Title

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Authors

Hall, P
Nakamura, S
Maiello, L
et al.

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Clinical and Angiographic Outcome After Palmaz–Schatz Stent Implantation Guided by Intravascular Ultrasound

Patrick Hall, MD, Shigeru Nakamura, MD, Luigi Maiello, MD, Yaron Almagor, MD, Antonio Gaglione, MD*, Steven L. Goldberg, MD, Jonathan M. Tobis, MD**, Giovanni Martini, CCP, Gina Tucci, RN, Marinella Di Maggio, MD, Antonio Colombo, MD

ABSTRACT: Intracoronary stents can be implanted with a low incidence of stent thrombosis (< 1%) when the stent procedure is guided by intravascular ultrasound. The long–term clinical and angiographic effects, however, have not been reported. This study assesses the 6 month clinical and angiographic results of a consecutive series of patients with intravascular ultrasound guided Palmaz–Schatz stent deployment that were not treated with subsequent anticoagulation after a successful stent implantation procedure.

From March, 1993 to April 1994, 411 patients underwent Palmaz–Schatz stent implantation. There were 26 patients that had uncomplicated Palmaz–Schatz stent implantation that were treated with a standard anticoagulation regimen that are not evaluated in this study. Thus, this study includes an assessment of 385 patients that had either a successful intravascular ultrasound guided stent implantation procedure and did not receive post procedure anticoagulation or had a procedural complication. Procedural success was achieved in 369 patients (96%). Clinical success (procedure success without early post procedure event) was achieved in 363 patients (94%). There were 2 acute stent thrombosis events (0.5%) and 1 subacute stent thrombosis (0.3%) in the group of 369 patients with 454 lesions treated without anticoagulation. At 6 month clinical follow–up the incidence of myocardial infarction was 4.9% and the rate of coronary bypass surgery was 6.2%. There was a 2.1% incidence of death. Emergency intervention (emergency angioplasty or bailout stent implantation was necessary in 3 patients (0.8%). The total incidence of repeat percutaneous intervention was 11.4%. By 6 months clinical follow–up, major events had occurred in 19.2% of patients. The angiographic lesion restenosis rate, according to 50% diameter stenosis criteria, was 19%. The incidence of restenosis per patient was 22%. In conclusion, intravascular ultrasound guided Palmaz–Schatz can be performed without subsequent anticoagulation with a low incidence of stent thrombosis and acceptable clinical and angiographic outcome at 6 month clinical follow–up.

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The potential utility of the intracoronary stent to decrease restenosis was first noted after the initial clinical evaluation of the self expanding Wall stent.[1] Subsequently, the early observational clinical trials with the Palmaz–Schatz stent suggested a similar potential benefit in reducing restenosis.[2-6] These early investigations led to multicenter randomized trials in America (STRESS) and Europe (Benestent) comparing elective Palmaz–Schatz stent implantation with angioplasty for the treatment of de novo coronary lesions. Both studies

From Centro Cuore Columbus, Milan, Italy, * Villa Bianca, Bari, Italy, ** University of California Irvine, Orange, California, USA.

Address for reprints: Antonio Colombo, MD, Centro Cuore columbus, Via M. Buonarotti 48, 20145 Milan, Italy.

demonstrated a significant reduction in the restenosis rate in the group treated with stents.[7,8] In addition, in the Benestent trial the reduction in restenosis rate was associated with a significant reduction in major clinical events in the group randomized to stents.[8] Despite the promising long–term results, both of these trials had excessive stent thrombosis and vascular complications.

More recently, a prospective study on intravascular ultrasound guided stent implantation has shown that intracoronary stents can be safely implanted without using post–procedure anticoagulation.[9,10] The short term benefit of this strategy is evident with regard to a low incidence of stent thrombosis (0.9%) and vascular complications (0.3%). Technical factors such as optimizing stent expansion by high pressure stent dilation and covering the extent of the lesion to reduce potential flow disturbances in conjunction with intravascular ultrasound confirmation of result all had an impact on reducing the rate of early post–procedural complications.

Although the short–term results of this prospective study are encouraging, the effects on restenosis and long term clinical outcome are not known. In particular, both media stretch by vigorous dilation[11-13] and the use of multiple stents[14] has been reported to have an unfavorable impact on increasing restenosis. The extent that these factors are balanced by the benefit derived from an increase in luminal diameter is not certain. The focus of this report is, thus, on the angiographic and cumulative 6 month clinical follow–up of the 369 consecutive patients that were treated only with antiplatelet agents following the completion of a successful intravascular ultrasound guided stent implantation procedure.

