A prospective, randomized trial of intravascular-ultrasound guided compared to angiography guided stent implantation in complex coronary lesions: The AVIO trial

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Background No randomized studies have thus far evaluated intravascular ultrasound (IVUS) guidance in the drug-eluting stent (DES) era. The aim was to evaluate if IVUS optimized DES implantation was superior to angiographic guidance alone in complex lesions.

Methods Randomized, multicentre, international, open label, investigator-driven study evaluating IVUS vs angiographically guided DES implantation in patients with complex lesions (defined as bifurcations, long lesions, chronic total occlusions or small vessels). Primary study endpoint was post-procedure in lesion minimal lumen diameter. Secondary end points were combined major adverse cardiac events (MACE), target lesion revascularization, target vessel revascularization, myocardial infarction (MI), and stent thrombosis at 1, 6, 9, 12, and 24 months.

Results The study included 284 patients. No significant differences were observed in baseline characteristics. The primary study end point showed a statistically significant difference in favor of the IVUS group (2.70 mm ± 0.46 mm vs. 2.51 ± 0.46 mm; $P = .0002$). During hospitalization, no patient died, had repeated revascularization, or a Q-wave MI. No difference was observed in the occurrence of non-Q wave MI (6.3% in IVUS vs. 7.0% in angio-guided group). At 24-months clinical follow-up, no differences were still observed in cumulative MACE (16.9%vs. 23.2 %), cardiac death (0%vs. 1.4%), MI (7.0%vs. 8.5%), target lesion revascularization (9.2% vs. 11.9%) or target vessel revascularization (9.8% vs. 15.5%), respectively in the IVUS vs. angio-guided groups. In total, only one definite subacute stent thrombosis occurred in the IVUS group.

Conclusions A benefit of IVUS optimized DES implantation was observed in complex lesions in the post-procedure minimal lumen diameter. No statistically significant difference was found in MACE up to 24 months. (Am Heart J 2013;165:65-72.)

Following the introduction of drug-eluting stents (DES) into clinical practice, restenosis rates have been dramatically reduced. Some concerns have been raised regarding the risk of late and very late stent thrombosis (ST) after DES implantation. However, the majority of ST still occur in the first 30-days following DES implantation,

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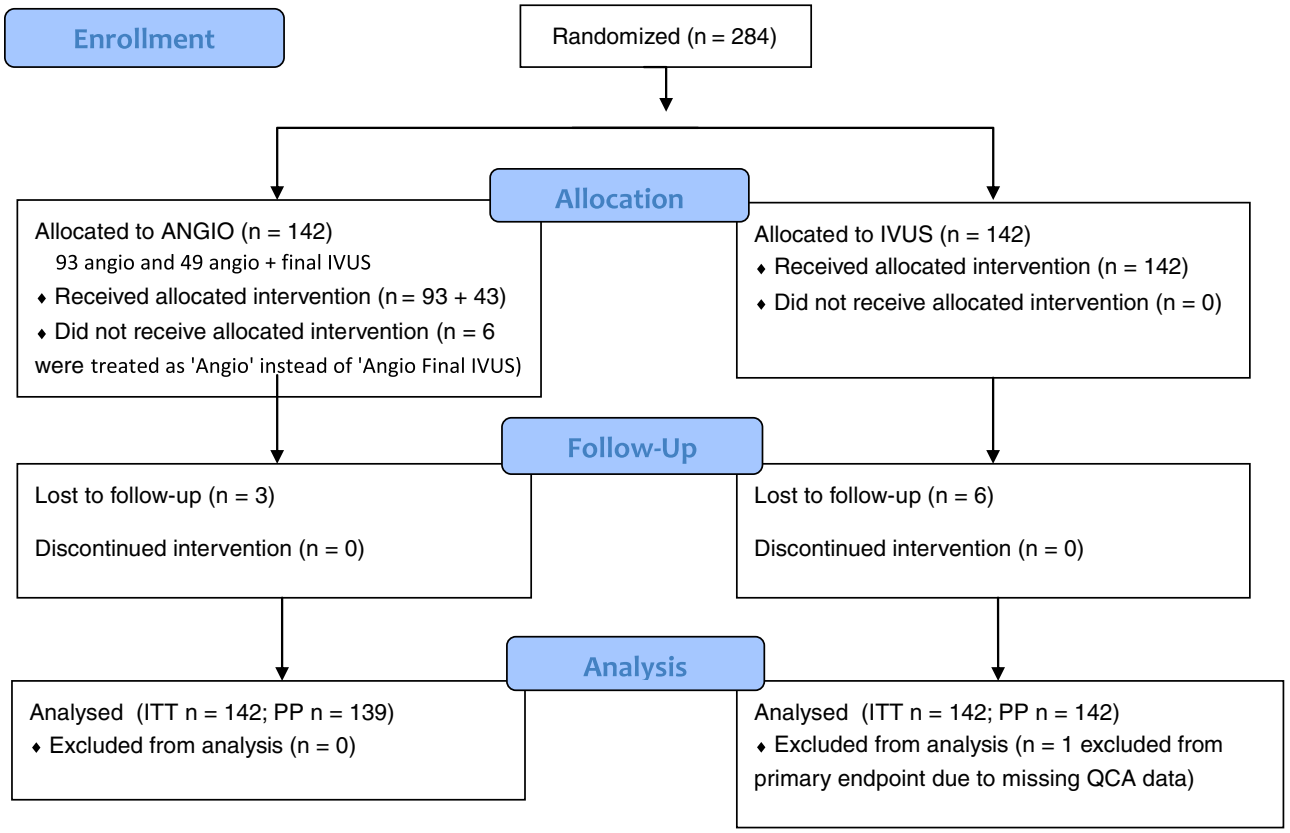
Figure 1



