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Subacute Stent Thrombosis in the Era of Intravascular Ultrasound-Guided Coronary Stenting Without Anticoagulation: Frequency, Predictors and Clinical Outcome

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Objectives. **This study was performed to determine predictors of subacute stent thrombosis (SST) in the era of intravascular ultrasound (IVUS)-guided coronary stenting without anticoagulation.**

Background. **The incidence of stent thrombosis has declined with the application of high pressure stent deployment with only antiplatelet therapy. However, no data are available on predictors of stent thrombosis in this era.**

Methods. **Between March 30, 1993 and July 31, 1995, 1,042 consecutive patients underwent coronary stenting without anticoagulation. For this analysis, we excluded patients who underwent coronary artery bypass surgery, died or had acute stent thrombosis within the 1st 24 h after stenting (41 patients). A total of 1,001 patients (1,334 lesions) were included: 982 patients (1,315 lesions) without SST and 19 patients (19 lesions) with SST.**

Results. **The rate of SST was 1.9% (per patient). There was no difference between the SST and No SST groups in rescue stenting (12% vs. 13.5%, p = 1.0) or mean ± SD reference diameter (3.11 ± 0.58 vs. 3.19 ± 0.53 mm, p = 0.54). A preexisting thrombus was present in 12% of the SST group and in 4.5% of the No SST group (p = 0.19). Predictors of SST by univariate analysis were low ejection fraction (p = 0.004), more stents per lesion (p = 0.049), use of combination of different stents (p = 0.012), smaller balloon size (p = 0.012) and suboptimal result in terms of smaller lumen dimensions by angiography (p = 0.016) and IVUS (p = 0.004), residual dissections (p = 0.027) and slow flow (p = 0.0001). In stepwise logistic regression analysis, ejection fraction (p = 0.019), use of a combination of different stents (p = 0.013) and postprocedure dissections (p = 0.014) and slow flow (p = 0.0001) were predictive of SST.**

Conclusions. **In the present era of stent implantation, factors that may predispose to SST are low ejection fraction, intraprocedural complications leading to utilization of more stents, particularly with different stent designs, and suboptimal final result in terms of smaller lumen dimensions and persistent slow flow and dissections.**

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Coronary stenting has been shown to reduce the morbidity of acute vessel closure (1) and to decrease clinical and angiographic restenosis in selected lesions (2,3). However, the rate of subacute stent thrombosis (SST) and vascular complications remained high in the era of low pressure stent deployment despite vigorous anticoagulation (4–6). Intravascular ultrasound (IVUS) guidance provided the insight that led to the application of high pressure stent deployment. These technical refinements have been shown (7,8) to decrease the rate of SST despite the use of antiplatelet therapy alone. Although the incidence of SST is reduced, limited data are available on predictors of SST with this new approach. This report presents a retrospective analysis of our experience, using a data base that was collected prospectively, in an attempt to highlight the factors associated with SST.

Methods

Study patients. From March 30, 1993 until July 31, 1995, 1,042 consecutive patients underwent intracoronary stenting at Centro Cuore Columbus Hospital in Milan, Italy. To analyze factors associated with SST, we excluded 41 patients: 6 patients (0.6%) who had acute stent thrombosis within 24 h of the index procedure, 29 patients (2.8%) who underwent coronary artery bypass surgery (27 emergently and 2 within the 1st 24 h after stenting) and 6 patients (0.6%) who died during the procedure. A total of 1,001 patients with 1,334 lesions were included in this study. Patients were classified into two groups: 982 patients (1,315 lesions) without SST and 19 patients (19 lesions) with SST.