METHODS

Between March 30, 1993 and April 1, 1994, there were 411 patients that underwent Palmaz–Schatz intracoronary stent implantation. Of this cohort there were 26 patients that were treated with anticoagulation following the stent procedure. This included 10 patients that did not have intravascular ultrasound performed, 8 patients that had an unsuccessfully attempted intravascular ultrasound evaluation, and 8 patients that had a suboptimal intravascular ultrasound evaluation. Although these patients, treated with a standard anticoagulation regimen consisting of short term heparin and coumadin did not have any early stent thrombosis events, they were excluded from analysis in this investigation in order to focus on the short–term and long–term effects of a strategy involving intravascular ultrasound guided stent implantation. In the remaining 385 patients with 484 lesions, 16 patients had procedural complications. Although 6 of these complications occurred after intravascular ultrasound was performed, all the patients with procedural complications were included for analysis in this study. This was felt to be particularly important to provide a prospective on the safety and long–term effect of aggressive stent implantation techniques such as high pressure balloon dilation and the frequent implantation of more than one stent to provide full lesion coverage as well as the impact of intravascular ultrasound and the safety of stent implantation without anticoagulation. The clinical evaluation relative to stent thrombosis, vascular complications, and restenosis concentrates on the 369 patients with 454 lesions that did not have subsequent anticoagulation after a successful intravascular ultrasound guided stent implantation procedures.

The criteria for study entry were: 1) coronary artery disease manifested by clinical symptoms or objective evidence of myocardial ischemia either on exercise test or by nuclear scintigraphy; and 2) angiographic evidence of single or multiple vessel coronary disease with target lesion stenosis > 70% by visual estimate. The exclusion criteria included: 1) small vessels less than 2.5 mm by visual estimate; and 2) angiographically diffuse distal disease that might compromise outflow after stent insertion. There were no specific age or ejection fraction limitations for study entry. Patients were not excluded on the basis of indication for stent implantation, lesion location, or complex lesion morphology. Thus, patients with ostial lesions, tortuous vessels, diffuse disease, long lesions, tandem lesions and lesions with thrombus or severe calcification were eligible for study entry.

Stent Implantation Procedure

Prior to the stent procedure, patients received Aspirin 325 mg and a calcium channel antagonist. A bolus of 10,000 units of heparin was given after sheath insertion. An additional bolus of 5,000 units was given to maintain an activated clotting time greater than 250 seconds. Patients did not

receive Dextran, persantine, or ticlopidine prior or during the stent procedure. Five different types of Johnson and Johnson tubular slotted stents were utilized during the course of this study: the Palmaz–Schatz stent and a short stent composed of one 7 mm tubular slotted segment were used most commonly. A 10 mm long biliary stent, a 20 mm renal stent composed of two 10 mm segments with a central articulation and a short (disarticulated) renal stent were infrequently used. A pre–mounted stent delivery system was also used sparingly during the study (n = 25). After pre–dilation, stents were hand crimped on balloons and implanted under fluoroscopic guidance. Further dilations (angiographic optimization) were performed to achieve an acceptable angiographic result with less than 20% residual stenosis by visual estimates. After the angiographic results was considered acceptable and the procedure would ordinarily be terminated, intravascular ultrasound was performed. All subsequent treatment decisions were based on the ultrasound results in conjunction with angiographic assessment.

Stent implantation was performed for a number of indications during the course of this investigation. The indications for placement of stents were defined as follows: *acute occlusion stenting* was undertaken to relieve ischemia associated with complete vessel closure (100%) following angioplasty with no or markedly delayed grade 0 or 1 Thrombolysis in Acute Myocardial Infarction (TIMI) flow; *threatened closure stenting* was performed when the angioplasty was complicated by a longitudinal or spiral dissection associated with > 50% luminal encroachment (with or without compromised flow), and evidence of ischemia; *suboptimal result stenting* was defined as insertion of a stent for a focal dissection or significant vascular recoil following angioplasty that resulted in > 50% luminal narrowing but was not associated with ischemia; *restenosis stenting* was performed for lesions with a history of restenosis following one or more previous angioplasty procedures; *chronic occlusion stenting* was performed after reopening a vessel that had been occluded for more than 2 months; *elective stenting* was performed when the operator believed a better result would be obtained with a stent instead of balloon angioplasty. *Multiple stents* was defined as the use of more than 1 Palmaz–Schatz® (15mm) stent. Short stents were counted as a half stent. Biliary, disarticulated renal stents and renal stents were counted as 1 stent each.

