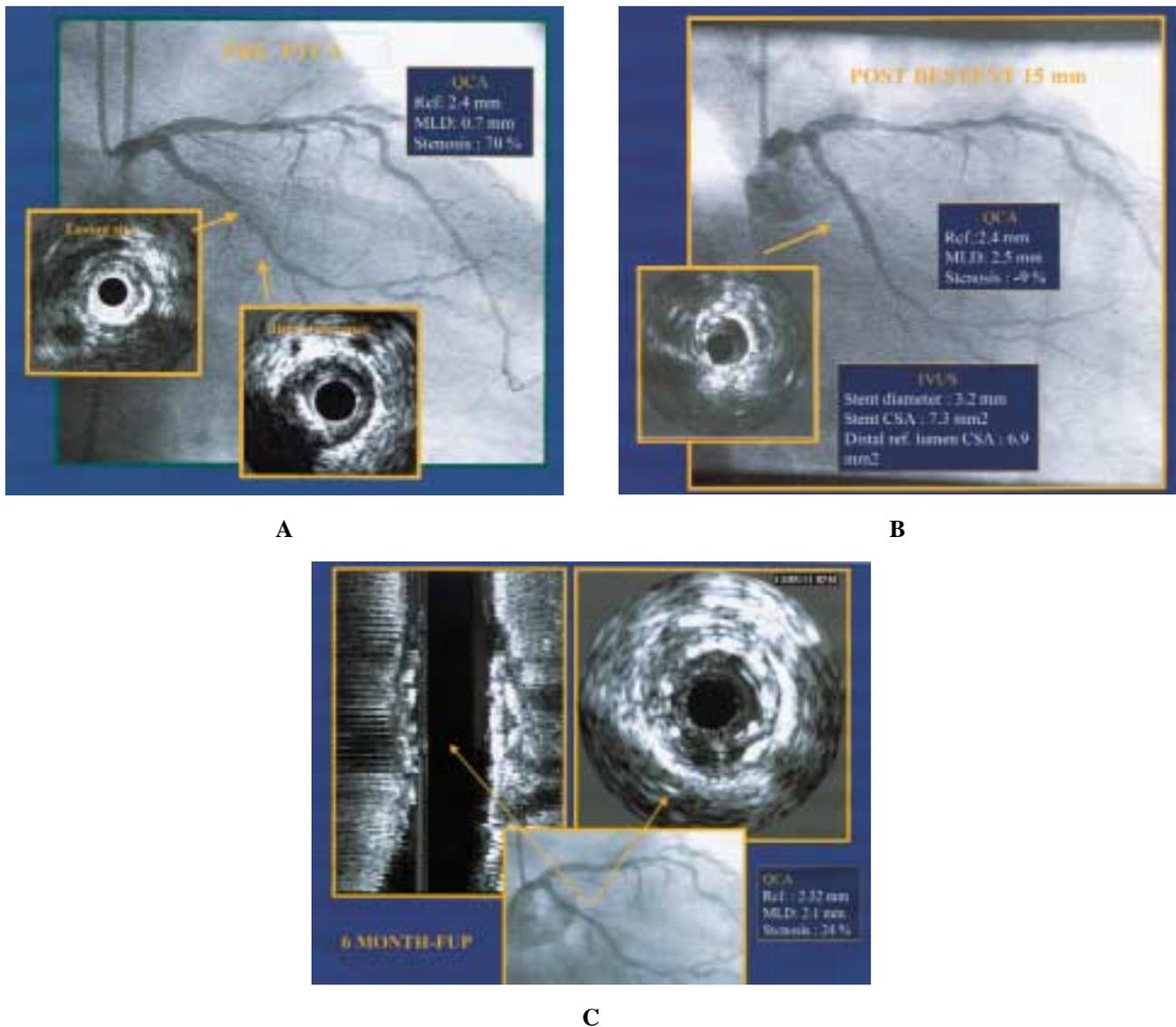
**Study design.** IVUS examination was performed before balloon predilatation with a commercially available electronic 3.5F ultrasound catheter (Vision F/X, Endosonic Corp., Rancho Cordova, CA, USA). Images were obtained using a mechanical pullback system at a constant speed of 0.5 mm/s. The position of the catheter at fluoroscopy was used to correlate the ultrasound image with the angiogram. The ultrasound runs (tomograms and longitudinal reconstruction) were stored on a super VHS videotape and on CD-ROM. Immediate quantitative analysis was performed after each pullback. Reference IVUS measurements were taken at the proximal and distal sites adjacent to the lesion that correlated with the apparently normal reference segments at angiography. The vessel size was measured at the medial-adventitial interface (external elastic membrane). The following measurements were taken during diastole at the lesion and reference sites: lumen diameters (minimal, maximal and mean; mm); vessel diameters (minimal, maximal and mean; mm); lumen CSA (mm<sup>2</sup>); vessel CSA (mm<sup>2</sup>); plaque CSA (mm<sup>2</sup>); mean diameter, determined at the proximal and distal reference sites using the following equation reported in the CLOUT study<sup>8</sup>: mean diameter = mean vessel diameter + mean lumen diameter/2. The mean diameter of the smaller reference sites was used to determine the site of an upsized balloon (Figs. 1 and 2).