Stent implantation procedure. Intracoronary stenting was performed by using techniques previously described (7–9). The Palmaz-Schatz coronary stent (Johnson & Johnson Interventional Systems) was the stent most commonly used. Other

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Abbreviations and Acronyms

ACC–AHA = American College of Cardiology–American Heart Association
IVUS = intravascular ultrasound
PTCA = percutaneous transluminal coronary angioplasty
SST = subacute stent thrombosis
TIMI = Thrombolysis in Myocardial Infarction

stents included the Gianturco-Roubin Flexstent (Cook Inc.), the Wiktor stent (Medtronic Interventional Vascular, Kerkrade, Netherlands), the AVE Micro stent (Applied Vascular Engineering Inc., Richmond, Canada), the Cordis stent (Cordis Corporation) and the Wallstent (Schneider Europe, Bulach, Switzerland).

After stent implantation, angiographic optimization was performed by using high pressure balloon dilation to achieve a good angiographic result with <20% residual stenosis by visual estimate. After the angiographic result was considered acceptable, IVUS studies were performed in 707 patients (72%) in the No SST group and 13 (68%) in the SST group. Subsequent treatment decisions were based on IVUS results (when available) in conjunction with angiographic assessment. The final IVUS evaluation was the last IVUS study that documented achievement of optimal stent expansion criteria (9).

Indications for stenting were defined as follows: *elective stenting* was performed when the operator elected to use stenting before starting the procedure; *suboptimal result stenting* was defined as insertion of a stent for a focal dissection or significant vascular recoil after percutaneous transluminal coronary angioplasty (PTCA) associated with >30% lumen narrowing without associated ischemia; *threatened closure stenting* was performed when PTCA was complicated by a longitudinal or a spiral dissection associated with >50% lumen encroachment (ischemia was not always present in the setting of threatened closure); *acute occlusion stenting* was performed to relieve ischemia associated with total or subtotal vessel closure after angioplasty with no or markedly delayed distal flow (Thrombolysis in Myocardial Infarction [TIMI] grade 0 or 1 flow); *total occlusion stenting* was performed after reopening a vessel that had been occluded before the procedure had begun; *restenosis stenting* was performed for lesions that recurred ≥3 months after an angioplasty procedure.

Angiographic analysis. Coronary angiography was performed in a routine manner. Patients received intracoronary nitroglycerin before initial, final and follow-up angiograms to achieve maximal vasodilation. Angiographic measurements were made with the use of digital electronic calipers (Brown and Sharp) and an optically magnified image in the projection that demonstrated the tightest stenosis. The guiding catheter was used as the reference for calibration. Previous studies (10,11) have shown that measurements obtained with digital calipers correlate closely with those obtained with computer-assisted methods, with a low interobserver and intraobserver variability.

The proximal and distal reference lumen diameters, lesion minimal lumen diameter and lesion length were measured on the preintervention film, with the final stent minimal lumen diameter measured on the final images. The mean reference lumen diameter was calculated as the average of the proximal and distal lumen diameters, and the percent diameter stenosis was calculated as the mean reference lumen diameter minus the minimal lumen diameter divided by the mean reference lumen diameter. The reference lumen diameters and minimal lumen diameter were measured during follow-up angiography, when similar calculations were performed.

Lesions were characterized according to the modified American College of Cardiology–American Heart Association (ACC–AHA) classification (12). Thrombus was defined as a filling defect seen in multiple projections surrounded by contrast medium. Angiographic findings such as the occurrence of dissection, vessel rupture or side branch compromise were recorded.

IVUS equipment and measurements. From March 1993 until November 1993, coronary arteries were imaged with a 3.9F monorail system with a 25-MHz transducer-tipped catheter (Interpret Catheter, InterTherapy/CVIS). A Cardiovascular Imaging System (CVIS) with a 2.9F catheter was used after November 1993. Validation of quantitative measurements and pathologic correlation with ultrasound measurements has been reported (13,14). Images were initially obtained with a manual pullback system, but starting in July 1994 a mechanical pullback device at a speed of 0.5 mm/s was always employed. The position of the catheter on fluoroscopy was used to correlate the ultrasound image with the angiogram. The ultrasound catheter was advanced distal to the stent, and images were recorded while the imaging catheter was pulled back. On-line quantitative measurements were performed during the procedure.