Intravascular Ultrasound Equipment Measurements and criteria for optimal stent expansion

The coronary arteries were imaged using a 3.9 Fr monorail system with a 25 MHz transducer tipped catheter (Interpret Catheter, Inter-Therapy/CVIS, Sunnyvale, Cal.) or a 2.9 Fr catheter from Cardiovascular Imaging Systems, Inc. (CVIS/Sunnyvale, Cal.). Images were obtained using a manual pullback system. On line quantitative measurements were performed during the procedure. All images were stored on super VHS videotape. After advancing the catheter distal to the stent, images were recorded during slow pullback. Measurements were made at a distal and proximal reference site and at the tightest point within the stent as previously described.[9,10,15,16] At the proximal and distal reference sites, the following measurements were made within 5 to 10 mm of the stented segment: Vessel cross–sectional area (CSA), vessel minimal and maximal diameters, lumen CSA, and lumen minimal and maximal diameters. The border of the vessel was defined on the ultrasound image as the outer boundary of the echolucent media surrounding the plaque. Lumen measurements were made at the inner border of the echo dense plaque. The tightest site within the stent was identified and lumen CSA, and diameter measurements were made. Intravascular ultrasound imaging was performed in the reference sites and in the stented segment at the initial intravascular ultrasound evaluation and after each series of balloon dilations. Measurements were made at the tightest point within the stented segment and after each series of balloon dilations.

Intravascular ultrasound was first performed after obtaining a good angiographic result. There were several qualitative and quantitative criteria for optimal stent expansion as previously reported.[9,10,15,16] The qualitative criteria for evaluation of the stent site involved the achievement of good stent apposition to the vessel wall with good plaque compression. The quantitative assessment of optimal stent expansion evolved during the course of the investigation. For the majority of the lesions (n = 339), 60% of the average of the proximal and distal cross–sectional vessel area was the

target for defining intravascular ultrasound success. The quantitative criteria for optimal stent expansion was altered in the last 115 lesions so that the goal was to achieve an intrastent lumen CSA ≥ the distal reference lumen CSA. A final ultrasound criteria was that the non–stented segments immediately adjacent to the stent (proximal or distal) did not reveal evidence of a significant lesion defined as a cross–sectional area stenosis > 60 percent relative to the adjacent reference lumen. When a significant lesion was observed in these segments, angioplasty or, more commonly, stent implantation was performed.

Balloon Dilation and Stent Implantation Strategy

The final stent balloon dilatations were performed with minimally compliant short balloons (generally the 9 mm Chubby, Schneider, Geneva, Switzerland) or non–compliant balloons (NC Shadow, Scimed Life Systems, Maple Grove, Minn., USA). The compliant short balloons were inflated up to 16 atmospheres and the non–compliant balloons up to 20 atmospheres.

Angiographic analysis

Coronary angiograms were analyzed by experienced angiographers not involved in the stenting procedure. The lesions were measured from an optically magnified image in a single, matched "worst" view using digital calipers (Brown and Sharp, North Kingston, RI). The guiding catheter was used as the reference object for magnification calibration. Previous studies have shown that digital calipers correlated closely with computer assisted methods with a low interobserver and intraobserver variability.[17,18] Minimal lumen diameter and percent diameter stenosis were obtained on the baseline, final angiograms and follow–up angiograms. The diameter of the proximal and distal vessel reference sites were averaged to obtain a mean reference diameter. The average reference diameter was used to calculate the percent diameter stenosis at baseline and final angiogram. Lesion length was measured on baseline angiography from the point at which the lumen was compromised by 50% at the proximal or distal reference vessel site. Long lesions were defined as a single continuous narrowing greater than 20 mm. Lesions were characterized according to the modified American College of Cardiology–American Heart Association (ACC/AHA) score.[19]

Post Procedure Medication Protocol and Follow–up

All patients in this study satisfied angiographic and intravascular ultrasound criteria for success and were treated only with antiplatelet therapy following the stent procedure. Sheaths were removed when the ACT had normalized to less than 150 seconds. When procedures were performed in the evening, heparin was infused overnight and the sheaths were removed the following morning. Patients received either aspirin 325 mg/day or a Ticlopidine 250 mg bid for 1 to 2 months with aspirin 325 mg/day for 5 days.

Patients underwent clinical evaluation within 4 weeks of hospital discharge, at 2 months and 6 months following the stent procedure. Follow–up angiograms were generally performed at 4 to 6 months. Follow up angiograms were performed sooner than 4 months if clinical symptoms warranted earlier evaluation. Only those angiograms performed after 3 months following the procedure were eligible for angiographic analysis.