Balloon predilatation was then performed under angiographic guidance. In general, balloons were sized approximately to the mean of the proximal and distal reference segments. Semicompliant balloons were mostly used. Following balloon predilatation, elective intracoronary stenting was performed using the BeStent (Medtronic, Minneapolis, MN, USA) hand-crimped on a semicompliant balloon. The size and type of the balloon were selected on the basis of an inflated balloon size equal to the IVUS-determined mean diameter. Quarter-sized balloons were routinely used for accurate sizing. If, according to the formula, the value was irregular, the closest-sized balloon was chosen. The adequacy of the final result was based on the angiographic visual assessment of the stent site and on IVUS evaluation. Before any IVUS evaluation, intracoronary isosorbide dinitrate (1 mg) was administered. IVUS success was defined as the achievement of a final minimal intrastent CSA > 90% of the distal (or smaller) reference lumen CSA. Additional balloon inflations were performed until the IVUS imaging criteria for stent expansion were reached. Patients received aspirin (100-300 mg) and continued their standard antianginal therapy before and after the procedure. A bolus of 70-100 IU/kg of heparin was administered after the insertion of the femoral sheath. After stent implantation all patients were treated only with antiplatelet therapy: ticlopidine (500 mg/day) for 1 month and aspirin (100-300 mg/day) indefinitely. Patients underwent clinical and angiographic evaluation at 6 months of follow-up.

**Quantitative coronary analysis.** Intracoronary isosorbide dinitrate (1 mg) was administered to all patients before the initial, post-procedure and follow-up angiograms



**Figure 1.** Methodology for intravascular ultrasound (IVUS)-guided stent overexpansion. Before standard angiographically guided angioplasty, vessel and lumen IVUS parameters are measured at the proximal and distal reference sites and at the lesion site. IVUS of the distal reference site revealed a mean lumen diameter of 2.5 mm and a mean vessel diameter of 3.25 mm. IVUS of the proximal reference site revealed a mean lumen diameter of 3.0 mm and a mean vessel diameter of 4.4 mm. The distal reference segment is thus the limiting site and according to the equation its mean diameter is 2.9 mm. Stent implantation would thus be performed with a BeStent hand-crimped on an upsized 2.9 mm balloon, regardless of the initial angiographically determined reference diameter.