Study flow diagram.

mostly due to technical and procedural factors. Some studies suggest that stent under expansion remains one of the most important causes of restenosis and ST.[1]

Intravascular ultrasound (IVUS) guidance has therefore been advocated as a possible solution to optimize the results of stenting and theoretically reduce the risk of ST, in addition to improving restenosis rates and consequently the need for repeated revascularization. The final minimum luminal diameter (MLD) has been regarded as one of the most important determinants of restenosis,[2,3] with IVUS having the potential to maximize the final MLD. Recently it has been reported in some DES registries that IVUS guidance was correlated with a lower occurrence of myocardial infarction (MI) and mortality.[4,5] To our knowledge, no randomized studies have thus far evaluated IVUS guidance in the DES era.

The aim of the AVIO (Angiography Vs. IVUS Optimization) study was to evaluate the safety and efficacy of IVUS guided post-dilatation in increasing the final MLD, as compared with angiographic guided post-dilatation, in the setting of complex lesions treated with DES.

Methods

AVIO was a multi-centre, international, randomized, open-label, investigator-driven study (NCT00936169). The study flow diagram is reported in Figure 1. All consecutive patients from 18 centers, with complex lesions suitable for DES implantation, were included in the study if considered by the investigators eligible for randomization. For study protocol, there was not a screening log for the patients not entered in the study because not evaluated as eligible for randomization by the investigators. Complex lesions were defined as one of the following: long lesions (>28 mm); chronic total occlusions (CTO), ie, a total occlusion of duration more than 3-months; lesions involving a bifurcation; small vessels (≤2.5mm) and patients requiring 4 or more stents. All patients provided written informed consent prior to randomization and inclusion in the study. The study protocol was approved by the ethics committee of each participating center.

Data handling, monitoring and clinical event adjudication, core-lab quantitative coronary angiography (QCA) and IVUS measurements as well as statistical analysis were performed independently by Mediolanum Cardio Research (MCR), Milan, Italy.

The sponsor of the study was Fondazione Evidence, Milan, Italy.

The exclusion criteria were: contra-indication to dual antiplatelet therapy; ejection fraction <30%; renal failure (creatinine >2 mg/dL); significant comorbidities precluding clinical follow-up; MI in the 48 hours prior to the procedure; in-stentrestenosis; prior brachytherapy; venous or arterial grafts; unprotected left main stem stenosis; thrombocytopenia <100,000; recipient of a heart transplant; a positive pregnancy test in women of child-bearing potential; acute infection; planned major surgery leading to discontinuation of anti platelet therapy or prior bare metal stent; or DES implanted in the target vessel less than 1 year before enrolment (including 1 year from any inter current restenotic or thrombotic event). Patients who satisfied the inclusion and exclusion criteria were randomized in a 1:1 ratio at the time of the angiogram, through sealed opaque envelopes, to either IVUS optimized or angiographic guided DES implantation.