Events

Major clinical events were considered death, emergency bypass surgery, elective bypass surgery, myocardial infarction (Q wave or non Q wave), emergency repeat intervention (bail out stenting or repeat angioplasty) and vascular complications. Specific major event definition were as follows: *death:* any death irrespective of cause. A diagnosis of *Q wave myocardial infarction* was made when there was the documentation of new pathologic Q waves (≥ 0.14 seconds) on an electrocardiogram in conjunction with elevation of creatine kinase to greater than twice the upper limit of normal. A diagnosis of *non Q wave myocardial infarction* was defined as elevation of the cardiac enzymes to greater than twice the upper limit of normal without the development of new pathologic Q waves. *Emergency coronary bypass surgery* was defined as bypass surgery involving immediate transfer of the patient from the catheterization laboratory to the operating room. *Elective coronary bypass surgery* was non–emergent bypass surgery performed more

than 24 hours after a stent procedure for procedural failure in the absence of ischemia or evolving myocardial infarction. *Acute thrombosis events* were defined as angiographically documented occlusion with TIMI grade 0 flow at the stent site occurring within 24 hours of the stent procedure. *Subacute thrombosis events* were angiographically documented occlusions with TIMI grade 0 flow at the stent site occurring beyond 24 hours of the stent procedure. *Emergency intervention:* Bail out stenting or emergency angioplasty performed for ongoing acute ischemia or evolving myocardial infarction in the setting of an angiographically documented stent thrombosis event. *Repeat angioplasty:* non emergency angioplasty performed for symptomatic restenosis. *Vascular complications* were defined as the occurrence of bleeding or hematoma formation at the access site requiring transfusion, vascular repair, or external compression.

Events were categorized as intraprocedural complications, post–procedural events that occurred during hospitalization (hospital events), events that occurred after hospital discharge up to two months (short–term post–hospitalization events) and late events that occurred between 2 and 6 months clinical follow–up. Cumulative events were reported at 6 months clinical follow–up. The separation of intraprocedural and early post–procedural events was done to evaluate the safety of the intravascular ultrasound guided stent implantation procedure and to assess the efficacy of antiplatelet therapy without anticoagulation following a successful stent procedure. Angiographic restenosis was defined as the occurrence of a 50% diameter stenosis at the time of angiographic follow–up.

Statistics

Normally distributed data is expressed as the mean ± one standard deviation (SD). Data that are not normally distributed are expressed as a median with a range of values. Comparisons between equivalent groups were performed by paired Student's t test. Subgroup comparisons of discrete variables were made by $\chi 2$ analysis. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Patient, Angiographic and Procedural Characteristics

The clinical characteristics and indications for use of a stent in the 385 patients undergoing Palmaz–Schatz stent implantation are shown in Table 1. Angiographic and procedural characteristics are presented in Table 2. The majority of stent procedures were performed electively (68%). There were a total of 473 lesions treated in 424 vessels. A total of 895 stents were implanted. Biliary and Renal stents were a minority of the total stents that were used. Similarly, the stent delivery system was used to deliver only 26 stents (2.9%). Multiple stents were implanted in 40% (188 of 473) of lesions, and in 53% (204 of 385) of patients. The mean number of stents per lesion was 1.44 ± 0.82 (range 0.5 to 9 stents/lesion), per vessel 1.60 ± 0.96 and per patient 1.80 ± 1.10.

Procedural Success

Procedure Success was achieved in 369 of 385 patients (96%). The 369 patients that had both a good angiographic result and adequate stent expansion by intravascular ultrasound criteria were treated with antiplatelet medications and did not receive additional anticoagulation (heparin or Warfarin). During the 2 month short term clinical follow up, there were 4 stent throm-

Table 1. Baseline Clinical Characteristics

	n	%
Study Patients	385	
Age (years) mean	58 ± 10	
Gender: Male	349	91%
Rick Factors		
Hypercholesterolemia	184	48%
Active Smoker	171	44%
Family History	156	41%
Hypertension	125	32%
Diabetes	51	13%
Previous Myocardial Infarction	194	50%
Previous Angioplasty*	69	18%
Previous Bypass	37	10%
Mean LV Ejection Fraction	57 ± 10	
Unstable Angina	139	36%
Multivessel Disease	179	46%

Table 2. Angiographic and Procedural Characteristics

n= 473	n	%
Indication for stent implantation		
Elective	320	68%
Restenosis	49	10%
Suboptimal result	51	11%
Emergency*	25	5%
Following chronic occlusion Recanalization	28	6%
Vessel dilated		
LAD	240	57%
RCA	108	25%
LCX	59	14%
Vein Graft	8	2%
Left Main	9	2%
Lesion site		
Ostial	32	7%
Proximal	186	39%
Mid vessel	218	46%
Distal	37	8%
Small Reference Vessel (< 3.0 mm)	107	23%
Long Lesion (> 20 mm)	45	10%
Modified AHA/ACC lesion type		
A	33	7%
B_1	184	40%
B_2	189	40%
C	67	14%
Type and number of stents		
Palmaz–Schatz	460	
short stent	406	
Biliary/Renal stent	29	
Total Stents	**895**	

* Threatened or Acute vessel closure

bosis events in the 369 patients (1.1%) with 399 lesions (0.9%) treated only with antiplatelet therapy and no anticoagulation.

