Intracoronary Stent Implantation Without Ultrasound Guidance and With Replacement of Conventional Anticoagulation by Antiplatelet Therapy

30-Day Clinical Outcome of the French Multicenter Registry

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Background Stenting reduces both acute complications of coronary angioplasty and restenosis rates but increases subacute thrombosis rates and hemorrhagic complications when used with coumadin anticoagulation.

Methods and Results To simplify postcoronary stenting treatment and to reduce these drawbacks, we evaluated the 1-month outcome of a prospective registry of 2900 patients in whom successful coronary artery stenting was performed without coumadin anticoagulation. Patients received 100 mg/d aspirin and 250 mg/d ticlopidine for 1 month. Low-molecular-weight heparin (LMWH) treatment was progressively reduced in four consecutive stages, from 1-month treatment to none. Event-free outcome at 1 month was achieved in 2816 patients (97.1%). Major stent-related cardiac events were subacute closure in 51 patients (1.8%), including death in 12 (0.5%), acute myocardial infarction in 17 (0.6%), and coronary artery bypass graft surgery in 9 (0.3%). Stent thrombosis was more frequent with balloon size of <3.0 mm (≤2.5 mm, 10%; 3.0 mm, 2.3%; ≥3.5 mm, 1.0%; $P<.001$), bail-out situations (6.67% versus 1.38%, $P<.001$), and patients with unstable angina or acute myocardial infarction (2.2% versus 1.12%, $P=.02$). Bleeding complications that required transfusion, surgical repair, or both occurred in 55 patients (1.9%). Bleeding complications were related to female gender (4.0% versus 1.51%, $P<.001$), duration of LMWH treatment (3.83% in phase II/III versus 0.69% in phase IV/V, $P<.001$), sheath size (6F, 0.52%; 7F, 1.04%; ≥8F, 4.23%; $P<.001$), bail-out situations (4.76% versus 1.67%, $P<.01$), and saphenous graft stenting (4.38% versus 1.75%, $P=.04$).

Conclusions These results suggest that poststenting treatment by ticlopidine/aspirin is an effective alternative to coumadin anticoagulation, achieving low rates of subacute closure and bleeding complications. LMWH treatment does not improve subacute reocclusion rates but increases bleeding complications. Furthermore, as bleeding complications were independently related to sheath size, we suggest that stenting with 6F guiding catheters may prevent local complications. Furthermore, the ticlopidine/aspirin combination allows a low-cost stenting strategy without ultrasound assessment of stent deployment and permits short in-hospital stay.(***Circulation*. 1996;94:1519-1527.**)

Key Words • coronary artery • stents • aspirin • ticlopidine

Percutaneous transluminal coronary angioplasty is a widely used revascularization technique in patients with coronary artery disease, but this technique is limited by its rate of restenosis, frequent unsatisfactory results, cardiac complications such as acute and subacute closure, and local bleeding complications. Stents have been developed to improve the acute and long-term results of coronary angioplasty. Compared with conventional balloon angioplasty, stents have demonstrated their ability to prevent abrupt closure of the artery in bail-out situations[1-3] and to reduce restenosis.[4,5] However, early experience with coronary stenting has been characterized by a marked increase in bleeding complications as a result of aggressive anticoagulation protocols based on coumadin administration, whereas acute and subacute thrombosis rates of the stented artery remained high.[2,3,6] In the phase I study,[7] which was designed to reduce subacute occlusion after stenting LMWH was used instead of coumadin in 237 consecutive patients. Despite this therapeutic change, subacute occlusion occurred in 10.3% of patients, suggesting that both coumadin and LMWH were ineffective in preventing thrombus formation at the site of stent implantation. Curiously, the peak of subocclusion was located between days 5 and 8, which corresponds to platelet half-life, and was not influenced by heparin treatment. Therefore, we hypothesized that subacute occlusion after stenting was more likely to be initiated by platelet aggregation than by contact activation of blood coagulation factors on foreign material. Because we suspected that there was an additive

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Selected Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
LMWH = low-molecular-weight heparin
MI = myocardial infarction
PTCA = percutaneous transluminal coronary angioplasty

inhibitory effect of aspirin and ticlopidine on platelet aggregation,[8] it appeared that the combination of these two treatments could reduce subacute closure of the stented artery in association with LMWH. The investigation on the beneficial effects of the ticlopidine/aspirin combination was conducted in four phases in which the LMWH treatment duration could be progressively reduced from 4 weeks to complete suppression.

The present study had three major purposes: to examine the clinical outcome of stented patients with a 1-month aspirin/ticlopidine treatment, to evaluate the risk-to-benefit profile of LMWH treatment, and to determine the clinical and procedural variables leading to subacute closure of the stented artery and to local bleeding complications.

Methods

Patients

From December 1992 to March 1995, 2900 consecutive patients were included in a prospective, nonrandomized, multicenter registry. At 25 participating centers, the 1-month results were evaluated of a new medication protocol after coronary artery stenting procedure. Advanced age, unstable angina, acute MI, low ejection fraction, or previous MI, CABG, or PTCA was not considered to be an exclusion criterion. All patients who had been successfully implanted with stents in the 25 participating centers were consecutively included in the registry. No other therapeutic approach was performed; in particular, at no participating center was coumadin administered to any of the stented patients, and no patient received intravascular ultrasound guidance for stent implantation.

Patients with contraindications to aggressive anticoagulation treatment, such as uncontrolled hypertension, peptic ulcer, or previous major bleeding events, were excluded from stenting and therefore from the study. Patients with contraindications or previously known side effects for ticlopidine or aspirin treatment were also excluded. Oral informed consent was obtained from all patients before any procedure.

Arteries

This study included planned stenting procedures (de novo lesion, restenosis, and vein graft stenosis) as well as unplanned procedures (dissection, elastic recoil, bail-out procedures). No selection was made on artery type or stenosis morphology or location, and the decision to stent was entirely left to the operator's judgment. Because high rates of artery occlusion had been observed after stent placement into small coronary arteries,[9,10] operators tried to avoid stenting of small arteries.