If patients were treated for more than one complex lesion meeting AVIO inclusion criteria, all the lesions had to be treated with the same DES, with all lesions treated according to the randomization with IVUS optimization or angiographic guidance. All patients were pretreated with ticlopidine or clopidogrelplus aspirin. A loading dose of 300 mg of clopidogrel was given to those patients not previously treated with thienopyridines.

Clinical follow-up was obtained at 30-days, 6, 9, 12 and 24 months (either by office visit or telephone contact). Angiographic follow-up was performed in patients who were symptomatic, had evidence of ischemia or equivocal results during non-invasive testing, or who had experienced an ischemic coronary event at any time following hospital discharge.

Angiography Guided Group

In patients randomized to the angiography guided group, all decisions regarding requirement for post-dilatation, balloon size for post-dilatation and the assessment of optimal stent expansion were based on angiography alone, being left to the discretion of the operator. However, post-dilatation was strongly recommended.

IVUS Guided Group and AVIO criteria for optimal stent expansion

In the IVUS guided group, IVUS was performed following DES implantation in order to assess optimal stent expansion. This was based on the optimal balloon size (OBS) that should be used for post-dilatation. The OBS was determined by averaging the media to media diameters of the distal and proximal stent segments, as well as at the sites of maximal narrowing within the stent. The value was rounded to the lower 0.00 or 0.50 mm. For values 3.5 mm or above, the operator could downsize the balloon diameter as per clinical judgment. Any segment inside the stent with a cross sectional area (CSA) less than the target criteria for the OBS (see AVIO criteria in Table I) was considered under expanded and post-dilatation was performed with a non-compliant balloon, selected according to the OBS. In order to avoid peri-stent dissections, the AVIO criteria were reduced by 10% at the proximal and distal stent edges. In lesions treated with overlapping or long stents, operators were encouraged to utilize multiple balloons of different sizes if tapering of the vessel was evident.

Table I. AVIO IVUS criteria

Optimal balloon size, mm	Nominal balloon area mm^2	Target area mm^2
2.50	4.91	4
3.0	7.07	6
3.5	9.62	8
4.0	12.56	10
4.5	15.90	12

Quantitative coronary angiography

Coronary angiograms were analyzed in an independent core angiographic laboratory (Angiographic Core Laboratory, MCR, Milan, Italy) with a semi automated edge contour detection computer analysis system (MedisQAngio XA 7.1) at baseline and following the procedure. The analysis was done in a blinded fashion: the technician did not know to which group the patient had been randomized. Quantitative analysis was performed of the "stent area" (in stent analysis including only the stented segment) and the in-segment area, which included the stented area as well as both 5 mm areas proximal and distal to the stent (in-segment analysis) and at the point of baseline MLD (in-lesion analysis). Since the primary endpoint of the AVIO study was the post procedural in-lesion MLD, in the post analysis the MLD was manually repositioned to the point of the original MLD (MLD pre-treatment). Acute gain was defined as the difference between the final MLD and the baseline MLD.

Quantitative IVUS

IVUS images were evaluated by an independent IVUS core laboratory (MCR, Milan, Italy). Measurements were performed at the following locations: the smallest lumen within the stent and the proximal and distal stent edges. The averages of the minimum and maximum lumen diameters at each location were used for diameter-related calculations. When 2 stents in a vessel overlapped, they were treated as a single segment for the current analysis. Analysis was performed of the first IVUS run performed after stent implantation and the final IVUS run after post-dilatation. Whether the AVIO criteria were met or not was evaluated by the IVUS core lab.

Study endpoints and definitions

The primary endpoint was post-procedural in-lesion MLD as evaluated by core laboratory QCA. This was the primary efficacy endpoint to test the superiority of the IVUS optimized over the angiography directed stent placement, in the intention to treat population.

Secondary endpoints were target lesion revascularization (TLR) at 9 months and major adverse cardiovascular event (MACE) at 30 days, 6, 9, 12, and 24-months. MACE was defined as the composite of any MI, cardiac death and target vessel revascularization (TVR).