**Figure 2.** A: pre-angioplasty (PTCA) angiographic and intravascular ultrasound (IVUS) images. In a vessel with an angiographically determined reference diameter of 2.4 mm, IVUS revealed, at the distal reference site, a mean lumen diameter of 3.0 mm and a mean vessel diameter of 4.0 mm. Thus, according to the equation the mean diameter was 3.5 mm. B: post-stent implantation angiographic and IVUS images. IVUS guidance allowed the safe use of stent implantation with an oversized balloon. C: angiographic and IVUS images obtained 6 months after the procedure. At follow-up, there was no angiographic evidence of restenosis. IVUS study (tomograms and longitudinal reconstruction) shows mild intrastent proliferation. CSA = cross-sectional area; MLD = minimal lumen diameter; QCA = quantitative coronary angiography.

to achieve maximal vasodilation. QCA was performed before PTCA, after the IVUS-guided upsized stent implantation and at the 6-month control angiography using the Philips analysis package. A 15-20 mm segment surrounding the stenosis was analyzed, using the guiding catheter for calibration. The reference segment was defined as the region adjacent to the stenosis which was used for the IVUS reference calculation at the time of the procedure. The mean reference diameter, the length of the stenosis, the lesion minimal lumen diameter, the acute gain, late loss and loss index were measured. The lesions were graded according to the modified American Heart Association/American College of Cardiology classification<sup>9</sup>. After IVUS-guided stent implantation the presence of intimal dissection was graded according to the

National Heart, Lung and Blood Institute classification<sup>10</sup>. The coronary flow in the study vessel was graded according to the TIMI classification<sup>11</sup>.

**Definitions.** The study endpoints were:

- the feasibility and safety of IVUS utilization in the setting of small vessels;
- in-hospital clinical events and the presence, at 6 months of follow-up, of angiographically diagnosed in-stent restenosis, defined as the presence of a QCA diameter stenosis  $\geq 50\%$  at the treated site.

The success of stent implantation was defined as  $< 30\%$  residual stenosis at QCA with no major procedural or in-hospital complications (death, emergency bypass surgery, myocardial infarction).

A diagnosis of a Q-wave myocardial infarction was made when there was documentation of new pathological Q waves ( $> 0.04$  s) at ECG in conjunction with an elevation in creatinine kinase serum levels to more than twice the upper limit of normal.

A diagnosis of a non-Q-wave myocardial infarction was made when an elevation in the serum levels of cardiac enzymes to more than twice the upper limit of normal was documented without the development of new pathological Q waves ( $> 0.04$  s). Emergency coronary artery bypass graft was defined as any coronary artery bypass graft performed before the patient was discharged.

Acute thrombosis events were angiographically documented stent thrombosis occurring within 24 hours of the procedure. Subacute thrombosis events were angiographically documented coronary occlusions at the site of the stent occurring between 24 hours and 2 months after stent implantation or sudden death occurring within 2 months of the procedure.

**Statistical analysis.** Categorical variables are presented as absolute numbers and percentages. Continuous variables are presented as mean  $\pm$  SD. Comparisons between categorical variables were performed by  $\chi^2$  analysis. Probability values  $< 0.05$  were considered statistically significant.

## Results

**Procedural and clinical in-hospital results.** The clinical and angiographic characteristics of the patients are shown in table I. In 9 patients, multivessel coronary artery disease was present. In 5 of them, multivessel stent implantation was performed in association with adjunctive treatment of a non-small vessel. The QCA mean reference vessel diameter was  $2.3 \pm 0.2$  mm (Table II). The mean percentage lesion stenosis was  $72.9 \pm 12.9\%$ . IVUS evaluation was feasible in all patients without any clinical or angiographic adverse events. In particular, during IVUS evaluation, no patient presented acute vessel occlusion, embolism, dissection or spasm. The IVUS mean vessel diameter at the lesion site was  $3.6 \pm 0.4$  mm ( $3.2 \pm 0.4$  mm at the distal reference site and  $3.8 \pm 0.6$  mm at the proximal reference site) (Table III). In most of these patients IVUS imaging showed fibrocalcific (71%) or fibrotic (21%) lesions. Pre-stent PTCA was performed using a balloon to artery ratio equal to 1.1 while stent deployment was done with a significantly higher balloon expansion (a balloon to artery ratio equal to 1.3) (Table IV). Procedural success was achieved in all 14 treated patients with implantation of a BeStent 15 mm. A TIMI III flow was obtained in all treated vessels. In 2 patients an asymptomatic dissection (1 type A and 1 type B) was detected after stent implantation. As seen in table II, following stent implantation the lesion minimal lumen diameter increased from  $0.7 \pm 0.2$  to  $2.45 \pm 0.3$  mm (acute gain  $1.8 \pm 0.4$  mm) and the lesion percentage stenosis decreased from  $72.9 \pm 12.9$  to  $0.75 \pm$