Unsuccessful Stent Implantation and Intraprocedural Events

Unsuccessful stent implantation associated with a major event occurred in 16 patients (4.2%) as shown in Table 3. In these 16 patients, myocardial infarction occurred in 11 patients (3.1%), only 5 of which were Q wave myocardial infarctions (1.4%). Emergency bypass was performed in 11 patients (3.1%), and elective bypass in 2 patients (0.6%). Intraprocedural death occurred in 3 patients (0.8%). Unsuccessful stent implantations associated with major clinical events were due to unsuccessful stent delivery in 5 patients (1.4%) and occurred after successful stent delivery to the lesion site in 11 patients (3.1%). Unsuccessful stent delivery was due to incomplete lesion coverage in 3 patients, left main dissection from guiding catheter trauma prior to stent delivery in 1 patient and from left anterior descending artery dissection that occurred during stent delivery into an angulated circumflex in 1 patient. Causes of complications after successful stent delivery included distal embolization in a degenerated vein graft in one patient, dissection from the intravascular ultrasound catheter in 1 patient. After successful stent delivery, stent site optimization complications were due to non occlusive dissections in 4 patients (1.1%), coronary vessel rupture occurred in 4 patients, and side branch compromise during stent optimization in 1 patient.

Early Post Procedural Events

Early post–procedural hospital events occurred in 6 patients (Table 3). Two patients had acute thrombosis events at the stent site 3 hours, 12 hours following the stent procedure. Both of these events were associated with Q wave myocardial infarctions. One of the patients underwent successful emergency angioplasty. The second patient had bailout stent implantation performed prior to undergoing emergency coronary bypass. There was 1 subacute stent thrombosis event associated with a Q wave myocardial infarction occurring 8 days following a stent procedure in 1 patient. The occlusion was reopened, an additional bailout stent placed at the site of a distal dissection and the patient continued on antiplatelet therapy. There was one other non Q wave myocardial infarction that occurred in the post procedure hospitalization period that was not due to stent thrombosis. This patient had undergone a combined Rotablator® and stent procedure and returned to the catheterization laboratory 2 days following the procedure for angiographic evaluation of an asymptomatic cardiac enzyme elevation. Angiographic and intravascular ultrasound evaluations, revealed a patent stent site and no evidence of thrombus. this, non

Table 3. Intraprocedural, early post–procedural, late and cumulative complications at 6 months follow–up

n= 385 patients 99% Clinical F/U	Intraprocedural complication		Early Events (≤ 2 months)		Late Events (2 to 6 months)		Total Events at 6 months	
	n	(%)	n	(%)	n	(%)	n	(%)
Myocardial infarction	11	(2.9%)	4	(1.0%)	4	(1.0%)	19	(4.9%)
Coronary bypass	13	(3.4%)	2	(0.5%)	9	(2.3%)	24	(6.2%)
Repeat intervention	0		4	(1.0%)	40	(10.4%)	44	(11.4%)
Stent thrombosis event	0		4	(1.0%)	0		4	(1.0%)
Death	3	(0.8%)	1	(0.3%)	4	(1.0%)	8	(2.1%)
Vascular complication	0		2	(0.5%)	1	(0.3%)	3	(0.8%)
Event per patient	16	(4.2%)	6	(1.6%)	52	(13.5%)	74	(19.2%)

Q myocardial infarction event was considered an embolic event related to a pre stent rotablation procedure. A final patient returned to the hospital with recurrent exertional angina, 17 days following a proximal LAD stent implantation. This patient underwent coronary bypass after an angiogram identified a distal left main dissection. There was one vascular complication and one death that occurred in the same patient. This patient underwent multiple percutaneous interventions and vascular surgical repairs for lower extremity ischemia, developed rhabdomyolylis, renal failure and, died 17 days after the stent procedure of multiorgan failure and sepsis.