Measurement of Coronary Arteries

In the present study, we report the results of a multicenter national registry without the use of a core laboratory, which represents a major limitation. However, the majority of the centers involved in this study were equipped with on-line quantitative coronary angiography, which enabled the physicians to measure the arteries, select the appropriate balloon size, measure the artery-to-balloon ratio, and assess residual stenosis. Because the equipment varied from center to center and the measurements were performed by the operators, no absolute value of artery diameter, stenosis diameter, or poststent residual stenosis could be accurately reported. The fact that no objective methodology was used to evaluate reference vessels diameter, lesion minimal lumen diameter, and results represents a major limitation of this study.

Definitions

Successful stenting was defined by correct placement of the stent, TIMI 3 flow, and residual stenosis of $<10\%$, with no distal embolism and no major side-branch occlusion.

Nonocclusive dissections were defined as types A, B, C, and D1 of the National Heart, Lung, and Blood Institute classification, and bail-out situations as clinical and/or ECG ischemia associated with type D2, E, and F dissections and TIMI grade ≤ 2 flow.

Major complications during the 1-month follow-up period included death, Q- or non–Q-wave MI with CK elevation of more than twice the normal value, CABG, or repeat PTCA at the same site.

In complicated cases of patients in whom angiographic control of the stented artery could not be performed, subacute occlusion was defined as sudden death; clinical symptoms of prolonged chest pain with ST elevation; new Q waves, with or without CK elevation; or an isolated CK raise occurring during the first month.

Severe local complications were defined as local swelling, hematoma, pseudoaneurysm, arteriovenous fistula, or retroperitoneal hematoma requiring surgical repair or blood transfusion.

For the purpose of this study and in an attempt to show a correlation between the operator's experience in stenting and the complication rate, the investigating centers were arbitrarily divided into two groups: investigators reporting <100 stenting procedures to the registry (low-volume centers) and investigators reporting >100 stenting procedures (high-volume centers).

PTCA and Stenting Routines

PTCA was performed using standard techniques. During catheterization, a 10 000 to 15 000 IU IV bolus of heparin was given immediately before the PTCA procedure and 250 mg aspirin IV was administered when the patient had not been pretreated with aspirin. In most cases, PTCA was performed via the femoral approach with a 6F to 9F guiding catheter. In 2.6% of patients, the radial approach with a 6F guiding catheter was used. Intracoronary vasodilators (molsidomine, isosorbide dinitrate, or nitroglycerin) were routinely administered before and after angioplasty to allow assessment of the maximal lumen. Indication and technical method for stent implantation were left to the operator's judgment. However, it was recommended that the size of the balloon be selected carefully, on the basis of an artery-to-balloon ratio of 1:1 to 1:1.2; that poststent inflation pressures of ≥ 10 atm be used; and that a residual stenosis of $\leq 10\%$ be obtained after stenting. In 80.0% of procedures, manually crimped stents were used. The arterial sheath was removed 4 to 24 hours after angioplasty, according to activated coagulation time levels, and compression was carried out either manually or mechanically. As investigators became more confident in the patients' clinical outcome during the study, patients were progressively discharged earlier.

Drug Management

No particular pretreatment was recommended before the procedure. When the patients were not receiving aspirin, they received a bolus of 250 mg aspirin IV during the procedure, which was reduced to 100 mg/d for 1 month after stent placement. Ticlopidine therapy (250 mg/d for <85 kg body wt and 500 mg/d for >85 kg body wt PO for 1 month) was initiated immediately after the stenting procedure. After withdrawal of the sheath, continuous heparin was administered for 48 hours, followed by subcutaneous LMWH (100 IU/kg BID) for 1 month in phase II and for 2 weeks in phase III. In phase IV, the patients did not receive postprocedural continuous IV heparin; however, subcutaneous LMWH was initiated after sheath removal. They received LMWH only for 1 week. No postprocedural heparin and no

LMWH were administered in phase V. Patients with acute MI as well as the majority of bail-out patients were excluded from phase V and included in phase IV. Blood analysis included anti–factor Xa activity at the peak of activity at day 3 and once a week afterward, as well as platelet count, hematocrit, fibrinogen, and liver enzymes once a week for 1 month.

Data Collection and Statistical Analysis

A case report was completed at 1 month for each patient and included patient baseline data, indication for PTCA, procedural information, and in-hospital follow-up. Because this multicenter study was conducted without a core laboratory and because the quantitative coronary angiography analysis differed throughout the 25 centers, we chose to use maximal balloon diameter as reference instead of measured arterial diameter. One-month follow-up included clinical data, ECG recordings, and biological measurements. All major and minor events were precisely recorded.

Statistical analysis was performed on a personal computer with SAS 6.08 software. Data were summarized as mean and SD values as continuous variables and frequencies for the categorical variables. The association measures between complication supervention and relevant factors were evaluated through the logit estimates of the odds ratios and their associated 95% CIs. The likelihood ratio χ^2 statistic was used to test the univariate hypotheses for categorized data even though the Kruskal-Wallis test was used for continuous data. All the univariate tests were considered to be statistically significant for a value of $P<.05$. The multivariate analysis with a stepwise logistic regression was performed to identify the independent predictors for general and local complications. Backward elimination and maximum likelihood estimations were used for the selection of factors in the model that was determined by a probability value of $P<.15$. Any selected factor was considered to be an independent predictor. For factors with three modalities, adjusted odds ratios and P values were provided for the 1 *df* comparisons between the first two modalities and between the last two modalities. The SAS Proc Catmod did not permit analysis of patients with missing data.

Results

Baseline Patient Characteristics

In this study, 2900 consecutive patients underwent successful stenting procedures. Most of the patients were men (84.5%; mean age, 61.1±10.6 years). Patients enrolled in the study exhibited unstable angina (1129; 38.9%), stress-induced angina (977; 33.7%), asymptomatic restenosis after PTCA (195; 6.7%), postinfarction documented ischemia (437; 15.1%), and post-CABG ischemia (76; 2.6%). Eighty-six patients (3.0%) were enrolled with evolving MI. Indications for stenting were planned stenting (1034; 35.7%), restenosis (439; 15.1%), suboptimal balloon angioplasty result(570; 19.7%), nonocclusive dissection (647; 22.3%), and occlusive dissection (210; 7.2%). Baseline clinical and procedural characteristics of the study population are detailed on a phase-by-phase in Table 1.