Q-wave MI was defined as the development of pathological Q-waves post-procedure lasting at least 0.4s in two consecutive leads with an elevation of creatinine kinase 2 times the upper reference limit. Non–Q-wave post-procedural MI was defined as

Table II. Clinical characteristics of the study population

	IVUS (n = 142)	Angio (n = 142)	P
Age (y)	63.9 ± 10.1	63.6 ± 11.0	.83
Gender (M/F)	117/25	109/33	.24
Diabetes (%)	23.9	26.8	.56
Hypercholesterolemia (%)	70.4	76.8	.18
Hypertension (%)	70.4	66.9	.58
Current smokers (%)	34.5	31.0	.55
Unstable angina (%)	29.6	26.1	.80
LVEF (%)	55.3 ± 8.5	55.9 ± 8.6	.63

an elevation of creatinine kinase two times the upper reference limit with an elevated creatinine kinase–MB 2 times the upper reference limit. Repeat revascularization was classified as TLR if it occurred inside the implanted stent or within 5 mm proximally or distally, or as TVR for any repeated intervention in the same vessel by percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery. ST was classified according to Academic Research Consortium definitions.[6]

Sample size

The objective of the study was to evaluate if IVUS optimized DES implantation in complex lesions was superior to angiographic guidance alone in achieving a larger final MLD. A sample size of 145 patients per group was calculated in order to meet the primary endpoint requirements. The power calculation was based on an expected mean and standard deviation of the post-procedural MLD of 2.9 ± 0.4 mm for the IVUS optimized versus 2.7 ± 0.5 mm for angiographic guided DES implantation.

Statistical analysis

Data were analyzed according to the intention to treat (ITT) and Per Protocol principles (SAS 9.2; SAS Institute, Cary, NC). The ITT population included all randomized subjects who were treated and had at least one assessment after baseline. The ITT population was the primary population for the analysis. The Per Protocol analysis compared patients who did and did not meet AVIO criteria and the angiography guided group. Descriptive statistics (arithmetic mean, median as indicated, minimum, maximum and standard deviation) were calculated for continuous variables. Absolute frequencies and percentages were obtained for qualitative variables. Summary 95% confidence intervals were provided for variables subject to statistical inference. A $P < .05$ was considered statistically significant and all tests were two-sided. The difference in MLD between the two groups was assessed with the unpaired *t* test (the homoskedasticity condition was fulfilled). As an additional statistical test, a covariance analysis was also performed with the baseline MLD as a covariate. This paired difference in MLD between the two groups has been assessed with the unpaired t-test. All binary outcomes were evaluated by the χ^2 test. Time-to-event data for MACE were analyzed with Kaplan-Meier survival curves and compared with the log-rank test.

The statistical analysis was performed by an independent statistician from MCR.

Table III. Lesion characteristics of the study population

	IVUS (n = 182)	Angio (n = 179)	P
CTO (%)	13.6	17.8	.18
Bifurcations (%)	23.1	27.2	.96
Long lesions (%)	62.1	58.0	.31
Small vessels (%)	21.9	23.7	.84
LAD location (%)	53.3	48.6	.13

LAD, Left anterior descending artery.

Table IV. Procedural characteristics

	IVUS (n = 182)	Angio (n = 182)	P
Stent diameter, mm	2.95 ± 0.38	2.86 ± 0.36	.19
Stent length, mm	23.9 ± 6.74	23.2 ± 6.51	.49
Stent pressure, atm	15.6 ± 3.1	15.3 ± 2.6	.26
Postdilatation balloon diameter, mm	3.39 ± 0.47	3.15 ± 0.40	.002
Postdilatation max pressure, atm	20.3 ± 4.82	19.6 ± 4.0	.89

Results

Two hundred eighty-five patients were randomized into the study. Of these, one was erroneously randomized but not treated. The remaining 284 patients were randomized as follows: 142 to the IVUS group and 142 to the angiography group. The baseline clinical and lesion characteristics were similar between the 2 groups (Tables II and III). Most of the lesions included were long lesions: 62.1% in the IVUS vs. 58.0% in the angiography guided group; bifurcation lesions respectively in 23.1% vs. 27.2% and small vessels in 21.9% vs 23.7%. Furthermore, CTOs were present in 13.6% in the IVUS vs 17.8% in the angiography guided group. Post-dilatation was most frequently performed to the lesions treated in the IVUS group (88.3% vs 68.4%; $P < .0001$). Table IV reports the procedural characteristics of the study groups.