Late Events

Long term follow–up was obtained in 381 patients (99%). Late events between 2 and 6 months occurred in 52 patients (13.5%) as shown in Table 3. Ischemia driven target lesion revascularization was necessary in 49 patients (12.7%). The majority of these events were repeat angioplasty which were performed in 40 patients (10.4%) for symptomatic restenosis. A total of 9 patients (2.3%) underwent non emergency coronary bypass during the late follow–up period for symptomatic restenosis. Myocardial infarction during the late follow–up was observed in 5 patients (1.3%). There were 4 deaths during the late follow–up period and all were cardiac related. One death occurred following a large inferior myocardial infarction in a patient 5.5 months after stent implantation in the left anterior descending artery. An angiogram performed 3 weeks prior to the death revealed a patent left anterior descending stent and moderate diffuse disease in the right coronary artery but no evidence of a critical lesion. A second late death was a witnessed in–hospital ventricular fibrillation event 4 months after the procedure. The patient had a history of an ischemic cardiomyopathy and refractory ventricular arrhythmias. The third late death also occurred in a patient with an ischemic cardiomyopathy due to refractory congestive heart failure without evidence of ischemia. The fourth death occurred in a patient that had clinical and angiographic restenosis of a left main stent 5 months following the initial procedure. On follow–up the patient had a balloon angioplasty performed at this site and had sudden death 2 days following the repeat angioplasty. This was a witnessed in–hospital event and was presumed to be an occlusion at the site of the initial stent implantation and subsequent angioplasty site.

Cumulative Events

Clinical follow–up at 6 months was achieved in 381 of 385 patients (99%). By 6 months clinical follow–up major events had occurred in 74 patients (19.2%) with some patients having more than 1 major event. Myocardial infarction was evident in 19 patients (4.9%). A total of 24 patients required coronary bypass (6.2%). This included the 13 emergency coronary bypass procedures (3.4%) that were performed for procedur-

Table 4. Quantitative Angiographic Measurements

	Baseline n = 473	**Final** n = 454	**Follow–up** n = 355
Reference Vessel Diameter (mm)	3.17 ± 0.50	3.17 ± 0.41	3.02 ± 0.55
Minimum Lumen Diameter (mm)	0.93 ± 0.51	3.34 ± 0.62	2.29 ± 0.94
Diameter Stenosis (%)	71 ± 16	-7 ± 24	24 ± 28
Lesion Length (mm)	11.2 ± 6.6		
Final Nominal Balloon Size (mm)		3.73 ± 0.52	
Balloon/Proximal Vessel Ratio		1.16 ± 0.19	
Maximal Pressure (atmospheres)		15.2 ± 2.9	

al or early post–procedural complications. A total of 44 patients required repeat angioplasty (11.4%). Emergency angioplasty or bailout stent implantation was necessary in 4 patients (1.0%). There were 3 patients that had vascular complications (0.8%). This included 1 procedural related pseudoaneurysm that required vascular repair, and 1 ischemic vascular vascular complication related to a femoral artery dissection at the time of follow–up angiogram.

Angiographic Analysis

As shown in Table 4, the baseline reference vessel diameter was 3.17± 0.50. The reference vessel diameter following the stent procedure was not significantly different. At follow–up the reference vessel diameter had decreased to 3.02 ± 0.55 ($p < 0.0008$). Baseline minimum lumen diameter was 0.93 ± 0.51 mm with a baseline percent diameter stenosis of 71 ± 16%. The final stent diameter was 3.34 ± 0.62 mm with a mean final percent stenosis of -7 ± 14%. At follow–up, the minimum lumen diameter was 2.29 ± 0.94 with a percent diameter stenosis of 24 ± 28. The lesion length was 11.2 ± 6.6 mm. The median length of the lesions was 9.6 (range 1.2 to 39 mm). The results were achieved using a mean pressure of 15.2 ± 2.9 atmospheres and a balloon to vessel ratio of 1.16 ± 0.19.

Angiographic follow–up was performed in 355 of the 454 eligible lesions (78.1%) and in 284 of the 369 eligible patients (77%) that had a successful IVUS guided stent implantation procedure. Mean follow–up was 5.1 ± 2.2 months. The cumulative distribution of the minimum lumen diameter is depicted in Figure 1. The cumulative distribution of the percent diameter stenosis is shown in Figure 2. By per protocol analysis, the incidence of lesion restenosis, according to the 50% diameter stenosis criteria, was 19% (66 of 355 lesions). Restenosis per patient was 22% (63 of the 284 patients).

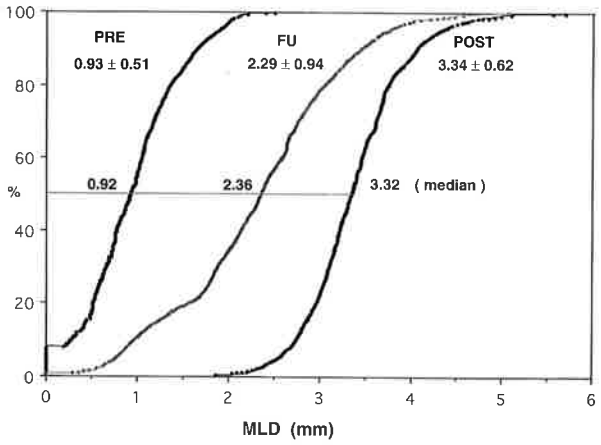

Figure 1. *Cumulative distribution showing the minimum lumen diameter before intervention, after intervention, and at follow up.*