The dilated lesions were located in the left anterior descending coronary artery (1248; 43.0%), right coronary artery (998; 34.4%), left circumflex artery (450; 15.5%), saphenous vein graft (160; 5.5%), protected left main coronary artery (25; 0.9%), or in another artery (ie, lateral or obtuse marginal branches) (19; 0.7%). The most frequently implanted stent was a Palmaz-Schatz stent (Johnson and Johnson) (2361; 81.3%); others included microstent (AVE) (312; 10.8%), Wiktor (Medtronic) (106; 3.7%), Gianturco-Roubin (Cook) (103; 3.6%), Strecker (Boston Scientific) (1), and multiple various types (17; 0.6%). Maximal balloon size used as an approximation to normal artery size was assessed for each angioplasty procedure. Results showed a slight decrease in maximal balloon size, which may reflect the confidence that operators progressively gained in stenting smaller arteries. Maximal balloon inflation pressure was recorded only in the two last phases of the study (mean, 12.4±3.5 atm). Because stenting arteries of <3.25 mm had been reported to be a high-risk procedure and because of the BENESTENT[5] and STRESS[4] protocols, as a rule operators did not try to stent arteries of <3.0 mm, except for bail-out procedures. Data regarding the size of the femoral sheath were collected from phases III through V but not in phase II. Table 1 provides a summary of the dramatic reduction in sheath size across the different phases of the study, probably reflecting the technical improvements in guiding catheters, balloons, and stenting procedures. The effects of this reduction in sheath size are discussed later. Finally, during the different phases of the study, we observed a significant regular decrease in global and poststent in-hospital stay ($P<.001$) (Table 1).

One-Month Clinical Outcome

Postprocedural success without major complications at 1-month follow-up was obtained in 2816 patients (97.1%). Eighty-four (2.9%) showed major cardiac events either during the in-hospital stay or 1-month follow-up. At 1 month, 17 patients (0.6%) had died, 44 (1.5%) had experienced Q-wave or non–Q-wave MI, 13 (0.5%) had repeat PTCA at the same site, and 10 (0.3%) had emergency or elective CABG. In 33 patients (1.1%)with complications, stent patency could be proved: among these 33 patients, 5 (0.2%) died, 1 had CABG, and 27 (0.9%) had acute MI, which was caused by a side-branch occlusion during stenting or, more frequently, by the transient artery occlusion before stenting in bail-out procedures.

Proven or Suspected Stent Occlusion

Fifty-one patients (1.8%) had suspected or proven stent thrombosis. Among these patients, 12 (0.5%) died, 17 (0.6%) had nonfatal Q-wave or non–Q-wave acute MI, 9 (0.3%) had emergency or elective CABG, and 13 (0.4%) underwent repeat PTCA at the same site. There was no statistical difference in cardiac complication rates throughout the four phases, during which LMWH treatment was progressively reduced.

Because patency of the stented artery could be proved in 33 of the 84 patients with complications, statistical analysis was performed in the remaining 51 patients with proven or suspected stented artery closure.

A slightly higher rate of complications (3.13% versus 1.59%, P=NS) was observed at low-volume centers (<100 stenting procedures). Age of >75 years was associated with a nonsignificant higher rate of subacute closure of the stented artery (3.38% versus 1.63%, P=NS). Some clinical characteristics of the patient increased the rate of subacute closure; there was a twofold increase in complication rates in patients dilated for unstable angina or acute MI compared with patients showing stable angina (2.24% versus 1.12%, $P=.02$).

Among procedural characteristics, two variables were found to be highly significant for major complications (Table 2): stenting with a balloon size of ≤2.5 mm was associated with a 10% rate of major complication, whereas with a 3.0-mm balloon, the risk decreased to 2.3%, and with balloons of ≥3.5 mm, the risk decreased to only 1.0% ($P<.001$). Concerning angiographic indication for stent-

TABLE 1. Clinical and Procedural Characteristics of the Patients Detailed by Phases