Lumen and vessel cross-sectional areas were measured with the use of a trackball to outline the lumen-intimal interface and the media-adventitia interface, respectively. The part of the lesion with the smallest lumen area was selected for measurements for each pass of the IVUS catheter. Reference lumen cross-sectional areas were measured proximal and distal to the stented segments in the closest most normal-appearing segments. The average reference vessel and lumen cross-sectional areas were calculated as the average of the proximal and distal reference vessel and lumen cross-sectional areas. Interobserver and intraobserver reproducibility of minimal lumen diameter and lumen cross-sectional area measurements have already been documented (15).

Definitions. *Angiographic success* was defined as a final angiographic residual diameter stenosis of <20% by visual estimate. *Clinical events* were defined as death, coronary artery bypass surgery, myocardial infarction (Q wave or non-Q wave), repeat angioplasty and vascular complications. *Death* was defined as any death irrespective of cause. However, only deaths occurring >24 h after stenting are included. A *Q wave*

myocardial infarction was diagnosed when there were documented new pathologic Q waves (>0.4 s) on an electrocardiogram in conjunction with elevation in creatine kinase levels to greater than twice the upper limit of normal. A *non-Q wave myocardial infarction* was diagnosed when an elevation of the cardiac enzymes to greater than twice the upper limit of normal was documented without the development of new pathologic Q waves. *Coronary artery bypass surgery* was defined as coronary bypass surgery occurring at ≥24 h after successful stenting. *Acute thrombosis events* were angiographic stent thrombosis occurring within 24 h of the procedure; those events were excluded from analysis because of the intent of this study. *SST events* were angiographically documented occlusions with TIMI grade 0 or 1 flow at the stent site occurring >24 h after the stent procedure, or sudden death occurring within 1 month after the procedure. *Repeat angioplasty* was nonemergency angioplasty performed for symptomatic restenosis. *Vascular complications* were defined as the occurrence of psuedoaneurysm, bleeding or hematoma formation at the access site requiring transfusion, vascular repair or external compression. Events in the two patient groups were compared at the end of 1 month.

Postprocedure management and follow-up. Starting on the day of the procedure all patients received aspirin, 325 mg/day indefinitely, but they did not receive dextran or dipyridamole. The general guidelines were that if the IVUS criteria for optimal stent expansion were met and the angiographic result was also acceptable, no further heparin was administered at the end of the procedure and sheaths were removed within 4 to 6 h. Patients with a final unsuccessful angiographic result received warfarin on the day of the procedure, and both heparin and warfarin were continued until the prothrombin time was >16 s (international normalized ratio 2.0 to 3.5), after which the heparin was stopped and warfarin continued for 1 month. After a successful procedure, patients were treated with antiplatelet agents alone (952 patients) (aspirin, 325 mg/day, either alone [253 patients] or in combination with ticlopidine, 250 mg orally twice daily for 1 month [699 patients]). The choice of antiplatelet regimen went through several phases during this study. We started our experience with stenting without anticoagulation by using a combination of aspirin and ticlopidine; because of encouraging results after an 8-month experience with this regimen we started using aspirin alone in all patients (150 patients). This phase was followed by a randomized trial of aspirin alone versus aspirin plus ticlopidine, during which an additional 103 patients received aspirin alone. After the end of this trial, all patients were given a combination of aspirin and ticlopidine.

One month follow-up was performed in all patients by an interview or a telephone conversation with the patient or the referring physician.

Statistical analysis. Data were analyzed with the SAS statistical software package. The patient was used as the unit for analysis. Categoric variables are presented as mean value ± SD. Differences between groups were evaluated by chi-square analysis or Fisher exact test for categoric variables and Student *t* test for continuous variables. Correlation between independent and dependent continuous variables was evaluated by simple linear regression analysis. The contribution of clinical, angiographic and procedural variables to the categoric outcome variable (stent thrombosis) was evaluated with logistic regression analysis. First, univariate analysis was performed to evaluate the contribution of each relevant variable independently; then variables that were found to be significant in univariate analysis were entered into a stepwise logistic regression model where selection of variables was achieved in a stepwise fashion. Probability values < 0.05 were considered significant.