**Table I.** Clinical and angiographic features of the patients.

No. patients	14
Age (years)	$66 \pm 7$
Female gender	5 (36%)
Diabetes	2 (14%)
LVEF (%)	$74 \pm 8.3$
Prior myocardial infarction	3 (21%)
Prior coronary artery bypass	0
Vessel disease	
1	5 (36%)
2	8 (57%)
3	1 (7%)
Angina (CCS)	
1-2	8 (57%)
3-4	6 (43%)
Treated vessel	
Left anterior descending	7 (50%)
Circumflex	5 (36%)
Right coronary artery	2 (14%)
Lesion site	
Proximal	2 (14%)
Middle	12 (86%)
Lesion type	
A	1 (7%)
B1	8 (57%)
B2	5 (36%)
C	0

CCS = Canadian Cardiovascular Society; LVEF = left ventricular ejection fraction.

**Table II.** Basal and post-stent implantation quantitative coronary angiography data.

	Basal	Post-stent	p
Reference diameter (mm)	$2.3 \pm 0.2$	$2.46 \pm 0.2$	NS
MLD (mm)	$0.7 \pm 0.2$	$2.45 \pm 0.3$	$< 0.0001$
% stenosis	$72.9 \pm 12.9$	$0.75 \pm 11.7$	$< 0.0001$
Lesion length (mm)	$8.7 \pm 1.9$		
Acute gain (mm)		$1.8 \pm 0.4$	

MLD = minimal lumen diameter.

**Table III.** Basal and post-stent implantation intravascular ultrasound data.

	Proximal reference	Lesion	Distal reference
Basal			
Vessel diameter (mm)	$3.8 \pm 0.6$	$3.6 \pm 0.4$	$3.2 \pm 0.4$
Lumen diameter (mm)	$2.8 \pm 0.3$	$1.6 \pm 0.3$	$2.5 \pm 0.3$
Vessel CSA (mm <sup>2</sup> )	$10.6 \pm 3.9$	$10.3 \pm 2.9$	$8.8 \pm 2.4$
Lumen CSA (mm <sup>2</sup> )	$6.9 \pm 1.6$	$2.3 \pm 0.8$	$5.2 \pm 1.1$
Plaque CSA (mm <sup>2</sup> )	$3.7 \pm 2.5$	$8.0 \pm 2.5$	$3.6 \pm 1.8$
% plaque area	$34.6 \pm 17.4$	$77.6 \pm 5.7$	$40.9 \pm 12.3$
Post-stent			
Vessel diameter (mm)	$4.0 \pm 0.5$		$3.4 \pm 0.6$
Lumen diameter (mm)	$2.9 \pm 0.3$	$2.7 \pm 0.3$	$2.5 \pm 0.3$
Vessel CSA (mm <sup>2</sup> )	$10.3 \pm 3.2$		$9.5 \pm 3.4$
Lumen CSA (mm <sup>2</sup> )	$7.1 \pm 1.4$	$5.6 \pm 1.1$	$5.4 \pm 0.8$

CSA = cross-sectional area.

**Table IV.** Procedural data.

PTCA balloon maximal diameter (mm)	2.57 ± 0.1
PTCA maximal pressure (atm)	7.4 ± 1.26
PTCA balloon/vessel ratio	1.1
Stent balloon maximal diameter (mm)	2.9 ± 0.2
Stent inflation pressure (atm)	13.8 ± 2.8
Stent balloon/vessel ratio	1.3
Implanted stents	
BeStent small 8 mm	8
BeStent small 15 mm	6
BeStent large 15 mm	1
Post-stent dissections	
A-B	2
C-D	0
Final TIMI flow	
0-1	0
2	0
3	14

TIMI = Thrombolysis in Myocardial Infarction; PTCA = percutaneous transluminal coronary angioplasty.