	Phase II	Phase III	Phase IV	Phase V	Total
Patients, n	237	520	986	1157	2900
Age±SD, y	59.8±9.2	60.7±10	61.1±10.5	61.5±11.1	61.1±10.6
In-hospital stay, d					
From admission	10.1±5.5	8.2±4.2	7±3.7	5.2±3.1	6.8±4.1
After stenting	7.4±4.2	6.4±4.4	5.4±3.1	3.7±2.4	5.1±3.5
Clinical indication for angioplasty, n					
Unstable angina	85 (35.9%)	180 (34.6%)	399 (40.5%)	465 (40.2%)	1129 (38.9%)
Restenosis	27 (11.4%)	59 (11.3%)	47 (4.8%)	62 (5.4%)	195 (6.7%)
Postinfarction	36 (15.2%)	65 (12.5%)	152 (15.4%)	184 (15.8%)	437 (15.1%)
Post-CABG angina	25 (10.5%)	19 (3.7%)	15 (1.5%)	17 (1.5%)	76 (2.6%)
Stress-induced angina	63 (26.6%)	185 (35.6%)	301 (30.5%)	428 (37%)	977 (33.7%)
Acute MI	1 (0.4%)	12 (2.3%)	72* (7.3%)	1* (0.1%)	86 (3%)
Indication for stenting, n					
Planned	80 (33.8%)	129 (24.8%)	281 (28.5%)	544 (47.0%)	1034 (35.7%)
Occlusive dissection	20 (8.4%)	65 (12.5%)	89 (9%)	36 (3.1%)	210 (7.2%)
Nonocclusive dissection	68 (28.7%)	136 (26.2%)	234 (23.7%)	209 (18.1%)	647 (22.3%)
Angiographic restenosis	39 (16.5%)	98 (18.8%)	166 (16.8%)	136 (11.8%)	439 (15.1%)
Suboptimal result	30 (12.7%)	92 (17.7%)	216 (21.9%)	232 (20.1%)	570 (19.7%)
Site of angioplasty, n					
LAD	75 (31.6%)	206 (39.6%)	425 (43.1%)	542 (46.8%)	1248 (43.0%)
LCx	42 (17.7%)	78 (15%)	138 (14%)	192 (16.6%)	450 (15.5%)
RCA	80 (33.8%)	187 (36%)	358 (36.3%)	373 (32.2%)	998 (34.4%)
SVG	36 (15.2%)	45 (8.7%)	48 (4.9%)	31 (2.7%)	160 (5.5%)
Left main	4 (1.7%)	4 (0.8%)	9 (0.9%)	8 (0.7%)	25 (0.9%)
Other			8 (0.8%)	11 (1%)	19 (0.7%)
Balloon size, mm					
2				5 (0.4%)	5 (0.2%)
2.5	2 (0.8%)	9 (1.7%)	38 (3.9%)	46 (4.0%)	95 (3.3%)
3	47 (19.8%)	135 (26%)	362 (36.7%)	468 (40.4%)	1012 (34.9%)
3.5	140 (59.1%)	273 (52.5%)	430 (43.6%)	492 (42.5%)	1334 (46%)
4	44 (18.6%)	93 (17.9%)	142 (14.4%)	126 (10.9%)	405 (14%)
4.5	3 (1.3%)	5 (1%)	9 (0.9%)	15 (1.3%)	32 (1.1%)
5	1 (0.4%)	5 (1%)	4 (0.4%)	5 (0.4%)	15 (0.5%)
5.5			1 (0.1%)		1 (0.03%)
Mean balloon size, mm	3.50	3.47	3.36	3.32	3.38
Maximal final inflation pressure, atm	NA	NA	12.4±3.11	12.4±3.0	12.4±3.05
Sheath size					
6F	NA	108 (20.8%)	493 (50.0%)	548 (47.4%)	1149 (43.1%)
7F	NA	81 (15.6%)	242 (24.5%)	442 (38.2%)	765 (28.8%)
≥8F	NA	323 (62.1%)	248 (25.2%)	162 (14%)	733 (27.5%)
Missing data	NA	8 (1.5%)	3 (0.3%)	5 (0.4%)	16 (0.6%)
Local bleeding complications, n					
Need for surgical repair	5 (2.1%)	12 (2.3%)	12 (1.2%)	4 (0.3%)	33 (1.1%)
Blood transfusion	4 (1.7%)	6 (1.2%)	2 (0.2%)	5 (0.4%)	17 (0.6%)
Blood transfusion and surgical repair		2 (0.4%)	3 (0.3%)		5 (0.2%)
Total	9 (3.8%)	20 (3.8%)	17 (1.7%)	9 (0.8%)	55 (1.9%)

LAD indicates left anterior descending coronary artery; LCx, left circumflex artery; RCA, right coronary artery; and SGV, saphenous vein graft.

The shortening of in-hospital stay after stenting procedure through the different phases was statistically significant ($P<.001$).

*During phase V of the study, patients with acute MI were preferentially moved to phase IV protocol.

NA indicates that data are not available for the early phases of the study.

ing, patients stented for occlusive dissection had a subacute occlusion rate of 6.67%, which compared unfavorably with the 1.38% subacute occlusion rate in patients stented for other reasons ($P<.001$).

Sex, type of stent, number of stents implanted in the same patient, sheath size, type of artery, and phase of the study were not discriminants for general complication rates (Table 2). In the 17 patients with multiple stent implantations, no cardiac event and no subacute stent thrombosis were observed.

The following variables were entered in the multivariate model: low- or high-volume centers, age, sex, type of stent, balloon size, number of stents per patient, sheath size, clinical presentation, indication for stenting, type of artery, and duration of LMWH therapy. For general variables, the independent predictors for subacute closure of the stented artery were unstable angina or acute MI ($P=.02$) and the volume of the centers ($P=.04$). For procedural variables, the independent predictors for poorer outcome were bail-out procedures ($P<.001$) and the use of a balloon of <3.0 mm for stenting ($P<.001$).

As we initially did not know the importance of this criterion, maximal final inflation pressure was reported only in phases IV and V of the study. Noteworthy, this proce-

TABLE 2. Clinical and Procedural Univariate and Multivariate Predictors of Subacute Stented Artery Occlusion at 1 Month Follow-up

	Subacute Closure		Univariate Analysis		Multivariate Analysis	
	Percentage of Patients (n=2900)	Complication Rate, %	Univariate *P*	Odds Ratio (CI)	Multivariate *P*	Adjusted Odds Ratio (CI)
Participating centers						
Nonexperiment	11.0	3.13	.07	2.01 (0.99-4.04)	.04	1.46 (1.03-2.08)
Experiment	89.0	1.59				
Age, y						
>75	7.1	3.38	.10	2.11 (0.94-4.74)	.14	1.36 (0.90-2.06)
≤75	92.9	1.63				
Sex						
Female	15.5	2.22	.43	1.33 (0.32-1.59)		
Male	84.5	1.67				
Type of stent						
Palmaz-Schatz	81.9	1.81	.40	1.40 (0.63-3.12)		
Other	18.1	1.34				
Balloon size, mm						
≤2.5	3.5	10.0	<.001	10.30 (4.67-22.73)	<.001‡	
3.0	34.9	2.3		2.16 (1.17-4.00)	<.01§	3.22 (1.92-5.26)
≥3.5	61.6	1.0			.32§	1.22 (0.83-1.81)
No. of stents/patient*						
One	82.1	1.72	.85	0.89 (0.44-1.79)		
Multiple	17.9	1.93				
Sheath size†						
6F	43.3	1.48	.49	0.77 (0.38-1.56)		
7F	29.0	2.21		1.16 (0.57-2.38)		
≥8F	25.2	1.99				
Maximal final inflation pressure, atm						
≤8	4	4.92	.23		.42	
8-15	70.8	2.03				
>15	25.2	1.30				
Clinical presentation						
Unstable angina/ acute MI	57.0	2.24	.02	2.02 (1.09-3.75)	.04	1.39 (1.02-1.90)
Stable angina/ elective/restenosis	43.0	1.12				
Reason for stenting						
Occlusive dissection	7.2	6.67	<.001	5.12 (2.72-9.63)	<.001	1.82 (1.02-2.54)
Other	92.8	1.38				
Vessel type						
Native artery	94.5	1.79	.60	1.4 (0.35-5.97)		
Graft	5.5	1.25				
Duration of LMWH therapy (phase)						
II-III	26.1	1.32	.27	0.68 (0.34-1.37)		
IV-V	73.9	1.91				