Table 1. Baseline Clinical Characteristics of the Study Patients

	No SST Group (n = 982)	SST Group (n = 19)	p Value
Age (yr)	58 ± 9	58 ± 9	1.0
Male	860 (88%)	17 (89%)	0.57
Previous myocardial infarction	536 (55%)	17 (89%)	0.002
LVEF (%)	57 ± 11	49 ± 15	0.002
Unstable angina*	193 (20%)	6 (32%)	0.19
Multivessel disease	485 (49%)	10 (53%)	0.78

*Canadian Cardiovascular Society angina classification. Data presented are mean value ± SD. LVEF = left ventricular ejection fraction; SST = subacute stent thrombosis.

Results

Incidence of SST. SST occurred in 19 patients (1.9%) at a mean postprocedure interval of 9 ± 7 days (range 3 to 27). It was angiographically documented in 17 patients; in the other 2 patients, who died suddenly within 3 weeks of undergoing multivessel stenting, the cause of death was assumed to be SST. Because there was no angiographic documentation of the precise vessel that thrombosed, procedural, angiographic and IVUS data in these two patients were not included in the analysis.

Patient characteristics and indications for stenting. The clinical characteristics of the two subgroups are shown in Table 1. There was no difference in age, gender, frequency of multivessel disease and unstable angina. However, the SST group had a lower ejection fraction (57 ± 11% vs. 49 ± 15%, p = 0.002), greater frequency of ejection fraction <45% (11% vs. 38%, p = 0.0005) and greater frequency of prior myocardial infarction (55% vs. 89%, p = 0.002) than did the No SST group.

There was no difference in indications for stenting between the No SST and SST groups. Elective stenting was performed in 539 patients (55%) in the No SST group versus 10 (58%) in the SST group (p = 0.94), stenting after suboptimal PTCA in 88 patients (9%) versus 3 (18%) (p = 0.20), bailout stenting in 132 patients (13.5%) versus 2 (12%) (p = 1.0), stenting after recanalization of total occlusion in 100 patients (10%) versus 2 (12%) (p = 0.69), stenting for restenosis in 118 patients (12%)

Table 2. Baseline Angiographic Characteristics of the Study Patients

	No SST Group (n = 982)	SST Group (n = 17)	p Value
Vessel dilated			
LAD	473 (48.5%)	10 (59%)	0.53
LCx	149 (15%)	2 (12%)	1.0
RCA	277 (28%)	4 (23%)	0.79
LMCA	12 (1%)	0	1.0
Intermediate	6 (0.5%)	0	1.0
Diagonal	22 (2%)	1 (6%)	0.33
Obtuse marginal	22 (2%)	0	1.0
SVG	31 (3%)	0	1.0
Lesion site			
Ostial	59 (6%)	0	0.62
Proximal	412 (42%)	11 (65%)	0.10
Midvessel	403 (41%)	4 (24%)	0.21
Distal	108 (11%)	2 (12%)	0.71
Thrombus	45 (4.5%)	2 (12%)	0.19
Modified AHA–ACC lesion type			
A	69 (7%)	1 (6%)	1.0
B1	344 (35%)	5 (33%)	0.82
B2	393 (40%)	7 (39%)	0.92
C	176 (18%)	4 (22%)	0.53

Data presented are number (%) of patients. AHA–ACC = American Heart Association–American College of Cardiology classification; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery; SST = subacute stent thrombosis; SVG = saphenous vein graft.

versus 0 (0%) (p = 0.25) and stenting in the setting of acute myocardial infarction in 5 patients (0.5%) versus 0 (0%) (p = 1.0).

Angiographic and procedural characteristics. Baseline angiographic characteristics are shown in Table 2. There was no difference in lesion location or complexity between groups. Thrombus was present in 45 patients (4.6%) in the No SST group versus 2 patients (12%) in the SST group (p = 0.19).