11.7%. The final IVUS stent CSA and the IVUS stent mean diameter were respectively  $5.6 \pm 1.1 \text{ mm}^2$  and  $2.7 \pm 0.3 \text{ mm}$  (Table III). The IVUS criteria of adequate stent implantation were reached in 11 patients (78.6%). In 3 patients the procedure was stopped due to angiographic evidence of overexpansion of the stent, in spite of the fact that the IVUS criterion had not yet been reached. No major complication was induced by excess stent dilation. The 2 patients who developed non-flow-limiting coronary dissection were asymptomatic and did not require additional stenting. One patient developed purpura on the lower extremities and reversible renal dysfunction due to cholesterol embolization. No episode of stent thrombosis occurred (Table V).

**Clinical and angiographic results at 6 months of follow-up.** No patient was lost to follow-up 6 months after the procedure. Except for the patient who presented with cholesterol embolism after the procedure and who was asymptomatic at 6 months of follow-up, all patients were submitted to angiographic evaluation. Three patients underwent IVUS imaging. No patient died or developed myocardial infarction during follow-up (Table VI). Four (30.7%) patients presented with intrastent diffuse restenosis and were submitted to target vessel revascularization (1 surgical and 3 PTCA). As shown in table VII, at 6 months of follow-up, the stent site minimal lumen diameter decreased from  $2.45 \pm 0.3$  to  $1.4 \pm 0.5 \text{ mm}$  (late loss  $1.1 \pm 0.6 \text{ mm}$ ) with a loss index of  $59.6 \pm 30.8\%$ .

**Discussion**

**Stent implantation in small vessels.** Coronary stent implantation is an established treatment for patients with symptomatic coronary artery disease and target vessels > 3 mm in diameter. Previous randomized studies<sup>3</sup> have shown that stent implantation in small vessels

**Table V.** In-hospital clinical events.

Procedural success	14 (100%)
IVUS-related complications	0
Death	0
Q-wave MI	0
Non-Q-wave MI	0
Urgent coronary artery bypass	0
Re-PTCA	0
Cholesterol embolization	1 (7%)

MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; IVUS = intravascular ultrasound.

**Table VI.** Six-month clinical follow-up (14 patients).

Death	0
MI	0
Surgical revascularization	1 (7%)
Re-PTCA	5 (36%)
Target vessel revascularization (PTCA or bypass)	4 (28%)
Non-target vessel revascularization	2 (14%)
Angina (CCS)	
1-2	3 (21.6%)
3-4	1 (7%)

Abbreviations as in table V.

**Table VII.** Post-stent and follow-up quantitative coronary angiography data (13 patients).

	Post-stent	6 months	p
No. patients	14	13	
Reference diameter (mm)	$2.46 \pm 0.16$	$2.3 \pm 0.2$	NS
MLD (mm)	$2.45 \pm 0.3$	$1.4 \pm 0.5$	< 0.0001
% stenosis	$0.75 \pm 11.7$	$41.6 \pm 18.6$	< 0.0001
Restenosis (≥ 50%)		4 (30.7%)	
Late loss (mm)		$1.1 \pm 0.6$	
Loss index (%)		$59.6 \pm 30.8$	

MLD = minimal lumen diameter.

is less effective than in vessels > 3 mm in diameter. In particular, a worse clinical outcome was reported for subsets of patients with a small vessel size associated with extensive lesions or diabetes<sup>6</sup>. However, in these “old” studies stents not designed for small vessels and at low inflation pressures were implanted and patients were submitted to anticoagulant therapy. More recently, Elezi et al.<sup>12</sup> demonstrated that in small vessel stent implantation the risk of restenosis decreases if a greater balloon to artery ratio is used during the intervention, implying that an aggressive approach may be very effective particularly in small vessels. Other recent cumulative data from the STRESS I and II studies<sup>13</sup> have shown that elective stent implantation in vessels with a reference diameter < 2.7 mm decreases the incidence of coronary restenosis (34% stent vs 55% PTCA,  $p < 0.001$ ) and improves the event-free survival (78% stent vs 67% PTCA,  $p < 0.001$ ). Several randomized trials designed