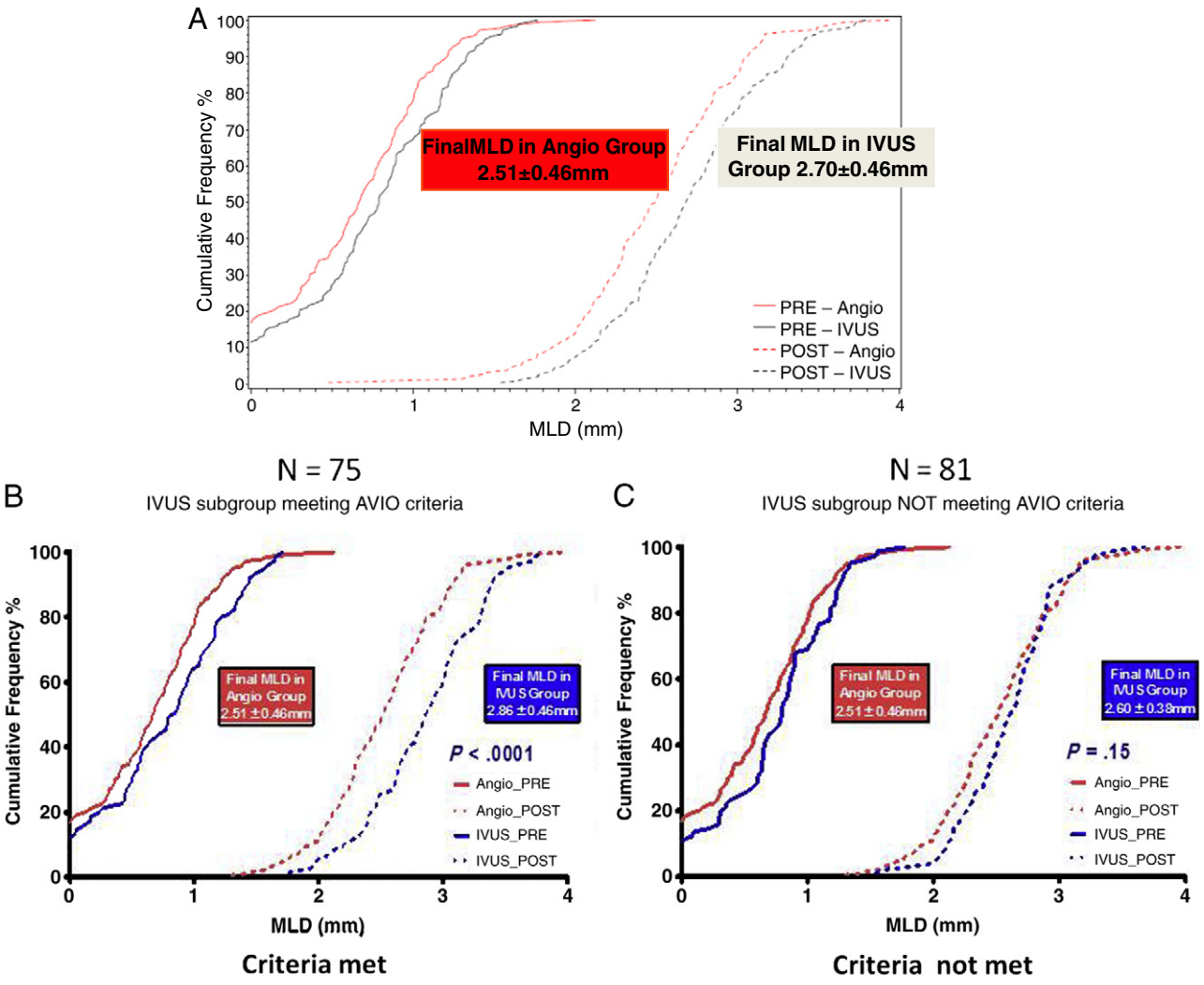
Primary study endpoint

The primary study endpoint (MLD in lesion) showed a statistically significant difference in favor of the IVUS group 2.70 ± 0.46 vs 2.51 ± 0.46 mm; $P = .0002$ for the unpaired *t* test for the analysis with lesions considered as independent; $P = .0207$ for analysis of covariance with lesions considered as not independent) (Figure 2A).

QCA measurements

QCA measurements are reported in Table V. A difference in baseline MLD was observed (0.76 ± 0.46 mm in IVUS vs. 0.65 ± 0.45mm in angiography guided group; $P = .01$). A larger final in-stent reference vessel diameter (RVD) and MLD (respectively 2.96 ± 0.46 vs

Figure 2



Cumulative frequency curves demonstrating the AVIO results. A, Primary study end point. Baseline and final MLD in angiography as compared to IVUS guided. B, Baseline and final MLD in angiography vs IVUS subgroup meeting AVIO criteria. C, Baseline and Final MLD in angiography vs IVUS subgroup not meeting AVIO criteria.