Procedural characteristics are shown in Table 3. The majority of stents used in this study were Palmaz-Schatz stents. A combination of different stent types was used in 69 patients (7%) in the No SST group versus 4 (24%) in the SST group (p = 0.03). Postprocedure residual dissections were present in 25 patients (2.5%) in the No SST group versus 2 (12%) in the SST group (p = 0.07) and slow flow was present in 3 patients in each group (0.3% vs. 18%, p < 0.0001). These markers of a suboptimal result persisted despite the use of more stents in an attempt to correct the problem. Multiple stents were used in 412 patients (42%) in the No SST group versus 11 (65%) in the SST group (p = 0.10).

Quantitative angiographic and IVUS analysis. Quantitative angiographic data are shown in Table 4. There was no difference in baseline proximal reference vessel diameter and lesion length between groups. However, the SST group had a smaller postprocedure minimal lumen diameter (3.14 ± 0.55 vs. 2.82 ± 0.48 mm, p = 0.017) and a higher residual percent diameter stenosis (−1.8 ± 14% vs. 5.4 ± 16%, p = 0.036).

IVUS measurements after the stent procedure were available for 707 patients in the No SST group (72%) and 13 in the SST group (68%) (p = 0.93). There was no significant difference in proximal reference vessel cross-sectional area between the No SST and SST groups (15.18 ± 4.6 mm^2 vs. 13.2 ± 4.8 mm^2, p = 0.12). However, the SST group had a smaller postprocedure minimal lumen diameter (2.88 ± 0.5 vs. 2.48 ± 0.36 mm, p = 0.004) and smaller lumen cross-sectional area (7.75 ± 2.52 vs. 5.87 ± 1.73 mm^2, p = 0.008) measured at the tightest point within the stent.

Table 3. Procedural Characteristics in the Two Study Groups

	No SST Group (n = 982)	SST Group (n = 17)	p Value
Type of stent			
Palmaz-Schatz	657 (67%)	10 (60%)	0.66
Gianturco-Roubin Flexstent	69 (7%)	0	0.62
Wiktor	74 (7.5%)	1 (6%)	1.0
AVE Micro	29 (3%)	0	1.0
Cordis	20 (2%)	1 (5%)	0.31
Wall	39 (4%)	1 (5%)	0.50
Angio	5 (0.5%)	0	1.0
NIR	20 (2%)	0	1.0
Combination of stents	69 (7%)	4 (24%)	0.03
Stents/lesion	1.5 ± 1	2 ± 1	0.041
Final balloon size (mm)	3.6 ± 0.5	3.3 ± 0.5	0.014
Final B/V ratio	1.14 ± 0.18	1.0 ± 0.24	0.001
Maximal inflation pressure (atm)	16 ± 3	17 ± 2	0.17

Data presented are mean value ± SD or number (%) of patients. B/V ratio = balloon diameter divided by proximal reference vessel diameter; SST = subacute stent thrombosis.

Postprocedure pharmacologic therapy and clinical events at 1 month. A combination of ticlopidine and aspirin was used in 688 patients (70%) in the No SST group versus 11 (59%) in the SST group (p = 0.25). Aspirin alone was used in 245 patients (25%) in the No SST group versus 8 (41%) in the SST group (p = 0.09). Forty-nine patients (5%) in the No SST group received warfarin in comparison with none in the SST group (p = 0.38).

All patients had clinical follow-up at 1 month after stenting. Major clinical events were significantly more frequent in the

Table 4. Quantitative Angiographic Measurements in the Two Study Groups

	No SST Group (n = 982)	SST Group (n = 17)	p Value
Preprocedure			
Reference vessel diameter (mm)*	3.19 ± 0.53	3.11 ± 0.58	0.54
Minimal lumen diameter (mm)	0.94 ± 0.56	0.74 ± 0.47	0.14
Percent diameter stenosis	69 ± 18	75 ± 17	0.17
Lesion length (mm)	10.26 ± 7.0	8.58 ± 5.0	0.32
Postprocedure			
Stent minimal luman diameter (mm)	3.14 ± 0.55	2.82 ± 0.48	0.017
Stent percent diameter stenosis	−1.8 ± 14	5.4 ± 16	0.036

*Proximal vessel diameter. Data presented are mean value ± SD. SST = subacute stent thrombosis.

