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## Articles

### Comparison of Immediate and Intermediate-Term Results of Intravascular Ultrasound Versus Angiography-Guided Palmaz-Schatz Stent Implantation in Matched Lesions

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## Abstract

**Background** Intravascular ultrasound (IVUS) provides more precise information than angiography about vascular dimensions. This information is used by some centers to optimize intracoronary stent implantation. There are no direct comparisons of the effects on restenosis of optimal IVUS-guided versus angiography-directed high-pressure stenting.

**Methods and Results** Lesions of patients who had a 6-month angiographic follow-up study were eligible for matching. From 445 consecutive lesions treated by Palmaz-Schatz (P-S) stenting guided by IVUS (IVUS group) in Milan, 173 lesions were individually matched with 173 of 476 consecutive lesions treated by P-S stenting directed by angiography (Angio group) in Hamburg. Lesions were selected by a computerized program according to baseline clinical, angiographic, and procedural variables. Immediate and 6-month angiographic results were retrospectively compared, distinguishing an "early phase" from a "late phase." This distinction was based on the more aggressive dilation strategy with larger balloons and more demanding IVUS criteria for optimal stent expansion used in Milan in the early phase. In both phases, a larger minimum lumen diameter (MLD) immediately after stenting and after 6 months was achieved in the IVUS group than in the Angio group. In the early phase, the dichotomous restenosis rate was lower in the IVUS group than in the Angio group (9.2% versus 22.3%;  $P=.04$ ). In the late phase, there was no difference in restenosis between the groups (22.7% versus 23.7%;  $P=1.0$ ).

**Conclusions** In matched lesions treated with high-pressure stenting, IVUS guidance achieved a larger MLD than angiographic guidance. However, in the IVUS group, the restenosis rate was lower only in the early phase, when balloons larger than currently used were selected to maximize the stent lumen area.

### Key Words:

stents  
coronary disease  
ultrasonics  
angiography  
restenosis

Early experience with IVUS evaluation after intracoronary P-S stent implantation demonstrated that when stents were expanded with balloon inflations at conventional pressures (up to 8 to 12 atm) and an acceptable angiographic result was achieved, >80% of stents were insufficiently expanded.<sup>1 2 3</sup> This required further dilation with larger balloons or higher inflation pressures. By the high-pressure technique with confirmation of adequate stent expansion by IVUS, patients could be treated with antiplatelet therapy only, without anticoagulation, yet a low stent thrombosis rate could be maintained.<sup>4</sup> At the present time, stenting with high-pressure (14- to 16-atm) final dilations without IVUS guidance has become standard practice in many centers,<sup>5 6 7</sup> with a low incidence of subacute stent thrombosis with aspirin and/or ticlopidine. However, the experience at some centers indicates that even after high-pressure balloon dilatation, 30% to 50% of lesions with optimal angiographic results after stenting require additional treatment to fulfill the IVUS criteria of optimal stent expansion (<10% stenosis and full stent apposition) and that IVUS-directed stent implantation safely leads to a higher final lumen enlargement.<sup>8 9 10</sup> According to the model of restenosis proposed by Kuntz et al,<sup>11 12</sup> the achievement of a greater "acute gain" reduces the risk of long-term angiographic restenosis. The aim of this retrospective dual-center study on matched lesions treated with high-pressure P-S stent implantation was to determine whether the use of IVUS for final stent optimization has an impact on the initial lumen gain and reduces the risk of restenosis.

## Methods

### General Patient Population

From March 1993 through September 1995, at Centro Cuore Columbus in Milan (Italy), 778 patients (919 lesions) underwent successful P-S stenting, frequently with IVUS guidance. From June 1994 through November 1995, at the Center for Cardiology Othmarschen in Hamburg (Germany), 546 patients (635 lesions) underwent P-S stenting with high-pressure dilatation directed only by angiography. For the purpose of this study, patients were

eligible for matching if they had an angiographic follow-up study with a quantitative coronary analysis (478 patients with 576 lesions in Milan; 393 patients with 476 lesions in Hamburg). Lesions were excluded from the Milan group when IVUS was not used to guide stent implantation (79 lesions, 13.7%). In addition, lesions were excluded from the Milan group when IVUS was also performed before stenting (52 lesions), because the balloon selection during the angiography-guided phase of stenting might have been influenced by the knowledge of the true vessel dimensions by IVUS. Thus, 445 lesions treated in Milan (IVUS group) and 476 lesions treated in Hamburg (Angio group) were eligible for matching.

### Matching Process

Matching was based on principles derived from the Thoraxcenter group (Rotterdam, Netherlands)<sup>13</sup>: (1) the angiographic dimensions of matched lesions are assumed to be "identical"; (2) the observed differences between the two identical lesions must be within the range of reproducibility of the quantitative angiographic analysis system.