2.83 ± 0.43 mm; $P = .005$ and 2.55 ± 0.46 mm vs 2.39 ± 0.42 mm; $P = .0006$) and lower final stenosis (13.9 ± 7.3% vs 15.5 ± 7.9%; $P = .05$) were seen in the IVUS group. A larger final RVD (2.94 ± 0.42 mm vs 2.81 ± 0.45 mm; $P = .004$) and lower final stenosis (8.4 ± 7.9% vs 10.5 ± 9.0%; $P = .02$) were observed in the IVUS group. No difference was observed in in-lesion acute gain (1.93 ± 0.59 mm in the IVUS vs 1.87 ± 0.63 mm in the angiography group; $P = .31$).

Clinical outcomes at 1 and up to 24 months

Clinical outcomes at 1 and 24 months are reported in Table VI. Interestingly, in our study only one coronary perforation occurred during the index procedure, which was observed in a patient in the angiography guided group. At 1 month, no patient had a Q-wave MI. No difference was observed in the occurrence of non-Q-wave MI (7.0% in both groups). One patient had a TLR in the IVUS group and one cardiac death occurred in the angiography group. In total, only one definite subacute ST occurred in the IVUS group.

At 24 months clinical follow-up, no differences continued to be observed in the occurrence of cumulative MACE in the IVUS vs the angiography guided group (16.9% vs 23.2 %). Additionally, no differences were found in the occurrence of cardiac death (0% vs 1.4%), MI (7.0% vs 8.5%), TLR (9.2% vs 11.9%) or TVR (9.8% vs 15.5%).

Table V. Quantitative coronary angiography measurements evaluated by independent core lab

	IVUS	Angio	*P* value
Baseline			
RVD (mm)	2.67 ± 0.46	2.62 ± 0.41	
Lesion length (mm)	27.4 ± 15.9	25.5 ± 15.0	
Baseline MLD (mm)	0.76 ± 0.46	0.65 ± 0.45	.01
Baseline stenosis (%)	71.6 ± 15.8	75.5 ± 16.1	
Post-procedure			
In Lesion			
Final RVD (mm)	2.94 ± 0.42	2.81 ± 0.45	.004
Final stenosis (%)	8.4 ± 7.9	10.5 ± 9.0	.02
Final MLD (mm)	2.70 ± 0.46	2.51 ± 0.46	.0002
Acute gain (mm)	1.94 ± 0.59	1.86 ± 0.63	.31
In stent			
Final RVD (mm)	2.96 ± 0.46	2.83 ± 0.43	.005
Final stenosis (%)	13.9 ± 7.3	15.5 ± 7.9	.05
Final MLD (mm)	2.55 ± 0.46	2.39 ± 0.42	.0006
In segment			
Final RVD (mm)	2.83 ± 0.55	2.72 ± 0.51	.05
Final stenosis (%)	26.8 ± 11.2	25.39 ± 11.7	.22
Final MLD (mm)	2.10 ± 0.58	2.03 ± 0.50	.35

Table VI. Major adverse cardiac events at 1 and 24 months

	IVUS (n = 142)	Angio (n = 142)
30 d MACE		
Q wave MI	0 (0%)	0 (0%)
Non-Q wave MI	10 (7.0%)	10 (7.0%)
TLR	1 (0.7%)	0 (0%)
TVR (including TLR)	1 (0.7%)	0 (0%)
Cardiac death	0	1 (0.7%)
Cumulative at 24-month MACE		
MI	10 (7.0%)	12 (8.5%)
TLR	13 (9.2%)	17 (11.9%)
TVR (including TLR)	14 (7.8%)	22 (15.5%)
Cardiac death	0	2 (1.4%)

P value was NS for all comparisons.