Table 5. Correlates of Stent Thrombosis by Logistic Regression Analysis

	Univariate Analysis		Stepwise Analysis	
	Likelihood Estimate ± SE	p Value*	Likelihood Estimate ± SE	p Value*
Preprocedure				
LVEF	−0.053 ± 0.019	0.004	−0.054 ± 0.023	0.019
Procedural				
Stent combination	1.46 ± 0.582	0.012	1.73 ± 0.696	0.013
Balloon size	−1.44 ± 0.576	0.012	—	—
Stents per lesion	0.254 ± 0.129	0.049	—	—
Postprocedure				
Slow flow	4.54 ± 0.859	0.0001	5.12 ± 1.033	0.0001
Dissections	1.71 ± 0.774	0.027	2.33 ± 0.945	0.014
Stent MLD (angiographic)	−1.09 ± 0.458	0.016	—	—
Stent MLCSA (IVUS)	−0.457 ± 0.159	0.004	—	—

*$p < 0.05$ is considered significant. Data presented are mean value ± SD. IVUS = intravascular ultrasound; LVEF = left ventricular ejection fraction; MLCSA = minimal lumen cross-sectional area; MLD = minimal lumen diameter.

SST group. Nonfatal myocardial infarction occurred in 1 patient (0.1%) in the No SST group versus 11 (58%) in the SST group ($p < 0.00001$). Coronary artery bypass surgery was performed in two patients (0.2%) in the No SST group versus three (16%) in the SST group ($p = 0.00006$), and death occurred in one patient (0.1%) in the No SST group versus five (26%) in the SST group ($p < 0.000001$). When all major clinical events are considered, only four patients (0.4%) in the No SST group had a major event compared with all patients in the SST group ($p < 0.000001$).

Correlates of SST. As shown in Table 5, univariate predictors of SST were low left ventricular ejection fraction, number of stents per lesion, use of a combination of different stent types, smaller balloon size, smaller postprocedure angiographic stent minimal lumen diameter and intravascular ultrasound stent cross-sectional area and residual dissections and slow flow. When all these variables were entered into stepwise logistic regression analysis, four factors predicted stent thrombosis: postprocedure slow flow or residual dissections, use of a combination of different stent types and low baseline left ventricular ejection fraction.

Discussion

Our findings demonstrate that SST in the era of high pressure stent optimization without subsequent anticoagulation is a multifactorial process. Clinical factors such as low ejection fraction and procedural factors such as suboptimal stent expansion and postprocedure complications leading to utilization of more stents per lesion without full correction of the problem, residual postprocedure dissections and slow flow are the major determinants of subsequent SST.

SST: a multifactorial process frequently procedure related. Large multicenter studies on patients undergoing elective stenting in the era of low pressure stent deployment and anticoagulation reported an incidence rate of stent thrombosis of 3% to 4% (2–4). When stenting was performed for bailout or emergency indications, the rate of stent thrombosis increased to 8% to 16% (1,16). In the same period, studies with the Palmaz-Schatz stent and the Wallstent (4,6,17,18) reported lesion-related factors predisposing to stent thrombosis including tortuous segments, undersizing of stents, intraluminal filling defects before or after stent implantation, acute ischemic syndromes, small vessels (<3 mm) and poor distal runoff. Agrawal et al. (19) reported that factors predisposing to stent thrombosis after use of the flexible coil stent with anticoagulation were residual dissections, persistent filling defects, small stent size (<2.5 mm) and multiple stents. Nath et al. (20) reported that lesion eccentricity, bailout stenting, unstable angina and subtherapeutic anticoagulation were factors predisposing to stent thrombosis with the coil stent.