to compare PTCA with elective stenting in small vessels are currently underway (Besmart, SISA, ISAR, RAP, STRESS IV). Unfortunately, preliminary data seem contradictory. In fact, while the Besmart trial (BeStent vs PTCA in vessels < 3 mm in diameter and with focal lesions) has shown a significant reduction in the 6-month restenosis rate (22.7% BeStent vs 48.5% PTCA,  $p < 0.001$ ) and target lesion revascularization rate in the stent group (13% BeStent vs 25% PTCA,  $p < 0.01$ ), the SISA (BeStent in vessels < 3 mm in diameter and with lesions < 12 mm in length) and the ISAR (Multilink in vessels < 2.8 mm in diameter) studies did not support these findings.

**Intravascular ultrasound in small vessels.** Several studies have shown that the final lumen diameter is the most important angiographic predictor of the long-term success after interventional procedures<sup>1-5</sup>. More recently, the use of IVUS has shown that even the final lesion plaque burden after PTCA and the final lesion CSA after stenting are important predictors of the long-term success<sup>7,14</sup>. In small vessel percutaneous procedures IVUS appears to be very useful. First of all, IVUS can demonstrate whether the vessel is a true small vessel or a pseudo-small vessel (normal vessel with diffuse disease). This finding may have practical consequences. In fact, in case of a pseudo-small vessel an approach similar to large vessel angioplasty could be safely undertaken. IVUS can also provide information about the plaque characteristics and thus facilitate the choice of the correct device for that lesion. Finally, IVUS guidance allows optimization of the procedure and thus attainment of the largest final CSA for that lesion. In fact, as documented in the randomized CRUISE study<sup>15</sup>, IVUS guidance makes it possible to achieve a significantly larger stent CSA ( $7.8 \pm 1.7$  vs  $7.1 \pm 2.1$  mm<sup>2</sup>,  $p < 0.001$ ). Interestingly, in that study, the lumen gain achieved in the IVUS group was associated with a 44% lower target vessel revascularization rate (8.5 vs 15.3%,  $p < 0.019$ ). No differences in mortality (0 vs 0.9%) or myocardial infarction (7 vs 6.1%) were detected between the two groups.

In a retrospective non-randomized study, Akiyama et al.<sup>16</sup> showed that with regard to small or large vessels, stent implantation under IVUS guidance was associated with a lower rate of restenosis compared to that observed for those patients in whom IVUS was not used. In particular, IVUS guidance resulted in a 9% decrease in the restenosis rate in small vessels (29 vs 38%,  $p < 0.002$ ). However, this benefit was primarily limited to patients in whom optimal stent expansion had been achieved. Unfortunately, in the small vessel cohort in that study, an optimal IVUS result could be achieved for only 71% of the lesions.

**Comments on our study.** The most important limitation of this report is the small sample size. However, this study is a pilot preliminary study and the main purpose