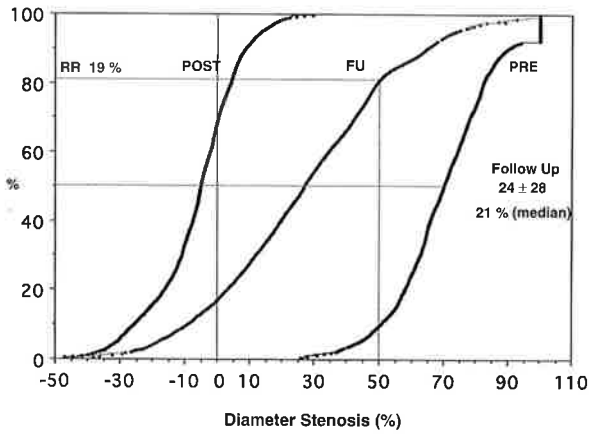

Figure 2. *Cumulative distribution showing the percent diameter stenosis before intervention, after intervention, and at follow up. By 50% diameter stenosis criteria the lesion restenosis rate was 19%.*

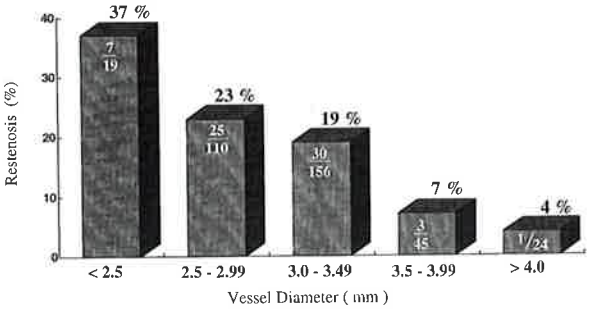

Figure 3. *Graph showing the relationship of restenosis to reference vessel diameter. The restenosis rate decreases with incremental increase in reference vessel diameter.*

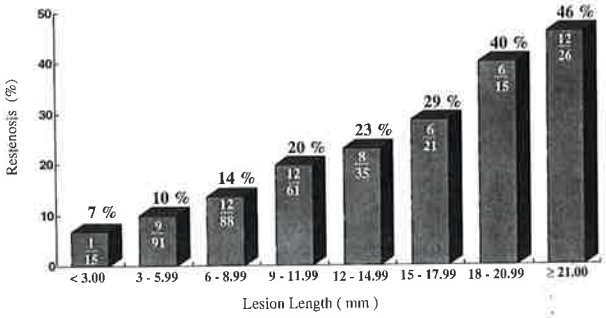

Figure 4. *Graph showing the relationship of restenosis to lesion length. The restenosis rate increases with incremental increase in baseline lesion length.*

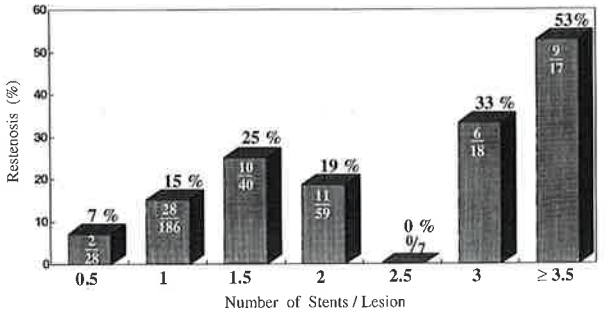

Figure 5. *Graph showing the relationship of restenosis to number of stents implanted. The lesion restenosis rate generally but not uniformly increases with increased number of stents implanted.*

The effect of vessel diameter is shown in Figure 3. There is a progressive increase in restenosis with smaller reference vessel size. The effect of lesion length on lesion restenosis is seen on Figure 4. The lesion restenosis rate is progressively higher with incremental increases in lesion length. The effect of number of stents on restenosis is depicted in Figure 5. The incidence of restenosis is less consistently related to increased number of stent implantation.

DISCUSSION

The short term results of this observational study on patients undergoing intravascular ultrasound guided intracoronary stent implantation indicate that anticoagulation can be safely withheld when adequate stent expansion is achieved and flow optimized at the stent site. The aggressive optimization techniques of expanding stents with high pressure balloon dilatation and using more than one stent to achieve full lesion coverage was also associated with a favorable restenosis rate and clinical event rate at 6 months follow–up.