Few data are available on clinical and procedural predictors of stent thrombosis in the era of no anticoagulation and only antiplatelet therapy. In the present study, proximal reference diameter was not predictive of stent thrombosis; 344 patients (35%) in the No SST group and 7 (41%) in the SST group had a proximal reference vessel diameter <3.0 mm ($p = 0.78$). In addition, there was no difference in lesion length and complexity (by ACC–AHA classification). There was a trend toward higher frequency of thrombus at the lesion site in the SST group ($p = 0.19$). There was no difference in stent thrombosis among the different stents used. However, the power of this study may be insufficient to evaluate this issue.

In univariate analysis, baseline left ventricular ejection fraction appeared to be an important clinical predictor of stent thrombosis, as a lower ejection fraction predicted a higher probability of stent thrombosis ($p = 0.004$). Among intraprocedural factors, the probability of stent thrombosis increased with the use of more stents per lesion ($p = 0.049$), a combination of different stent types ($p = 0.012$) and a smaller balloon size during final stent optimization ($p = 0.012$). The final stenting result led to an increased probability of stent thrombosis, when smaller final lumen dimensions were achieved as measured by angiography ($p = 0.016$) or IVUS

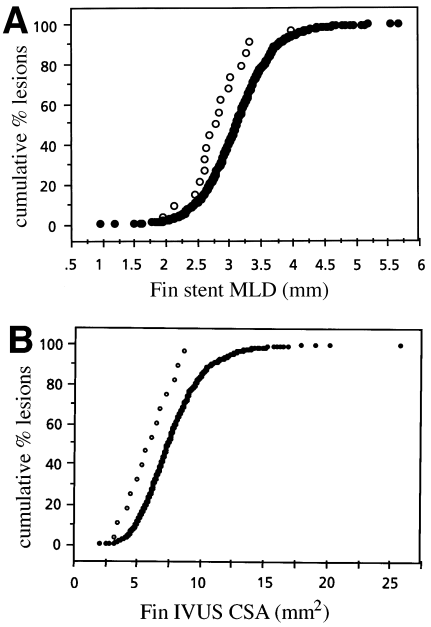

Figure 1. A, Comparison of the percentile distribution curves for final angiographic stent minimal lumen diameter (Fin stent MLD) for the groups with and without subacute stent thrombosis (SST). **B,** Comparison of the percentile distribution curves for final intravascular ultrasound cross-sectional area (Fin IVUS CSA) in the stented segment for the two groups. **Solid circles** = no SST; **open circles** = SST.

(p = 0.004) and when slow flow (p = 0.0001) or residual dissections (p = 0.027) persisted after the procedure. In stepwise logistic regression analysis, four factors remained significant in predicting a higher probability of stent thrombosis: low ejection fraction (p = 0.019), use of a combination of stents (p = 0.013), postprocedure slow flow (p = 0.0001) and dissections (p = 0.014). However, the use of stepwise regression analysis with a low event rate can cause important correlations to drop out in the presence of real or accidental stronger relations.

One possible explanation for these findings is that more angiographic complications (dissections, coil stent deformity, plaque prolapse) occurred at the time of initial stent deployment in the SST group. Subsequently, more stents (often of different types) were required in an attempt to correct this problem. Nevertheless, the final result in this particular group was frequently suboptimal with a smaller final angiographic stent minimal lumen diameter (Fig. 1A) and smaller stent cross-sectional area by IVUS (Fig. 1B). An alternative explanation for the influence of stent combinations on stent thrombosis may be that the use of several different stent types may create a nonlinear flow pattern that increases the propensity for thrombosis.