was to assess the safety and feasibility of IVUS utilization in really small vessels. In our study IVUS guidance was feasible in all patients and did not cause procedural complications. It safely allowed the achievement of a significant stent overexpansion (stent-artery ratio 1.3, residual stenosis  $0.75 \pm 11.7\%$ ). No episodes of stent thrombosis occurred in our study. Previous studies using coil stents and oral anticoagulants have suggested that the rate of stent thrombosis is higher when stents are implanted in angiographically small vessels<sup>17,18</sup>. The absence of stent thrombosis observed in our study is in agreement with other reports in which aggressive stent expansion was associated with post-procedure antiplatelet therapy<sup>16,19</sup> and highlights the importance of adequate stent expansion particularly in small vessel disease. In the present study, at 6 months of follow-up, the incidence of angiographically diagnosed restenosis was 30%, a result that is comparable with that (29%) found by Akiyama et al.<sup>16</sup> in the subgroup of patients with a small vessel size (mean reference diameter  $2.6 \pm 0.3$  mm) and IVUS-guided stent implantation. In that report<sup>16</sup>, patients submitted to IVUS-guided stent implantation showed, in both small and large vessels, a significant reduction in the restenosis rate (17 vs 26%,  $p < 0.0222$  in large vessels; 29 vs 38%,  $p = 0.0426$  in small vessels). Furthermore, the incidence of long-term restenosis observed in our study was strictly related to the intrastent post-procedure CSA ( $5.6 \pm 1.1$  mm<sup>2</sup>). In fact, in a group of stented lesions with an IVUS post-procedural minimal stent CSA (5.0 to 5.9 mm<sup>2</sup>) in the range of the values obtained in this study, Moussa et al.<sup>20</sup> found a restenosis rate of 32%. In the present study, IVUS success was defined as the achievement of an intrastent minimal lumen area  $\geq 90\%$  of the distal lumen CSA. In a recent retrospective analysis of selected patients in whom various non-randomly assigned IVUS criteria were evaluated, Moussa et al.<sup>21</sup> showed that these IVUS criteria applied to small or large vessels did not significantly reduce the long-term incidence of stent restenosis probably because it does not represent the maximal potential of lumen gain. A recent randomized trial that compared stent implantation with either IVUS or angiographic guidance, using an intrastent minimal lumen CSA  $\geq 80\%$  of the reference lumen CSA as the IVUS endpoint, did not show any significant difference in the restenosis rate between the two groups<sup>22</sup>. The IVUS criterion that, in the report of Moussa et al.<sup>21</sup> was associated, in both large and small vessels, with a higher probability of freedom from restenosis was an intrastent minimal lumen area  $\geq 55\%$  of the average reference vessel CSA, a criterion that was achievable in 69% of the patients. In particular, the achievement of this criterion on the basis of vessel rather than lumen size was associated with a 42% decrease in the restenosis rate (22 vs 38%) and in the subgroup of patients with an angiographic reference diameter < 3 mm, resulted in a restenosis rate of 22%. Unfortunately, to date no clinical trial specifically dedicated to small vessel stent implantation

has utilized this more aggressive IVUS criterion. Obviously, randomized trials will be required to definitely prove the role of IVUS guidance in small vessel stent implantation. The preliminary results of the AVID trial<sup>23</sup> in which IVUS guidance in the subgroup of patients with vessels < 3.25 mm in diameter produced a significant benefit in terms of the 12-month target vessel revascularization rate (8.6 vs 17.2%) seem encouraging.

In conclusion, IVUS-guided stent implantation is a safe and feasible procedure even in small vessels and renders the achievement of optimal angiographic results with a low incidence of acute or subacute stent thrombosis possible. However, owing to a restenosis rate higher than that observed for larger vessels, long-term results remain unsatisfactory. The implantation of more customized stents coupled with a broader and more aggressive use of IVUS, the utilization of pharmacological agents such as the IIb/IIIa platelet receptor inhibitors (at least in diabetic patients) or the application of radiation intravascular therapy are newer emerging techniques that could help to improve the results in this field of interventional cardiology.