Of the 445 lesions in the IVUS group, 173 were matched successfully with 173 of the 476 lesions in the Angio group. Matching was performed by a computerized program written in dBASE language that iteratively scanned the two databases chronologically and selected for each lesion in the Milan database the first lesion encountered in the Hamburg database that satisfied the selection criteria. The stented lesions were individually matched according to the following clinical, angiographic, and procedural selection variables: (1) sex, (2) history of diabetes, (3) previous PTCA at the same site, (4) vessel treated, (5) reference diameter  $\pm 0.3$  mm, (6) baseline MLD  $\pm 0.1$  mm, and (7) number  $\pm 0.5$  of stents deployed (the PS104 stent and the disarticulated 7-mm PS153 stent were counted as half stents). Lesion length was not entered into the matching model.

### Stent Implantation Procedure

In Milan, patients received aspirin 325 mg before stent deployment and did not receive dextran or dipyridamole before, during, or after the stent procedure. In Hamburg, patients received aspirin 100 mg before the procedure and in addition received intravenous low-molecular-weight dextran (dextran 40, given at a dose of 100 mL/h for 2 hours before stenting and at a dose of 50 mL/h during and after the procedure, for a total volume of 1 L). A bolus of 10 000 U heparin was given after sheath insertion, with a repeat bolus of 5000 U given as needed to maintain the activated clotting time  $>250$  seconds in Milan or hourly in the event of a prolonged procedure in Hamburg. Only P-S tubular slotted stents (Johnson & Johnson Interventional Systems) were implanted in the patients who entered this study: the standard 15-mm PS153 stent with a central linear articulation, a disarticulated 7-mm PS153 stent, a 14-mm PS154 stent, a 10-mm PS104 stent, an 18-mm PS204 stent with multiple spiral bridges, a 10-mm biliary stent, and a 20-mm renal stent. For calculating the number of stents per lesion, the short stents ( $<10$  mm) were counted as half stents. Biliary stents were counted as one stent each. All other stents were counted as one stent. Indications for stenting and their definitions were as previously reported.<sup>4</sup>

### Angiography-Guided Stenting in Milan and Hamburg

In Milan, the approach to angiography-guided stenting evolved as experience progressed. Until September 1993, after deployment of all stents, most angiography-guided postdilations were performed with minimally compliant balloons, usually 9 mm long,  $\approx 0.5$  mm larger than the reference lumen diameter, and inflated at moderate to high pressure (8 to 20 atm). In this "early phase," the angiographic evidence of a step up into the stented area and a step down into the distal unstented segment was considered the end point.<sup>2</sup> Subsequently, when the IVUS criterion for optimal stent expansion was altered ("late phase"), the approach to angiography-guided stenting was modified: most postdilations were performed with noncompliant balloons, more closely approximating the size of the angiographic vessel diameter by visual estimate, and inflated at high pressure ( $\geq 14$  atm up to 20 atm). In this phase, a final angiographic result with  $<10\%$  residual DS by visual estimate was considered acceptable. In Hamburg, stent implantation strategy did not change over time: postdilations were performed with noncompliant balloons, closely sized to the angiographic vessel diameter by visual estimate, and inflated at high pressure ( $\geq 14$  atm up to 21 atm). A final angiographic result with  $<15\%$  residual DS by visual estimate was considered acceptable.

### IVUS-Guided Stenting

In Milan, after an acceptable angiographic result was achieved, IVUS was performed.

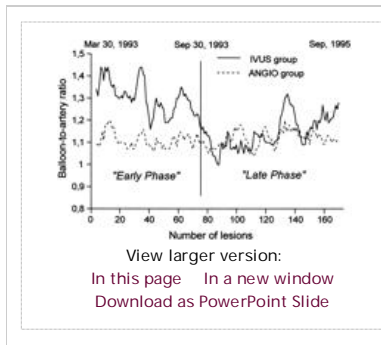
#### *IVUS Equipment and Measurement*

Imaging was performed with a 3.9F monorail system with a 25-MHz transducer-tipped catheter (Interpret Catheter, InterTherapy/CVIS) or a 2.9F or 3.2F monorail system with a 30-MHz transducer-tipped catheter (Scimed-Boston Scientific Co). Validation of quantitative measurements and pathological correlation with ultrasound measurements have been reported.<sup>14 15</sup> Interobserver and intraobserver reproducibility of MLD and lumen CSA measurements have been reported previously.<sup>4 16</sup> Images were obtained with a manual or an automated pullback system. Data were stored on 0.5-in Super VHS videotape. Measurement sites were as previously reported.<sup>2 4</sup> The initial IVUS was the first ultrasound examination performed after the initial angiographic success was achieved. The final IVUS was the last IVUS evaluation, which documented that the criteria for optimal stent expansion were achieved. Further balloon dilatations or stent implantations performed after the initial IVUS imaging were called IVUS-guided stent optimization.