The occurrence of unstable angina and bailout stenting did not predict the risk of SST. This conclusion highlights the unique importance of the achievement of an optimal final result. The message is that bailout stenting and stenting for dissections carry a high risk of SST only when the underlying angiographic problem is not fully corrected. The final result

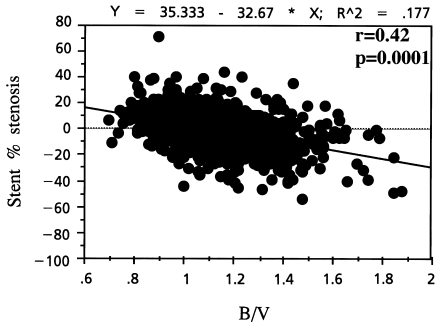

Figure 2. Linear regression analysis of balloon/vessel ratio (B/V) and final residual angiographic percent diameter stenosis after stenting.

remains the common denominator. The only exception to this statement is the presence of a baseline low ejection fraction, which may create a slow flow condition that is difficult to correct by lumen optimization. This setting may require a more potent antiplatelet regimen to diminish the risk of SST.

Role of IVUS and balloon sizing. IVUS provided information regarding the adequacy of stent deployment and reference vessel dimensions. This information was essential for appropriate balloon sizing and for maximizing the probability of optimal stent expansion. IVUS-guided stenting was used in 13 patients in the SST group; however, final IVUS imaging documented smaller lumen dimensions in this group than in the No SST group (Fig. 1B). The other six patients in the SST group did not have IVUS interrogation; in three of the six, this lack was due to unavailability of appropriate equipment at the time of the procedure, and in the other three, procedural complications made ultrasound interrogation potentially unsafe. In these six patients, the adequacy of stent deployment and balloon sizing was determined with angiography. Therefore, no firm conclusions could be made in regard to the role of IVUS as such, because this study was not a randomized comparison between angiography and IVUS guidance of coronary stenting.

Balloons were undersized in the SST group. Five patients (27%) in this group, had a balloon versus 86 (8.8%) in the No SST group, vessel ratio <0.9 (p = 0.01). This finding is of critical importance because the balloon/vessel ratio in this study correlated inversely with postprocedure angiographic residual percent diameter stenosis (r = 0.42, coefficient = −32.67, p = 0.0001, confidence interval = −36.76 to −28.57) (Fig. 2).

Role of antiplatelet therapy. The value of ticlopidine in diminishing SST is the subject of ongoing clinical trials. Recently, we (21) reported a randomized comparison between ticlopidine and aspirin versus aspirin alone after coronary stenting, with a positive trend favoring the combination of antiplatelet agents in reducing the rate of stent thrombosis. The present study cannot provide data to support the superiority of one antiplatelet regimen over the other by virtue of design and absence of systematic randomization.

Study limitations. Several important limitations should be noted when interpreting the results of this study. It is a

retrospective analysis; multiple different designs of stents were used, a situation that does not allow one to draw conclusions regarding the role of a specific stent design in inducing thrombosis; the assignment of antiplatelet regimens was not based on a randomized protocol, thus limiting conclusions in regard to the best post-stenting pharmacologic regimen. In addition, because of the low event rate (SST) in this cohort, two common problems might arise: Chance occurrences may suggest significant observations, and true relations may not achieve nominal significance. Therefore, ideally in the present era of stent implantation, a larger cohort of patients is necessary to determine predictors of SST with high statistical power. Despite these limitations, this is the first large study to examine predictors of SST in the era of high pressure stent deployment without anticoagulation, and it provides a practical insight into the multifactorial nature of this process.

Conclusions. SST in this era of stent implantation without subsequent anticoagulation has diminished. However, despite aggressive management, it is still associated with serious clinical events. This study has identified several factors that predispose to SST: low ejection fraction, intraprocedural complications with postprocedure residual dissections or slow flow leading to a final suboptimal angiographic or IVUS result. Other adverse factors that may have a role in SST include preexisting thrombus and use of multiple stents. The role of different regimens of antiplatelet therapy, including some new, more specific antiplatelet agents, needs to be further investigated, particularly in high risk groups. In addition, new stent designs with a higher rate of successful implantation in complex and unfavorable anatomic settings may further decrease the number of patients who have a final suboptimal result.

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