Sub-analysis according to AVIO criteria

An IVUS image run was available for analysis in 156 (86.0%) of 182 treated lesions. In the 26 remaining lesions, IVUS analysis was not possible, either due to the IVUS not being performed, poor image quality or technical issues regarding the digital storage of IVUS images. Only 75 (48.1%) of 156 of the lesions in the IVUS group met the AVIO criteria for optimal stent expansion. In this subgroup, the primary study end point was met (2.86 ± 0.46 vs 2.51 ± 0.46 mm; $P = .0001$) (Figure 2, Panel B). Also, the in-lesion acute gain was significantly higher in this group than the angiography-guided group (2.07 ± 0.59 vs 1.87 ± 0.63 mm; $P = .02$). Conversely, in the 81/156 (51.9%) lesions that did not meet the AVIO criteria, the primary study end point was not met (2.6 ± 0.38 vs 2.51 ± 0.46 mm; $P = .15$) (Figure 2C). Furthermore, acute gain was not different in this group compared with the angiography guided cohort (1.84 ± 0.52 vs 1.87 ± 0.63 mm; $P = .70$).

Discussion

The main findings of this study are: (1) a larger final in-lesion MLD was obtained with IVUS-guided DES post-dilatation (primary end point); (2) IVUS guided post-dilatation was a relatively safe procedure (no difference in 30-day MACE); (3) no difference was observed in cumulative MACE between IVUS and angiography guided procedures at 24-months; (4) a sub-analysis evaluating patients who did or did not meet AVIO criteria, confirmed that achieving the criteria was associated with a higher final MLD and acute gain; conversely in patients who did not meet the AVIO criteria, no advantage was observed in the IVUS group and (5) with current lesion preparation, stent delivery and post-dilatation technologies, optimal stent expansion could only be achieved in 48% of lesions randomized to IVUS guidance.

At the present time, the utility of IVUS guidance is debated due to the perceived minimal clinical benefit from a procedure that requires extra cost and time[7] and also due to the significant reduction inrestenosis that has occurred following the introduction of DES into clinical practice. However, concerns have been raised regarding the risk of late and very late ST after DES implantation. Delayed endothelialization, under-expansion and incomplete stent apposition have been proposed as causally related to stent thrombosis.[8-10]In addition, the problem of DES restenosis is far from being resolved.[11] Recently data from some DES registries suggested that IVUS guidance is correlated with lower MI and mortality rates.[4,5]Only 2 randomized trials have demonstrated a modest clinical benefit from bare metal stent using IVUS guidance.[12,13] The TULIP study (thrombocyte activity evaluation and effects of ultrasound guidance in long intracoronary stent placement) demonstrated a significant improvement in clinical TLR (4% vs 14%; $P < .05$), but the study was confined to lesions longer than 20 mm and with a stent diameter >3 mm.[12]In this study, the difference between the final MLD post-stenting between the IVUS guided group and the angiography guided group was 0.21 mm, a value relatively high compared to prior studies. The larger randomized AVID trial (angiographic versus IVUS direct stent placement), reported a trend towards a significant reduction in 12-month clinically driven TLR (8% vs. 12%; $P < .08$).[13]However, significance was achieved only in vessels of about 2.5–3.5 mm in diameter (TLR: 4% vs. 10%; $P < .01$) and in PCI for saphenous vein graft lesions (TLR: 5% vs. 21%; $P < .01$). This study had limitations similar to those of the TULIP study, with only modest differences in the final MLD and in-stent CSA between lesions using angiographic guidance versus IVUS guidance.

One major problem in the field of IVUS guidance has been the lack of consensus regarding the definition of optimal stent placement. To date, there have been numerous studies utilizing different criteria to determine optimal IVUS-guided balloon dilatation or stenting. The majority of these studies utilized the MUSIC (Multicenter Ultrasound Stenting In Coronaries) criteria.[14] In the original study, 81.0% of lesions fulfilled all three criteria, a figure which has been difficult to replicate in subsequent IVUS guided studies (48.0% in AVID[13] and 56.0% in OPTICUS[15] using IVUS optimization to reduce in-stentrestenosis). Recently, we introduced the PRAVIO criteria, adapted from our previous experience regarding stent under-expansion and IVUS-guided DES implantation. The theory was to perform stent optimization based on selecting a post-dilatation balloon according to the vessel size that is consistent with positive or negative remodeling of the atherosclerotic artery. The advent of newer generation non-compliant balloons improved the capacity to perform more aggressive post-dilatation, while minimizing the risks of coronary rupture. In the PRAVIO study,[7] our target criteria for optimal stent expansion was to achieve a final minimum stent CSA of at least 70% of the hypothetical CSA of the fully inflated balloon used for post-dilatation. The size of this balloon did not follow any specific recommendations. However, we observed that in many lesions, we were able to obtain a larger CSA than our proposed target. This finding led us to propose new criteria (AVIO criteria, see Table I) based on the actual achievable target. It is interesting to note that for each specific final balloon size, the mean value proposed minus one standard deviation is quite close to 70% of the CSA of the utilized balloon. An important attribute of the AVIO criteria is that they can be useful in long lesions, as the stent is evaluated at different segments throughout its length. In addition, these criteria take advantage of the larger vessel size due to positive remodeling.