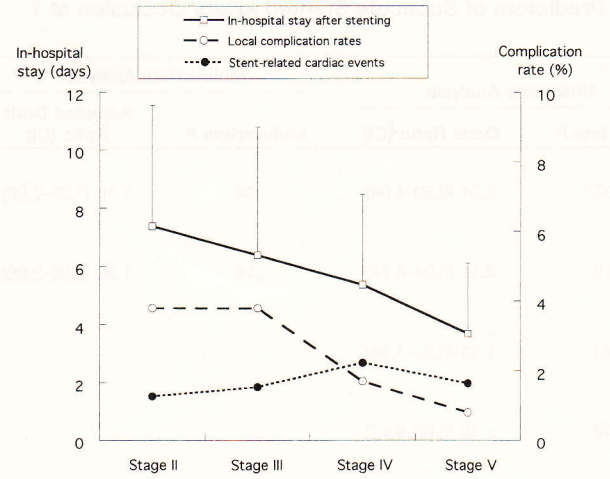
Factors not included in the multivariate model analysis ($P>.15$).
*For methodological reasons, patients with multiple various stent implantation procedures were excluded from this analysis.
†Data were not available for phase II.
‡Compared with the third level.
§Overall comparison.

dural variable had no significant effect on subacute thrombosis rates.

Local Vascular Complications

An overall incidence of 1.9% (55 patients) of local complications occurred during the 1-month follow-up. A detailed distribution of these complications is given in Table 1; there is a progressive decrease in local complication rates through the different phases of the study (Figure). We studied the effects of the following variables on local bleeding complications. Clinical variables were high- or low-volume centers, age and gender of the patients, clinical presentation, and duration of LMWH therapy. Procedural variables were stenting indication, size of the balloon used for stenting, type of stent, number of stents implanted per patient, vessel type, and sheath size.

Female gender was significantly associated with an increase in local bleeding complications (4.0% versus 1.51%, $P=.001$). There was no increase in local bleeding rate in elderly patients. Sheath size and LMWH therapy duration were the strongest predictors of bleeding complications (both $P<.001$). The rate of bleeding increased exponentially with sheath size: 0.52% for 6F, 1.04% for 7F, and 4.23% for ≥8F ($P<.001$). Conversely, bleeding complications decreased linearly with the shortening of LMWH therapy duration: 3.83% for 4 or 2 weeks of LMWH treatment, 1.72% for 1 week of treatment, and 0.69% when no LMWH treatment was administered after



In-hospital stay after stenting procedure, stent-related cardiac events, and local bleeding complication rates during the different phases of the study.

the stenting procedure ($P<.001$). Bail-out procedures for occlusive dissection or saphenous vein graft stenting were associated with a higher rate of bleeding complications ($P=.002$ and $P=.04$, respectively). Conversely, experience of the participating center, clinical presentation, type of stents, and number of stents implanted had no effect on bleeding complication rates (Table 3).

Gender, sheath size, stenting indication, saphenous vein graft stenting, and duration of LMWH were found to be independent predictors of bleeding complications in the multivariate analysis, whereas age of patient and type and number of stents implanted were not selected in the multivariate model as significant predictors (Table 3).

Hematological Side Effects

Investigators were not asked to report results of blood analyses. However, 23 cases (0.8%) of reversible leukopenia were reported. No major hematological complication was reported in this series.

Discussion

Study Design and Limitations

We report the 1-month results of the multicenter registry with a new poststenting antiplatelet therapy in which the combination of ticlopidine and aspirin is associated with decreasing duration of LMWH treatment. Because the exclusion criteria for stenting were very limited, the study population was representative of routine interventional practice in France. Although 49.2% of patients had an unplanned procedure, complication rates remained low (1-month mortality, 0.6%; overall major complications, 2.9%; proven or suspected stent thrombosis, 1.8%; severe groin bleeding complications, 1.9%).

This study has major limitations: it presents the results of a volunteer, consecutive, nonrandomized, multicenter registry, which cannot be compared with a randomized trial. However, the size of the study population and the absence of exclusion criteria underline the consistency of the statistical results.

Because the lack of an independent central core laboratory and the various angiographic equipment of the different investigating centers did not allow reproducible quantitative coronary angiography analysis, we chose to use maximal balloon size as an approximation of mean luminal artery size. Consequently, the study design did not permit the analysis of the effects of preprocedural and postprocedural angiographic characteristics in the occurrence of subacute closure and clinical outcome. We are aware that if balloon size allows an approximation of the artery size, the real artery-to-balloon ratio cannot be accurately determined. Nevertheless, a balloon-to-artery ratio of 1:1 to 1:1.2 was recommended in an attempt to reduce discrepancies between balloon and artery sizes.

It is important to emphasize that there was some degree of overlap between phases IV and V, whereas the previous phases were strictly consecutive. Thus, in patients admitted for acute MI and bail-out procedures, investigators were able to choose between phase IV and phase V strategy. Almost all of these patients were switched to receive phase IV strategy with a 1-week LMWH treatment. This could account for the trend toward higher rates of systemic and local complications in the phase IV group. Finally, the recruitment of the patients did not allow 6-month follow-up, and therefore, data for restenosis are not available in this study.