#### *IVUS Criteria for Optimal Stent Expansion*

The first criterion was a qualitative evaluation of the achievement of complete stent apposition to the vessel wall. The second criterion was based on a quantitative evaluation of stent expansion. Between March 1993 and September 1993 (early phase of the Milan experience), the target for defining IVUS success was the achievement of a stent lumen CSA of 60% of the average of the proximal and distal vessel CSAs (measured at the media). This target criterion was initially chosen to accommodate compensatory dilation that occurs with early atheroma deposition, as observed in both pathological and IVUS investigations even in angiographically normal reference sites.<sup>14 17 18</sup> In this phase, IVUS-guided stent optimization was performed with minimally compliant balloons, usually 9 mm long, sized close to the IVUS average distal vessel (media-to-media) diameter. These balloons were oversized to the angiographic vessel diameter by visual estimate and were inflated at moderate to high pressure. As previously reported,<sup>4</sup> in September 1993 the IVUS criterion for optimal stent expansion was rapidly altered (late phase): the goal was to achieve a stent lumen

CSA equal to or greater than the distal reference lumen CSA. In this phase, IVUS-guided stent optimization was generally performed with noncompliant balloons inflated at high pressure. The balloons were selected with a calculated nominal CSA 25% to 30% larger than distal lumen CSA, based on the observation that the ratio of the final stent CSA to the calculated nominal balloon CSA was 0.75 to 0.80 in the early phase. The rapid change in the final balloon-to-artery ratio over time in Milan, reflecting the change in IVUS-guided balloon selection compared with Hamburg (angiography-guided), is shown in Fig 1. The third IVUS criterion for optimal stent expansion was that the nonstented adjacent inflow and outflow segments should not reveal evidence of a significant lesion, defined as plaque area >60% of the total vessel lumen.



**Figure 1.**

Smoothed curve plot (moving average of 7 data points) of ratio of nominal diameter of final balloon selected to angiographic reference vessel diameter in Milan and Hamburg over time. In Hamburg, dilation strategy did not change over this time period. In Milan, when target for defining IVUS success was achievement of 60% of average of proximal and distal total vessel CSA, postdilations were performed with balloons angiographically oversized (early phase). From September 1993, IVUS criterion for optimal stent expansion was rapidly altered (late phase). Goal was to achieve stent CSA equal to or greater than distal lumen CSA. In this phase, use of smaller balloons inflated at higher pressure resulted in significantly lower balloon-to-artery ratio than in early phase.

### Angiographic Analysis

Both in Milan and in Hamburg, coronary angiograms were analyzed by experienced technicians not involved in the stenting procedure. Angiographic measurements of baseline, final, and follow-up angiograms were performed in a single matched view (working projection) at end diastole. The lesions were measured with a digital electronic caliper (Brown and Sharp) from an optically magnified image. The guiding catheter was used as the scaling device for calibration. Previous studies have shown that digital calipers correlate closely with computer-assisted methods, with a low interobserver and intraobserver variability.<sup>19 20</sup> The diameters of the proximal and distal lumen reference segments were averaged to obtain a mean reference diameter. MLD and % DS were measured in the baseline, posttreatment, and follow-up angiograms. Lesion length was measured on the baseline angiogram as the distance between the proximal and distal shoulders of the lesion, detected as the point at which the lumen becomes compromised by 50%. Lesions were characterized according to the modified American College of Cardiology/American Heart Association score.<sup>21</sup> Thrombus was defined as a filling defect seen in multiple projections surrounded by contrast in the absence of calcification.

### Postprocedure Medication Protocol

After a successful result was achieved, no further heparin was administered, and sheaths were removed in 4 to 6 hours. When procedures were performed in the evening, in Milan, heparin was infused overnight and the sheaths were removed the following morning, whereas in Hamburg, the sheaths were removed within 4 to 6 hours. In Milan, 155 patients (98%) were treated either with a combination of ticlopidine 250 mg BID for 1 month and long-term aspirin 325 mg/d or long-term aspirin alone 325 mg/d; only 3 patients (2%) were treated with anticoagulation. In Hamburg, 151 patients (98%) were treated with a combination of ticlopidine 250 mg BID for 3 months and long-term aspirin 100 mg/d, and only 3 patients (2%) were treated with anticoagulation.

### Events and Follow-up

Stent thrombosis, MI (Q-wave MI or non-Q-wave MI), CABG, repeat percutaneous intervention, or vascular complications were considered major clinical events. Stent thrombosis, MI (Q-wave MI or non-Q-wave MI), CABG, and vascular complications were defined as previously reported.<sup>4</sup> Repeat percutaneous intervention was defined as the need for repeat PTCA involving the site of the previously treated lesion within the first 6 months ( $\pm 60$  days) after the initial revascularization. The indication for a second intervention or CABG had to be substantiated by symptoms or by laboratory evidence of myocardial ischemia. After a successful procedure, patients were generally discharged from the hospital within 1 to 2 days. Follow-up angiography was performed at 6 months unless early restudy was indicated by symptoms, after a mean interval of 5.21 months in Milan and 5.23 months in Hamburg.

### Restenosis

The primary end point of this study was the incidence of restenosis defined in a dichotomous manner as a DS  $\geq 50\%$  at follow-up angiography. The analysis included assessment of the MLD and %DS immediately after stenting and at follow-up and their cumulative distributions. Finally, according to a continuous geometric model of restenosis proposed by Kuntz et al,<sup>11 12</sup> seven derived indexes were examined: (1) acute gain=MLD (poststenting)-MLD (preprocedure), (2) relative gain=acute gain $\div$ reference diameter before stenting, (3) late loss=MLD (poststenting)-MLD (at follow-up), (4) relative loss=late loss $\div$ reference diameter before stenting, (5) net gain=acute gain-late loss, (6) net gain index=net gain $\div$ reference diameter before stenting, and (7) loss index=late loss $\div$ acute gain.