In our study, only complex lesions were included, such as CTO, bifurcations, small vessels and long lesions that we know are associated with higher restenosis rates even in the era of DES. Because of the exploratory nature of our study, the primary study endpoint was the final MLD. Nevertheless, there is a large body of data suggesting that a large final MLD is a major determinant of the follow-up MLD.[2,3] In the overall population, the primary study endpoint was achieved, with a significant advantage in the final MLD in favor of the IVUS guided group (2.70 vs 2.51 mm; $P = .0002$). As expected, when we analyzed separately patients who did and did not meet the AVIO criteria, the advantage in the final MLD and acute gain with IVUS guidance was significantly higher in the subgroup of patients who met the criteria. However, in the subgroup of patients who did not meet the criteria there was no advantage observed. Interestingly, when comparing the baseline clinical and lesion characteristics in the IVUS guided subgroup, whether the optimal criteria were reached or not, there was no difference between the 2 groups. It is important to emphasize that AVIO criteria were met in only 48% of the lesions. It is not clear if this is due to the fact that these criteria were too ambitious to be obtained in such complex lesions or that the operators did not feel comfortable and had anxieties regarding the possible complications of aggressive post-dilatation. Nevertheless, in our study, IVUS-guided post-dilatation was confirmed to be safe and no complications occurred during the index PCI in this group. Furthermore, no coronary perforations were observed in the IVUS-group; conversely one perforation occurred in the angiography-guided group.

Moreover, at 1 month, no patients had a Q-wave MI and no difference was observed in the occurrence of non-Q-wave MI (7.0% in both groups). Despite the fact that the IVUS group met the primary endpoint, no significant differences were observed in TLR (9.2% vs. 11.9%) and TVR (9.8% vs. 15.5%) or in the composite of MACE at 24 months. Clearly, the low rate of angiographic follow-up lowered the possibility of detecting asymptomatic restenosis and in addition the protocol did not contemplate a formal non-invasive evaluation at follow-up in order to detect silent ischemia. Angiographic follow-up was only performed in approximately 30% of the patients and in this group of patients, the restenosis rates were 28.6% in the angiography vs 17.5% in the IVUS group.

Another factor that should be taken into consideration is that the top enrolling center has a large experience in IVUS guidance. In all possibility, such an extensive experience may have lowered the potential difference between angiography and IVUS guidance, due to the fact that in this center experienced operators develop an "IVUS eye" leading to an ability to perform very aggressive post-dilatation even with only angiographic guidance. In support of this hypothesis, is the fact that when the primary endpoint was analyzed center by center, there was no difference in the final MLD between the IVUS and angiography guidance groups in the top enrolling center. Another possible limitation explaining the low percentage of patients meeting AVIO criteria, is the fact that IVUS was not performed prior to stent implantation. Pre-intervention IVUS may have given a clearer idea of the "true" media-to-media diameter of the vessel and the need for better lesion preparation. A final consideration is the need of better technologies to allow this optimal lesions preparation and stent post-dilatation in order to achieve a larger stent expansion in a greater number of lesions.

Regarding ST, only one patient had a definite subacute ST, which occurred in the IVUS group, with no patient having a probable or possible ST in either of the groups. It is interesting to note that the patient with a subacute ST at

7 days after the procedure had a focal area of severe under-expansion on IVUS, with a final minimal stent CSA of 1.94 mm^2. Certainly because of the small study population, we could not anticipate to detect any differences in such a rare event as ST. A larger study is warranted in order to test if the AVIO criteria could translate into a clinical advantage, reducing repeated revascularization and furthermore ST.

Conclusions

A larger post-procedural MLD was obtained with IVUS-optimized DES implantation compared to angiographic-guidance. No difference was found at 24-months in the occurrence of MACE.

Disclosures

None

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