Subacute Closure and Cardiac Complications

The beneficial effects of stenting in reducing acute complications and restenosis rates compared with conventional PTCA have been reported by the BENESTENT[5] and STRESS[4] studies. The main limitations of coronary stenting that have been reported in the literature are the high rate of subacute closure and the significant rate of bleeding complication when associated with an aggressive coumadin-based anticoagulation protocol.[2,3,6,11,12] Predictors of subacute occlusion have been reported to be multiple stents, bail-out implantation, artery diameter of <3.25 mm, and impaired left ventricular ejection fraction.[9,10,13] Furthermore, coumadin treatment requires a prolonged hospital stay, which dramatically increases the cost of the procedure. Recently, Colombo et al[14] hypothesized that subacute thrombosis was more likely to be caused by incomplete deployment of the stent and impaired rheologic conditions in the stented artery than by the thrombogenic properties of the stent. Therefore, this group proposed a stenting strategy based on endo/echographic assessment of the stent deployment without anticoagulation.[14] A previous study[7] carried out by our group replaced coumadin with LMWH in an attempt to reduce the subacute occlusion rates after stenting. Unfortunately, this protocol failed, and subacute closure rates remained as high as with coumadin. Because the peak of subacute closure at 5 to 8 days was the same, we were able to eliminate the heparin/coumadin switch as the mechanism of stent thrombosis. The major role of platelet aggregation in stenting despite heparin treatment has been well documented in experimental models[15] as well as in clinical situations.[16] Recently, Barragan et al[17] reported a low subacute occlusion rate after stenting with the use of a new combination of ticlopidine and subcutaneous heparin. Ticlopidine is a potent inhibitor of ADP-induced platelet aggregation,[18,19] whereas inhibitory effects of acetylsalicylic acid are directed against thromboxane A_2. Therefore, we assumed that an aggressive antiplatelet treatment based on ticlopidine/aspirin could be an effective alternative to anticoagulation with coumadin. This treatment was instituted for 1 month, which is the time needed to ensure a complete covering of the stent by endothelial cells. In association with

TABLE 3. Clinical and Procedural Univariate and Multivariate Predictors of Local Bleeding Complications at 1-Month Follow-up

	Local Bleeding Complications		Univariate Analysis		Multivariate Analysis	
	Percentage of Patients (n=2900)	Complication Rate, %	Univariate *P*	Odds Ratio (CI)	Multivariate *P*	Adjusted Odds Ratio (CI)
Participating centers						
Experiment	89.0	2.01	.15	2.17 (0.67-7.14)		
Nonexperiment	11.0	0.94				
Age, y						
>75	7.1	2.90	.31	1.61 (0.68-3.81)		
≤75	92.9	1.82				
Sex						
Female	15.5	4.00	.001	2.70 (1.53-4.76)	<.001	1.96 (1.40-2.72)
Male	84.5	1.51				
Type of stent						
Palmaz-Schatz	81.9	1.95	.52	1.28 (0.6-2.72)	.15	1.39 (0.89-2.18)
Other	18.1	1.53				
No. of stents/patient						
One	82.1	1.81	.46	0.78 (0.41-1.47)	.12	1.33 (0.92-1.94)
Multiple*	17.9	2.31				
Sheath size†						
≥8F	27.7	4.23	<.001	8.45 (3.49-20.26)	<.001‡	
7F	29.0	1.04		2.00 (0.69-5.80)	<.01§	3.13 (1.61-6.09)
6F	43.3	0.52			.90§	1.03 (0.58-1.87)
Clinical presentation						
Stable angina/elective/ restenosis	43.0	1.92	.93	1.02 (0.60-1.75)		
Unstable angina/acute MI	57.0	1.88				
Reason for stenting						
Occlusive dissection	7.2	4.76	.002	2.94 (1.46-5.92)	<.01	1.72 (1.18-2.49)
Other	92.8	1.67				
Vessel type						
Graft	5.5	4.38	.04	2.56 (1.14-5.88)		
Native artery	94.5	1.75				
Duration of LMWH therapy (phase)						
II-III	26.1	3.83	<.001	5.08 (2.39-10.75)	.12‡	
IV	34.0	1.72		2.23 (1.00-5.05)	.06§	1.55 (0.97-2.50)
V	39.9	0.69			.62§	1.12 (0.71-1.75)

Factors not included in the multivariate model analysis ($P>.15$).
*For methodological reasons, patients with multiple various stent implantation were excluded from this analysis.
†Data were not available for phase II.
‡Overall comparison.
§Compared with the third level.

subcutaneous treatment, this protocol was previously tried out by our group in phase II of the study and gave encouraging results, with lower subacute closure rates and lower bleeding events than occurred with the usual coumadin-based protocols.[20] Because we assumed that these good results were due to the ticlopidine/aspirin combination, we progressively reduced the LMWH therapy duration to complete suppression, as planned in the beginning of the study. In addition, this strategy allowed earlier discharge of the patients, which led to a progressive significant decrease in in-hospital stay after the stenting procedure (Figure).

In this study, the overall mortality (0.6%) as well as the rate of major cardiac events (2.9%) remained low compared with rates of other series of stented patients.[11,12] In all cases, in the absence of angiographically proven subacute closure of the stented artery, the occurrence of a systemic event was, by convention, assumed to be due to subacute thrombosis of the stent.

Predictors of major complications were the same as those described in the literature. Analysis exhibited a higher risk of subacute thrombosis in stenting small arteries of <3.0 mm. Due to the design of the study, which assimilates the size of the artery to the size of the balloon, we cannot determine whether the higher incidence of subacute closure is caused by the artery diameter rather than by an inadequate undersizing of the balloon. Nevertheless, our data are consistent with previous studies exhibiting higher complication rates in small arteries. Stenting for unstable angina or acute MI also appeared to be at higher risk. The instability of the atheromatous plaque, as encountered in the subset of unstable angina, as well as bail-out situations seemed to be associated with an increasing rate of subacute thrombosis. The presence of thrombus at the angioplasty site linked to an unstable and more complex plaque could account for the increased rate of complications in these situations. Bail-out circumstances were also associated with a higher risk of subacute closure. The occurrence of balloon angioplasty complications is usually due to more complex lesions or is associated with high-risk clinical presentation (ie, women or elderly patients). This could explain why, in this subset, stenting leads to worse angiographic results and to higher rates of subacute closure.

Surprisingly, maximal final inflation pressure was not a predictor of subacute stent thrombosis, but this result remains questionable due to missing data in phases II and III.

Finally, a volume-related effect appeared to be statistically significant ($P=.04$; odds ratio, 1.46). High-volume centers reported a lower rate of major complications, suggesting a learning curve effect.