### Statistical Analysis

Data were expressed as mean $\pm$ SD (for normally distributed variables), median with a range of values (for other continuous variables), and percentage (for categorical variables). The Kolmogorov-Smirnov test was used to test the departure of the distribution of continuous variables from normality. Comparison of continuous variables between the groups was performed with the unpaired Student's *t* test (two-tailed) for normally distributed data or the Mann-Whitney *U* test for other continuous data. Comparisons of categorical variables were made by  $\chi^2$  and Fisher exact tests as appropriate. Differences were considered statistically significant at a value of  $P < .05$ .

### Results

### Patient, Baseline Angiographic, and Procedural Characteristics

The baseline clinical characteristics of the patients in the IVUS (173 lesions in 158 patients) and Angio (173 lesions in 154 patients) groups are shown in Table 1↓. In the Angio group, compared with the IVUS group, left ventricular ejection fraction was higher, the number of patients with two-vessel disease was lower, there were more patients with three-vessel disease and hypercholesterolemia, and fewer patients were current smokers. Sex, previous angioplasty at the same site, diabetes, and unstable angina were not different between the two groups. Matching for angiographic and procedural variables resulted in two groups of lesions with superimposable baseline angiographic and procedural characteristics. In the Angio group, however, the percentage of calcific lesions identified by angiography was lower than that in the IVUS group (Table 2↓). Furthermore, in the Angio group, the percentage of lesions in which a half stent per lesion was deployed was higher, with a lower percentage of lesions in which one and two stents per lesion were implanted (Table 3↓). Consequently, in the Angio group, the mean total number of stents per lesion was slightly lower ( $1.05 \pm 0.46$  versus  $1.17 \pm 0.44$ ,  $P = .014$ ).

**Table 1.**

Baseline Clinical Characteristics

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**Table 2.**

Baseline Angiographic Characteristics

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**Table 3.**

Stent Implantation Procedure Characteristics

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### Clinical Events

As shown in Table 4↓, no stent thrombosis occurred in either group. Moreover, the percentages of patients who had MI and CABG during hospitalization and after discharge were not statistically different between the groups. The percentage of patients who needed a repeat percutaneous intervention during follow-up was lower in the IVUS group than in the Angio group (5.1% versus 11.7%;  $P = .05$ ). However, the percentage of patients who needed a repeat revascularization (CABG+PTCA) was not significantly different between the groups (7% versus 11.7%;  $P = .17$ ).

**Table 4.**

Frequency of In-Hospital (<24 hours) and Postdischarge Events

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### Angiographic Analysis

Table 5↓ summarizes the quantitative angiographic results of the matched lesions in the IVUS and Angio groups during the early phase and the late phase. Reference vessel diameter, MLD, and %DS immediately before stenting were similar in the IVUS and Angio groups, indicating that the matching process was adequate.

**Table 5.**

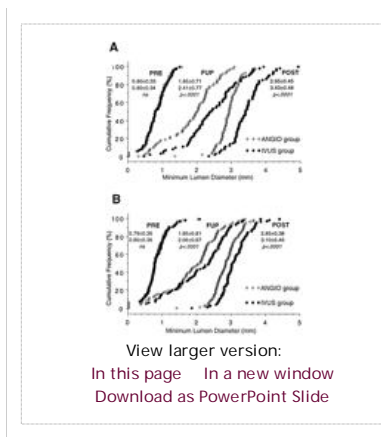
Comparison of Quantitative Angiographic Results of the Matched Lesions in the Early Phase and Late Phase

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As illustrated in Fig 2↓, IVUS-guided stent deployment produced a significantly greater acute gain than angiography-guided stenting in both the early phase and the late phase. A similar late loss of 1.0 to 1.1 mm was observed at 6-month follow-up angiography in the two groups in both phases. This resulted in a higher net gain and a lower loss index in the IVUS group than in the Angio group, with a statistically significant difference in the early phase, which translated into a lower dichotomous restenosis rate (9.2% versus 22.3%;  $P = .04$ ). In the late phase, there was no difference in restenosis between the groups (22.7% versus 23.7%;  $P = 1.0$ ). Furthermore, in the early phase, the balloons used to optimize stent expansion were larger in the IVUS group than in the Angio group, with a higher balloon-to-artery ratio (Fig 1↑). In the late phase, although the size of the final balloon was greater in the IVUS group than in the Angio group, the balloon-to-artery ratio was not different between the groups. In addition, in the early phase, the maximal balloon inflation pressure was lower in the IVUS group than in the Angio group. Finally, lesions were slightly longer in the IVUS group than in the Angio group. However, the calculated total length of the stented lesion was not different between the groups.

**Figure 2.**

Cumulative frequency distribution curves of baseline (PRE), poststenting (POST), and follow-up (FUP) MLD of Angio and IVUS groups during early phase (A) and late phase (B). In both phases, MLD immediately after stenting was significantly larger in IVUS than Angio group and remained significantly larger at 6-month follow-up. There was a greater difference in poststenting MLD between groups in early phase (A),



when larger balloons than currently recommended were used in Milan to maximize stent lumen CSA. In Angio group, curves in two phases were superimposable.