Short– term results

The present study is a consecutive series of patients that have undergone intravascular ultrasound guided stent implantation. Overall procedural success of 96% is favorable in comparison to other angioplasty investigations. Procedural complications were high in the initial experience largely due to the use of oversized balloon in the initial experience. The inclusion of patients with complex or high risk anatomy such as left main stenosis or patients with long lesions was also a factor in higher than expected procedural complications. With the use of non–compliant balloons and more careful attention to balloon vessel sizing during final stent dilations, overall procedural complications were reduced.

Although the findings of this study represent a departure from previous doctrine regarding coronary stents, there is increasing evidence that improved operator experience and technique is associated with the reduction in both acute and subacute stent thrombosis. Recent multicenter studies, with a spectrum of operators with different degrees of experience, reported a stent thrombosis rate of 3.5%.[7,8] In contrast, previous single center studies of Palmaz–Schatz stent implantation treated with subsequent anticoagulation were associated with stent thrombosis rates of 0.5 to 2.2%.[3,20] These trials appeared to have good stent expansion as represented by the increased final stent minimum lumen diameter and lower final stent percent diameter stenosis. Despite these beneficial results, these trials were associated with a 4.4 to 16% incidence of vascular complications due to the use of anticoagulation therapy following the stent procedure.[3,20] More recently, several investigations using the technique of high

pressure balloon dilation to optimize stent expansion and post stent treatment with ticlopidine and various combinations of low molecular weight heparin have also achieved a low stent thrombosis rate.[21,22] Morice and Marco report a 0.5 to 1.5% incidence of stent thrombosis after elective Palmaz Schatz stent implantation.[21,22] There was a 2.3% to 3.8% incidence of vascular or bleeding complications with these non coumadin anticoagulation regimens that included low molecular weight heparin.[21,23] The factor common to all these stent investigations is the achievement of optimized stent expansion at the end of the stent implantation procedure. The use of low molecular weight heparin and, particularly, ticlopidine, may also be a factor in the achievement of a low stent thrombosis rate in the studies that did not use post–procedure coumadin.[21-23]

Long–term Results

The lesion restenosis rate in the present study, by 50% diameter stenosis criteria, was 19%. The restenosis in patients that had a single stent or less implanted with 14%. It is somewhat problematic to compare the restenosis rates achieved in this study with those of others because of differences in study inclusion criteria and different methods of performing quantitative angiography. Nonetheless, the absolute restenosis results in our investigation compare favorably with the incidence of restenosis in other reported studies on stent implantation. The follow–up angiographic results are in keeping with the theory of that the achievement of a large final minimum lumen diameter is the strongest predictor of freedom from angiographic restenosis.[4,5] The restenosis rate appears to be strongly influenced by both the reference vessel size and lesion length. The absolute number of stents was less consistently associated with increased restenosis. The benefit of improved stent expansion with high pressure dilations, slight balloon oversizing (if necessary), and optimization of the lumen at the stent margins (when lesions are apparent) by treatment with additional stents may partially outweigh the effects of using more than one stent. However, placement of 3 or more stents to treat long lesions does appear to be associated with a prominent increase in angiographic restenosis. Restenosis rates were significantly affected by the use of high pressures or oversized balloons for final stent dilation.

The low angiographic restenosis rate in the present study was associated with acceptable clinical results at 6 months. Despite the complexity of the patients in this cohort, the clinical event rate at 6 months of 19.2% compares favorably with the 19.5-20% reported in other recent stent investigations. The late clinically driven target lesion revascularization in our study of 12.7% also appears acceptable in comparison to the target lesion revascularization rates of other recent studies.[7,8] The procedural complications in the early experience and the inclusions of patients with low ejection fraction contribute to the cumulative 2.1% death rate reported at 6 months.

Study Limitations

Several limitations of the study need to be emphasized. One drawback to the technique of using intravascular ultrasound to assess the adequacy of stent expansion and lesion coverage is the increased number of stents and balloons and a longer procedure time. A more accurate analysis of the overall cost of this technique, however, should weigh the expense of increased procedural resources together with an evaluation of the savings from a decrease in post–procedural complications, a reduction in hospital stay and the elimination of laboratory costs associated with monitoring anticoagulation regimens, and possibly, reduced restenosis and clinically driven late target revascularization rates. It is not possible to determine if improved stent implantation technique without intravascular ultrasound guidance could yield the same short–term and long–term clinical and angiographic results. In view of the important clinical and economic ramifications, a randomized, multicenter trial would perhaps best answer this issue. Finally, the assessment of clinical events at 6 months underestimates total and ischemia driven late events and as such an evaluation of events at 1 year is also warranted.

CONCLUSIONS

The present study provides additional evidence that Palmaz–Schatz stent can be deployed in coronary arteries with a low rate of thrombosis and negligible vascular complications. This strategy also appears to concur an acceptable incidence of restenosis. The late target lesion revascu-

larization and 6 month event rates also appear to be favorable.

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