Predisposing factors for local vascular complications were identified in previous studies. These factors include age of >75 years, female gender, sheath size of >8F, duration of sheath insertion, duration of PTCA procedure, and periprocedural use of heparin.[21-24] In our study, a higher rate of local complications was associated with female gender ($P=.001$), saphenous vein graft stenting ($P=.04$), bail-out procedures ($P=.002$), subcutaneous LMWH therapy duration ($P<.001$), and sheath size ($P<.001$). The relation between local bleeding complications and saphenous vein graft stenting or bail-out situations was not clear. We suggest that in these more complex or complicated procedures, we observed a higher rate of local bleeding complications because the need for intraaortic counterpulsation or intracoronary thrombolysis, and therefore intraprocedural administered doses of IV heparin, was higher, sheath size was larger, and duration of sheath insertion was longer. In our study, the two strongest univariate and multivariate predictors of bleeding complications were the increase in LMWH therapy duration and sheath size. Concerning the duration of postprocedural anticoagulation, our study led to the same conclusions as those of other series. In observation of a significant reduction in the rate of local complications from phase II to phase III without a rise in subacute thrombosis rates, we were tempted to pursue the shortening of postprocedural anticoagulation to reduce local complications further. This strategy resulted in complete suppression of heparin therapy in phase V, which did not increase subacute thrombosis rates of the stented arteries. Concerning factors determining femoral complications, Popma et al[25] suggested that there was no relation between sheath size and the occurrence of local bleeding. Our results led to the opposite conclusion, as we found a proportional decrease in local bleeding complications with the downsizing of the sheath diameter. Nevertheless, the range of sheath sizes used in the series of the Washington group was 8F to 11F, whereas in our study sheath sizes were commonly 6F to 8F and exceptionally over 8F. Because there was no overlap in sheath sizes in these two studies, it cannot be excluded that an inflection point in local complication rates exists around the 8/9F sheath size. An almost constant rate of complications for large sheath size and a regular decrease in this rate in sheath sizes of <8F could be evoked. In addition, stringent anticoagulation protocols were used by Popma et al that could in part account for their high rates of local bleeding complications, thus minimizing the proper effects of sheath size. Nevertheless, on the basis of our results, we plead for the routine use of 6F guiding catheters, even for stenting, whereas larger sheath sizes should be reserved for new PTCA devices or for particular stents. Conversely, the experience of the center in stenting, age of patients, clinical indication for PTCA, and procedural characteristics such as maximal balloon size, type of stent, and number of stents per patient did not influence the local complication rates in our series.

Incomplete apposition or inadequate sizing of the stent has been described as a major determinant of restenosis and subacute thrombosis. Therefore, Colombo et al[14] proposed optimization of the stent delivery through the use of high-pressure inflations and systematic intracoronary ultrasound imaging without coumadin. Nevertheless, some issues of this study remain unclear; the respective effects of high-pressure inflation and ultrasound imaging of the correct embedding of the stent in the arterial wall in reducing subacute thrombosis were not evaluated separately. In addition, intracoronary ultrasound is a time-consuming and costly investigation that is not affordable for a wide range of interventional catheter laboratories. Finally, this technique requires the use of accurate, highly experienced operators, since intravascular ultrasound images are not as self-explanatory as quantitative coronary angioplasty online measurements of residual stenosis. Thus, our approach, which favors relatively high-pressure inflations and angiographic assessment of the deployment of the stent associated with ticlopidine/aspirin antiaggregation, allows a low-cost, rapid, effective stenting procedure. In addition, the avoidance of ultrasound imaging allows widespread use of 6F guiding catheters, which appear to reduce local bleeding complications without increasing subacute thrombosis rates. Nevertheless, the effects of this strategy compared with ultrasound assessment of the stent deployment on restenosis rates should be assessed through additional randomized studies.

Conclusions and Future Directions

On the basis of these results, we suggest that intracoronary stenting can be performed without coumadin treatment with a sole antiaggregating treatment with the combination of aspirin and ticlopidine. Stent-related cardiac events remain very low; our results compare favorably with other studies. Adjunctive LMWH treatment does not appear to be useful because its progressive reduction did not increase stent thrombosis but rather significantly reduced local bleeding complications. Major factors associated with an increase of subacute thrombosis in the stented artery were small balloon size, used as an approximation to the artery reference diameter, and clinical subset of unstable angina or acute MI. Major factors associated with an increase of local bleeding complications were female gender, large sheath size, bail-out situations, and additional treatment with subcutaneous LMWH. We conclude that a strategy based on ticlopidine/aspirin treatment alone in association with small guiding catheters appears to be safe, allowing increased use of stenting to provide the benefit of decreased PTCA complications and, probably, decreased restenosis rates. In addition, this strategy is easy to perform, with no need for intracoronary ultrasound assessment of the stent deployment, thus reducing patient hospital stay and procedural costs.

Further randomized studies should investigate the effects of this strategy on restenosis rates and on the long-term outcome of the patients. Local drug delivery (ie, heparin) via coated stents could be another promising way of reducing subacute stent closure without increasing bleeding complications.