### Early Phase Versus Late Phase in Milan and Hamburg

In the IVUS group, larger final balloons were selected, with a higher balloon-to-artery ratio, and inflated at a lower maximal inflation pressure in the early phase than in the late phase. This resulted in a greater acute gain and net gain, which translated into a lower restenosis rate in the early phase. In the Angio group, no significant differences in the quantitative angiographic results were observed between the early phase and the late phase, and there was no difference in the observed restenosis rate between the two phases.

### IVUS Analysis

Comparisons of quantitative IVUS results between the early phase and late phase of the Milan experience are presented in Table 6. There were no differences in the measurements at the proximal reference site between the two groups of lesions. At the distal reference site, the vessel CSA and vessel diameters were significantly larger in the lesions treated during the early phase, with a trend toward a greater percentage of plaque area. This resulted in a greater calculated average vessel CSA and vessel diameters at the stent site in the lesions treated during the early phase. Furthermore, after the initial IVUS evaluation, a higher percentage of lesions required further therapy to achieve an adequate IVUS result in the early phase than in the late phase (83% versus 44%;  $P<.001$ ), and a greater increase in the stent CSA was noted after optimization ( $51\pm 36\%$  versus  $28\pm 35\%$ ;  $P=.002$ ). During the early phase, the balloons selected for final stent expansion were exactly sized to the average of the distal minor and major vessel diameters and to the distal vessel CSA, whereas in the late phase, they were slightly undersized (ratio of balloon diameter/IVUS average distal vessel diameter,  $1.00\pm 0.12$  versus  $0.95\pm 0.14$ ,  $P=.005$ ; balloon CSA/IVUS distal vessel CSA,  $1.00\pm 0.25$  versus  $0.89\pm 0.26$ ,  $P=.007$ ). Finally, the ratio of the final stent CSA to the calculated nominal balloon CSA was slightly lower during the early phase ( $0.78\pm 0.11$  versus  $0.82\pm 0.16$ ;  $P=.03$ ).

**Table 6.**

Comparison of Quantitative IVUS Results Between the Early Phase and the Late Phase of the Milan Experience

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### Discussion

The immediate and late angiographic results of the present dual-center study on matched lesions treated with high-pressure P-S stent implantation were markedly influenced by the two different balloon dilation strategies used in Milan during the early phase and the late phase. In Milan, a more aggressive dilation strategy for stent optimization was used in the early phase than in the late phase, with final balloons selected sized to the IVUS average distal vessel (media-to-media) diameter (angiographically oversized). This strategy was initially used to maximize protection against stent thrombosis in a large, unselected, and consecutive series of patients who were for the first time undergoing stent implantation without subsequent anticoagulation. Although this strategy was protective against stent thrombosis, in this phase a high procedural complication rate and a high incidence of intracoronary vessel rupture were observed,<sup>2,4</sup> possibly related to the use of oversized balloons. In the late phase, with the experience gained from IVUS imaging together with an evaluation of the clinical results, the final balloons selected were smaller than in the early phase, with a size slightly larger than the IVUS lumen diameters (not angiographically oversized), and higher pressures were used to provide adequate expansion within the stented segment. This adjustment in the balloon dilation strategy resulted in a lower intraprocedural complication rate without increasing the incidence of stent thrombosis. In Hamburg, balloon dilation strategy did not change over time: balloons were selected sized to the angiographic vessel diameter.

### Restenosis

In the early phase, the aggressive balloon dilation strategy used in the IVUS group produced a significantly greater postprocedure MLD than in the Angio group (Fig 2A), which resulted in a significantly lower angiographic dichotomous restenosis rate (9.2% versus 22.3%;  $P=.04$ ). In the late phase, although the postprocedure MLD was greater in the IVUS group than in the Angio group, as displayed in Fig 2B, the difference was slight and did not translate into a lower restenosis rate (22.7% versus 23.7%;  $P=1.0$ ). Our findings confirm the importance of the immediate result in determining the late result, as reported by Kuntz et al,<sup>11,12</sup> but deviate from the model of restenosis proposed by these authors in that the higher acute gain observed in the IVUS group versus the Angio group was not associated with a greater late loss, which was similar (1.0 to 1.1 mm) in the two groups in both phases. Coronary artery stenting prevents negative remodeling; thus, late loss within a stent results almost exclusively from intimal hyperplasia, as recently demonstrated by a serial IVUS study.<sup>22</sup> The present study demonstrates that in the IVUS group, the more aggressive balloon dilation strategy used in the early phase, which possibly increased vessel wall injury, was not accompanied by a greater hyperplastic response. A possible mechanism for this result could be that after stenting, the extent of subsequent intimal hyperplasia is more dependent on plaque mass before intervention, as we

have recently reported,<sup>23</sup> with the preintervention plaque area measured by IVUS, than on the greater final strain (overstretch) applied to the vessel wall by a larger balloon correctly sized to the media-to-media vessel dimensions.