## References

- Schunkert H, Harrel BS, Palacios IF. Implications of small reference vessel diameter in patients undergoing percutaneous coronary revascularization. *J Am Coll Cardiol* 1999; 34: 40-8.
- Hirshfeld JW Jr, Schwartz JS, Jugo R, et al. Restenosis after coronary angioplasty: a multivariate statistical model to relate lesion and procedure variables to restenosis. The M-HEART Investigators. *J Am Coll Cardiol* 1991; 18: 647-56.
- Azar AJ, Detre K, Goldberg S, et al. A meta-analysis of the clinical and angiographic outcomes of stent vs PTCA in the different vessels size in the BENESTENT and STRESS I/II trials. (abstr) *Circulation* 1995; 92 (Suppl I): I-475.
- Foley D, Melkert R. Influence of coronary vessel size on re-narrowing process and late angiography outcome after successful balloon angioplasty. *Circulation* 1994; 90: 1239-51.
- Kuntz R, Gibson C. Generalized model of restenosis after conventional balloon angioplasty, stenting and directional atherectomy. *J Am Coll Cardiol* 1993; 21: 15-25.
- Rozenman Y, Sapoznikov D. Long-term angiographic follow-up of coronary balloon angioplasty in patients with diabetes mellitus: a clue to the explanation of the results of the BARI study. *Circulation* 1997; 30: 1420-5.
- Mintz G, Hoffmann R, Pichard A, et al. Intravascular ultrasound: insights into the mechanisms and predictors of the restenotic process. *Intravascular Imaging* 1997; 1: 34-42.
- Stone GW, Hodgson JM, St Goar FG, et al. Improved procedural results of coronary angioplasty with intravascular ultrasound-guided balloon sizing: the CLOUT pilot trial. Clinical Outcomes With Ultrasound Trial (CLOUT) Investigators. *Circulation* 1997; 95: 2044-52.
- Ellis SG, Roubin GS, King SB, et al. Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. *Circulation* 1988; 77: 372-9.
- Holmes D, Faxon D, Kent K, Bentivoglio LG, Detre K, and the Investigators of the National Heart, Lung and Blood Institute Percutaneous Transluminal Angioplasty Registry. Comparison of complications during percutaneous transluminal angioplasty from 1977 to 1981 and from 1985 to 1986. *J Am Coll Cardiol* 1988; 12: 1149-55.
- The TIMI Study Group. The Thrombolysis in Myocardial Infarction (TIMI) Trial: phase 1 findings. *N Engl J Med* 1985; 312: 932-6.
- Elezi S, Kastrati A, Neumann FJ, et al. Vessel size and long-term outcome after coronary stent placement. *Circulation* 1998; 98: 1875-80.
- Savage MP, Fischman DL, Rake R, et al. Efficacy of coronary stenting versus balloon angioplasty in small coronary arteries. Stent Restenosis Study (STRESS) Investigators. *J Am Coll Cardiol* 1998; 31: 307-11.
- Mintz GS, Popma JJ, Pichard AD, et al. Intravascular ultrasound predictors of restenosis following percutaneous transcatheter coronary revascularization. *J Am Coll Cardiol* 1996; 27: 1678-87.
- Fitzgerald P, Oshima A, Hayase M, et al, for the CRUISE Investigators. Final results of the Can Routine Ultrasound Influence Stent Expansion (CRUISE) Study. *Circulation* 2000; 102: 523-30.
- Akiyama T, Moussa I, Reimers B, et al. Angiographic and clinical outcome following coronary stenting of small vessels. A comparison with coronary stenting of larger vessels. *J Am Coll Cardiol* 1998; 32: 1610-8.
- Agrawal S, Ho D, Liu M, et al. Predictors of thrombotic complications after placement of the flexible coil stent. *Am J Cardiol* 1994; 73: 1216-21.
- Nath F, Muller D, Ellis S, et al. Thrombosis of a flexible coil coronary stent: frequency, predictors and clinical outcome. *J Am Coll Cardiol* 1993; 21: 622-7.
- Moussa I, Di Mario C, Reimers B, Akiyama T, Tobis J, Colombo A. Subacute stent thrombosis in the era of intravascular ultrasound-guided coronary stenting without anticoagulation: frequency, predictors and clinical outcome. *J Am Coll Cardiol* 1997; 27: 6-12.
- Moussa I, Di Mario C, Moses J, et al. The predictive value of different intravascular ultrasound criteria for restenosis after coronary stenting. (abstr) *J Am Coll Cardiol* 1997; 29: 60A.
- Moussa I, Moses J, Di Mario C, et al. Does the specific intravascular ultrasound criterion used to optimize stent expansion have an impact on the probability of restenosis? *Am J Cardiol* 1999; 83: 1012-7.
- Schiele F, Meneveau N, Vuilleminot A, et al. Impact of intravascular ultrasound guidance in stent deployment on 6-month restenosis rate: a multicenter, randomized study comparing two strategies with and without intravascular ultrasound guidance. *J Am Coll Cardiol* 1998; 32: 320-8.
- Russo RJ, Atiubato MJ, Davidson CJ, et al. Angiography ultrasound directed stent placement: final results from AVID. (abstr) *Circulation* 1999; 100: I-234.