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References

1. Herrmann HC, Buchbinder M, Clemen M, Fishman D, Goldberg S, Leon MB, Schatz RA, Tierstein P, Walker CM, Hirshfeld JW. Emergent use of balloon-expandable stenting for failed percutaneous transluminal coronary angioplasty. *Circulation.* 1992;86:812-819.
2. George BS, Voorhees WD III, Roubin GS, Fearnot NE, Pinkerton CA, Raizner AE, King SB III, Holmes DR, Topol ER, Kereiakes DJ, Hartzler GO. Multicenter investigation of coronary stenting to treat acute or threatened closure after percutaneous transluminal angioplasty: clinical and angiographic outcomes. *J Am Coll Cardiol.* 1993;22:135-143.
3. Hearn JA, King SB III, Douglas JS Jr, Carlin SF, Lembo NJ, Ghazzal ZM. Clinical and angiographic outcomes after coronary artery stenting for acute or threatened closure after percutaneous transluminal angioplasty: initial results with a balloon expandable, stainless steel design. *Circulation.* 1993;88:2086-2096.
4. Fischman DL, Leon MB, Baim D, Schatz RA, Penn I, Detre K, Savage MP, Veltri L, Ricci D, Nobuyoshi M, Cleman M, Heuser R, Almond D, Teirstein P, Fish D, Colombo A, Brinker J, Moses J, Hirshfeld J, Bailey S, Ellis S, Rake R, Goldberg S. A randomized comparison of coronary stent placement and balloon angioplasty in the treatment of coronary artery disease. *N Engl J Med.* 1994; 331:496-501.
5. Serruys PW, De Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, Emanuelsson H, Marco J, Legrand V, Materne P, Belardi J, Sigwart U, Colombo A, Goy J-J, Van den Huevel P, Delcan J, Morel MA, for the BENESTENT Study Group. A comparison of balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. *N Engl J Med.* 1994;331: 489-495.
6. Sutton JM, Ellis SG, Roubin GS, Pinkerton CA, King SB III, Raizner AE, Holmes DR, Kereiakes DJ, Topol EJ. Major clinical events after coronary stenting: the multicenter registry of acute and elective Gianturco-Roubin stent placement. *Circulation.* 1994;89:1126-1137.
7. Bourdonnec C, Biron Y, Didier B, Guerin Y, Labrunie P, Lienhard Y, Morice MC, Royer T, Valeix B. Coronary stenting without coumadin. *Eur Heart J.* 1993;14:350. Abstract.
8. De Caterina R, Sicari R, Bernini W, Lazzerini G, Buti SG, Gianessi D. Benefit/risk profile of combined antiplatelet therapy with ticlopidine and aspirin. *Thromb Haemost.* 1991;65:504-510.
9. Diaz L, Fajadet J, Cassagneau B, Robert G, Marco J. The short-term results and angiographic predictors of subacute thrombosis in the coronary implantation of the Palmaz-Schatz endoprothesis. *Rev Esp Cardiol.* 1994;47:747-753.
10. Chan CN, Tan AT, Koh TH, Koh P, Lau KW, Gunawan SA, Chakraborty B. Intracoronary stenting in the treatment of acute or threatened closure in angiographically small coronary arteries (<3.0 mm) complicating percutaneous transluminal coronary angioplasty. *Am J Cardiol.* 1995;75:23-25.
11. Schatz RA, Baim DS, Leon M, Ellis SG, Goldberg S, Hirshfeld JW, Cleman MW, Cabin HS, Walker C, Stagg J, Buchbinder M, Teirstein PS, Topol EJ, Savage M, Perez JA, Curry RC, Whithworth H, Sousa JE, Tio F, Almagor Y, Ponder R, Penn IM, Leonard B, Lewine SL, Fish SL, Palmaz JC. Clinical experience with the Palmaz-Schatz coronary stent: initial results of a multicenter study. *Circulation.* 1991;83:148-161.
12. Serruys PW, Strauss BH, Beatt KJ, Bertrand ME, Puel J, Rickards AF, Meier B, Goy JJ, Vogt P, Kappenberger L, Sigwart U. Angiographic follow-up after placement of self-expanding coronary artery stent. *N Engl J Med.* 1991;324:13-17.
13. Iniguez A, Macaya C, Goicolea J, Alfonso F, Hernandez R, Fernandez R, Silva JC, Zarco P. Angiographic and clinical factors related to subacute Palmaz-Schatz stent occlusion in native vessels: a prospective study. *Eur Heart J.* 1993;14:323.
14. Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, Gaglione G, Goldberg SL, Tobis SL. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation.* 1995;91:1676-1688.
15. Parsson H, Cwikiel W, Johansson K, Swartbol P, Norgren L. Deposition of platelets and neutrophils in porcine iliac arteries after angioplasty and Wallstent placement compared with angioplasty alone. *Cardiovasc Intervent Radiol.* 1994;17:190-196.
16. Kopp DT, Tio FO, Ciaravinao V, Schatz RA, Rees C, Alvaredo R, Lancaster JL, Borchert RD. Balloon expandable intra-arterial stents: effects of antithrombotic medication on thrombus formation. In: Zeitler E, ed. *Pros and Cons in PTA and Auxilliary Methods.* Berlin, Germany: Springer-Verlag; 1989:170-178.
17. Barragan P, Sainsous J, Silvestri M, Bouvier JL, Comet B, Simeoni JB, Charmasson C, Bremondy M. Ticlopidine and subcutaneous heparin as an alternative regimen following coronary stenting. *Cathet Cardiovasc Diagn.* 1995;32:133-138.
18. Gent M, Blakely JA, Easton JD, Ellis DJ, Hachinski VC, Harbison JW, Panak E, Roberts RS, Sicurella J. The Canadian American Ticlopidine Study (CATS) in thromboembolic stroke. *Lancet.* 1989; 1:1215-1220.
19. Cattaneo M, Akkawat B, Lecchi A, Cimminiello C, Capitanio AM, Mannucci PM. Ticlopidine selectively inhibits human platelet response to adenosine diphosphate. *Thromb Haemost.* 1991;66: 694-699.
20. Morice MC, Zemour G, Benveniste E, Biron Y, Bourdonnec C, Faivre R, Fajadet J, Gaspard P, Glatt B, Joly P, Labrunie P, Lienhart Y, Marco J, Petiteau PY, Royer T, Valeix B. Intracoronary stenting without coumadin: 1-month results of a French multicenter study. *Cathet Cardiovasc Diagn.* 1995;35:1-7.
21. Oweida SW, Roubin GS, Smith RB III, Salam AA. Postcatheterization vascular complications associated with percutaneous transluminal coronary angioplasty. *J Vasc Surg.* 1990;12:310-315.
22. McCann RL, Schwartz LB, Pieper KS. Vascular complications of cardiac catheterization. *J Vasc Surg.* 1991;14:375-381.
23. Muller DW, Shamir KJ, Ellis SG, Topol EJ. Peripheral vascular complications after conventional and complex percutaneous coronary interrventional procedures. *Am J Cardiol.* 1992;69:63-68.
24. Berge PG, Winter UJ, Hoffmann M, Albrecht D, Hopp HW, Hilger HH. Local vascular complications in heart catheter studies. *Z Kardiol.* 1993;82:449-456.
25. Popma JJ, Satler LF, Pichard A, Kent KM, Campbell A, Chuang YC, Clark C, Merritt AJ, Bucher TA, Leon MB. Vascular complications after balloon and new device angioplasty. *Circulation.* 1993;88: 1569-1578.