Late loss (and restenosis) has been reported to be influenced by some clinical, angiographic, and procedural factors.<sup>24</sup> The effects of these factors in our study were well balanced in the two groups; in particular, the higher percentages of patients with hypercholesterolemia and three-vessel disease in the Angio group were counterbalanced by the lower percentage of patients currently smoking, by the slightly shorter lesion length, and by the lower percentage of calcific lesions. Furthermore, the differences in the type and number of stents per lesion were negligible. In fact, in Milan, two disarticulated 7-mm-long PS153 stents, instead of one standard 15-mm-long PS153 stent, were implanted in 53% of the lesions in which only disarticulated PS153 stents were implanted. This result is also inferable by the fact that, although the percentage of half stents implanted was higher in the IVUS than in the Angio group (46.2% versus 28.1%), the percentage of lesions in which only a half stent was implanted was lower in the IVUS group (6.9% versus 20.2%). Finally, although the mean number of stents per lesion was higher in the IVUS than in the Angio group (1.17 versus 1.05), the majority of patients had one stent per lesion, and the calculated stented lesion length was equal in both groups in both phases (Table 5↑). Other established risk factors for restenosis (diabetes, unstable angina, and chronic total occlusion) were not different between the groups.

After stenting, the inhibition of intimal hyperplasia would be the ideal therapy to reduce restenosis. The results of the present study indicate that restenosis can also be reduced mechanically by trying to achieve as large an MLD as possible and that IVUS is better than angiography guidance to achieve this goal, because angiography may underestimate the extent of atherosclerotic disease in coronary arteries that undergo compensatory enlargement, thus leading to underestimation of the size of the final balloon that can be selected to safely expand the stent and maximize the stent lumen CSA. The use of IVUS guidance allows one to better oversize the balloon (by angiography) and to obtain a larger final MLD that would not be achieved by inflating a smaller balloon at higher pressure.

### **IVUS-Guided Stent Optimization**

In the early phase, IVUS-guided stent optimization was performed with larger balloons than in the late phase, and with this strategy, a greater increase in the stent CSA was obtained after stent optimization ( $51\pm 36\%$  versus  $28\pm 35\%$ ;  $P=.002$ ). Although there was no difference in the angiographic reference vessel diameter, the vessel CSA measured at the distal reference site by IVUS was significantly smaller in the lesions treated during the late phase as a result of a lower percentage of plaque area. However, this finding cannot by itself explain the lower increase in CSA achieved in the late phase, which probably would have been greater if the final balloons selected had been larger and sized to the IVUS average distal vessel diameter.

### ***IVUS Guidance Permits the Use of Balloons Traditionally Considered Oversized***

In the IVUS group, in the 76 matched lesions treated in the early phase, there were no more complications or vessel ruptures, compared with the 97 lesions treated in the late phase and with the lesions in the Angio group, suggesting that in the presence of arterial remodeling identified by IVUS, target lesions can safely accommodate larger balloons. This hypothesis is supported by the favorable results of the CLOUT trial,<sup>25</sup> in which oversized balloons were safely used in 73% of the lesions in which IVUS identified the presence of arterial remodeling and the absence of heavy calcification. This technique increased the balloon-to-artery ratio from 1.12:1 after standard PTCA to 1.30:1 after IVUS-guided PTCA and resulted in significantly improved luminal dimensions without increasing the rate of major dissections. Furthermore, as previously reported,<sup>2</sup> vessel rupture during the early phase of the Milan experience occurred only when the operator exceeded the true distal vessel size measured at the media by IVUS. In the whole Milan database, 6 patients sustained vessel rupture in the early phase. In 4 of these 6 patients in whom IVUS was performed, the balloons used for stent optimization were oversized to the average distal vessel diameter by IVUS, and in 2, the event was probably caused by bursting of the balloon. Moreover, in the 2 patients with vessel rupture in whom stenting was guided only by angiography, a correctly sized balloon burst in 1 patient, whereas in the other, the balloon was oversized (balloon-to-artery ratio, 1.44). The use of balloons larger than the IVUS average distal vessel diameter was due to the inability to obtain an adequate lumen inside the stent with smaller balloons. At present, this goal could possibly be reached by use of pre-stent rotational atherectomy in hard, fibrocalcific lesions, in which we can expect difficulties in achieving an optimal final stent expansion.

### ***Comparison With Other Studies (Late Phase)***

The results of the late phase of the Milan experience (Table 6↑) are comparable to those obtained in the CRUISE substudy,<sup>8</sup> in which 49% of the IVUS-guided lesions required stent optimization, with an increase in stent CSA from 6.59 to 7.28 mm<sup>2</sup>. In the AVID trial,<sup>9</sup> in the ultrasound group, 33% of patients required additional therapy to fulfill ultrasound criteria, in which an increase in luminal diameter of 0.59 mm and an increase in CSA of 32% were noted. Our data are also consistent with those of another report,<sup>10</sup> in which 53% of the stents required additional balloon inflations after IVUS evaluation. In that study, additional balloons with an increase in balloon size of 0.20 mm were used in 44% of cases and produced an increase in mean stent lumen CSA from 85% to 103% of the reference lumen CSA. In Milan, in the late phase, balloons were selected with a calculated nominal CSA 25% to 30% larger than distal lumen CSA. This strategy is similar to that recently reported by another group,<sup>26</sup> in which the achievement of an optimal IVUS result (>90% of the average reference lumen CSA) was most frequently reached when the ratio of the calculated balloon CSA to the reference lumen CSA was >1.2.

### **Intraprocedural Complications and Postprocedure Clinical Events**

The true complication and clinical event rates of the two different methodologies cannot be correctly analyzed from the data presented in this study, in which a clear selection bias was introduced, including only the patients who had a follow-up angiographic study. However, the results observed in this selected population are likely to reflect the results of the overall population. The patients were selected by a computerized procedure from a larger patient cohort, which can be considered representative of the initial cohorts. In fact, in both centers after stenting, all patients were scheduled for a coronary angiography at 6 months, and a similar percentage of patients (61.4% of the Milan population versus 71.9% of the Hamburg population) had an angiographic follow-up. The rest did not undergo a repeat angiographic study, mostly because they were asymptomatic and refused the study.

### **Study Limitations**



There are several limitations in the present study. It is a nonrandomized, observational retrospective study, limited to a subset of patients who had a follow-up angiographic study. The quantitative coronary angiographic analysis was not computerized. The balloon-to-artery ratio was calculated from the nominal balloon size and not the actual size of the inflated balloon. Although matching for angiographic, procedural, and clinical variables can be used to compensate for some of the limitations of nonrandomized trials, not all bias of lesion selection can be excluded. However, this study represents the first comparison of the 6-month restenosis rate using IVUS to guide stent implantation compared with angiography from two European centers with extensive experience in placing coronary artery stents.

### Conclusions and Future Directions

In the present study on matched lesions treated with high-pressure P-S stenting, MLD immediately after treatment and at 6-month follow-up was larger when stent implantation was directed by IVUS as opposed to angiography. In addition, in the IVUS group, the 6-month restenosis rate was lower only in the early phase, when balloons sized to the IVUS average distal vessel (media-to-media) diameter (angiographically oversized) were used to maximize the stent lumen CSA. This early technique was modified because of an increase in complications, possibly related to the use of oversized balloons not only by angiography but also by IVUS, that is, larger than the IVUS distal vessel diameters. When balloons were subsequently selected to achieve the currently used IVUS criteria for optimal stent expansion (late phase), the 6-month restenosis rate was not statistically different from that of the Angio group. These results suggest that a significant reduction in restenosis may be safely realized if the size of the balloon selected to optimize the stent lumen CSA is equal to the IVUS average distal vessel diameter. Furthermore, it is important that the operator avoids choosing a larger balloon even when unable to obtain an adequate stent lumen CSA, because this strategy increases the risk of vessel rupture, especially in hard, fibrocalcific lesions. It may be that in these types of lesions, plaque pretreatment with rotational atherectomy is a better strategy than trying to forcefully overcome the lesion with a bigger balloon inflated at high pressure.

### Selected Abbreviations and Acronyms

Angio	=angiography (group)
CABG	=coronary artery bypass graft surgery
CSA	=cross-sectional area
DS	=diameter stenosis
IVUS	=intravascular ultrasound
MI	=myocardial infarction
MLD	=minimum lumen diameter
P-S	=Palmaz-Schatz
PTCA	=percutaneous transluminal coronary angioplasty

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### References

- Goldberg SI, Colombo A, Nakamura S, Almagor Y, Maiello L, Tobis JM. Benefit of intracoronary ultrasound in the deployment of Palmaz-Schatz stents. *J Am Coll Cardiol*. 1994;24:996-1003. [Medline](#)
- Nakamura S, Colombo A, Gardlione A, Almagor Y, Goldberg SI, Maiello L, Finci L, Tobis JM. Intracoronary ultrasound observations during stent implantation. *Circulation*. 1994;89:2026-2034. [FREE Full Text](#)
- Görge G, Haude M, Ge J, Voegele F, Gerber T, Rupprecht HJ, Meyer J, Erbel R. Intravascular ultrasound after low and high inflation pressure coronary artery stent implantation. *J Am Coll Cardiol*. 1995;26:725-730. [CrossRef](#) [Medline](#)
- Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, Gardlione A, Goldberg SI, Tobis JM. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation*. 1995;91:1676-1688. [Abstract/FREE Full Text](#)
- Morice MC, Breton C, Buncuf P, Cattan S, Etchepanoff H, Henry M, Joly P, Livarek B, Pillere P, Rioux P, Shaulding C, Zémour G. Coronary stenting without anticoagulation, without intravascular ultrasound: results of the French registry. *Circulation*. 1995;92(suppl I):I-796. Abstract.
- Barragan P, Silvestri M, Sainous J, Simoni JB, Bayat G, Bouvier H, Comet B. Prevention of subacute occlusion after coronary stenting with ticlopidine regimen without intravascular ultrasound guided stenting. *J Am Coll Cardiol*. 1995;25:182A. Abstract.
- Dav PP, Lowe HC, Walter BW, Barron DW, Cavaghan TP, Morgan H. Intracoronary stenting without intravascular ultrasound guidance followed by antiplatelet therapy with aspirin alone in selected patients. *Am J Cardiol*. 1996;77:1105-1107. [CrossRef](#) [Medline](#)
- Metz JA, Fitzgerald PJ, Oshima A, Hayase M, Weissman NJ, Diver DJ, Moses J, Benine CI, Uren NG, Oesterle SN, Yock PG. Impact of intravascular ultrasound guidance on stenting in the CRUISE substudy. *Circulation*. 1996;94(suppl I):I-109. Abstract.
- Rissen PJ, Teirstain PS, and the A.V.I.D. Investigators. Angiography versus intravascular ultrasound-directed stent placement. *J Am Coll Cardiol*. 1996;27:306A. Abstract.
- Vardi GM, Fishman PE, Meyers SN, Schaechter AG, Goodreau JM, Davidson CJ. Benefit of intracoronary ultrasound after angiographically optimal Palmaz-Schatz stent deployment. *Circulation*. 1996;94(suppl I):I-262. Abstract.
- Kuntz RE, Safian RD, Carrozza JP, Fishman PE, Mansour M, Baim DS. The importance of acute luminal diameter in determining restenosis after coronary atherectomy or stenting. *Circulation*. 1992;86:1827-1835. [Abstract/FREE Full Text](#)
- Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. Generalized model of restenosis after conventional balloon angioplasty, stenting and directional



- atherectomy. *J Am Coll Cardiol*. 1993;21:15-25. [Medline](#)
13. Ilmans VA, Keane D, Quaerdylien P, Serruys PW. Matching to guide the design and predict the outcome of randomized atherectomy trials. *Am Heart J*. 1995;130:1135-1143. [CrossRef](#) [Medline](#)
  14. Tobis JM, Mallory J, Mahon D, Lehman K, Zalesky P, Griffith J, Gassart J, Moriuchi M, McPae M, Dwyer MI, Green N, Henry WL. Intravascular ultrasound imaging of human coronary arteries in vivo: analysis of tissue characteristics with comparison to in vitro histological specimens. *Circulation*. 1991;83:913-926. [Abstract/FREE Full Text](#)
  15. Nishimura RA, Edwards WD, Warnes CA, Reeder GS, Holmes DR Jr, Taitik AJ, Yock PG. Intravascular ultrasound imaging: in vitro validation and pathologic correlation. *J Am Coll Cardiol*. 1990;16:145-154. [Medline](#)
  16. Nakamura S, Hall P, Blannino S, Maiello L, Itoh A, Martini G, Finci L, Colombo A. Reproducibility of intravascular ultrasound measurements. *Eur Heart J*. 1995;16:P1193. Abstract.
  17. Glagov S, Weisenberg E, Zarins CK, Stankunavicius K, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. *N Engl J Med*. 1987;361:1371-1375.
  18. Stiel GM, Stiel LC, Schofer J, Donath K, Mathay DG. Impact of compensatory enlargement of atherosclerotic coronary arteries on angiographic assessment of coronary disease. *Circulation*. 1989;80:1603-1609. [Abstract/FREE Full Text](#)
  19. Soblianko DP, Brown G, Mitten S. A new digital electronic caliper for measurement of coronary arterial stenosis: a comparison with visual and computer assisted measurements. *Am J Cardiol*. 1984;53:689-693. [CrossRef](#) [Medline](#)
  20. Theron HT, Lambert CR, Pepine CJ. Video densitometry versus digital calipers for quantitative coronary angiography. *Am J Cardiol*. 1990;66:1886-1890.
  21. Ryan TJ, Faxon DP, Gunnar RM, Kennedy JW, King SB III, Leon ED, Peterson KL, Reeves TJ, Williams DO, Winters WL Jr. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on assessment of diagnostic and therapeutic cardiovascular procedures. *Circulation*. 1988;78:486-502. [FREE Full Text](#)
  22. Hoffmann B, Mintz GS, Dussault GR, Popma JJ, Richard AD, Sattler JF, Kent KM, Griffin J, Leon MR. Patterns and mechanism of in-stent restenosis: a serial intravascular ultrasound study. *Circulation*. 1996;94:1247-1254. [Abstract/FREE Full Text](#)
  23. Moussa I, Di Mario C, Moses I, Di Francesco I, Reimers B, Tobis J, Colombo A. The impact of preintervention plaque area determined by intravascular ultrasound on luminal renarrowing following coronary stenting. *Circulation*. 1996;94(suppl 1):I-261. Abstract.
  24. Popma JJ, Topol EJ. Factors influencing restenosis after coronary angioplasty. *Am J Med*. 1990;88:1N,16N-24N. [Medline](#)
  25. Stone GW, Lincoff AM, Frey A, Mudra H, St Goar EG, Sheehan H, Hodson J. Incidence and implications of coronary dissection after PTCA using oversized balloons with intravascular ultrasound guidance: the CLOUT trial. *Circulation*. 1996;94(suppl 1):I-261. Abstract.
  26. Vardi GM, Fishman PE, Ailwadi GA, Parker MA, Meyers SN, Davidson CJ. Interaction of balloon size and pressure for optimal stent deployment using intracoronary ultrasound guidance. *Circulation*. 1996;94(suppl 1):I-262. Abstract.

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