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ST-Segment Elevation Myocardial Infarction Due to Early and Late Stent Thrombosis

A New Group of High-Risk Patients

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Objectives The aim of this retrospective study was to compare clinical and angiographic outcomes between patients presenting with ST-segment elevation myocardial infarction (STEMI) due to stent thrombosis (ST) and de novo coronary thrombosis.

Background There are limited data for procedural and mid-term outcomes of patients with ST presenting with STEMI.

Methods From January 2004 to March 2007, 115 definite ST patients were observed: 92 (80%) of them presented as STEMI and were compared with a consecutive group of 98 patients with de novo STEMI. All patients underwent primary percutaneous coronary intervention. Primary end points were successful angiographic reperfusion and distal embolization. Major adverse cardiovascular and cerebrovascular events (MACCE), evaluated at 6-month follow-up, were defined as death, nonfatal myocardial reinfarction, target vessel revascularization, and cerebrovascular accident.

Results Successful reperfusion rate was lower in patients with ST ($p < 0.0001$), whereas distal embolization rate was higher ($p = 0.01$) in comparison with patients with de novo STEMI. Stent thrombosis proved to be an independent predictor of unsuccessful reperfusion at propensity-adjusted binary logistic regression (odds ratio 6.8, $p = 0.004$). In-hospital MACCE rate was higher in patients with ST ($p = 0.003$), whereas no differences were observed at 6-month follow-up among hospital survivors between the 2 groups ($p = 0.7$).

Conclusions Stent thrombosis identifies a subgroup of patients with STEMI with poor angiographic and early clinical outcomes, suggesting that the management of these patients should be improved. (J Am Coll Cardiol 2008;51: 2396–402) © 2008 by the American College of Cardiology Foundation

Stent thrombosis (ST) is a recognized complication occurring in 0.5% to 2.2% (1,2) of patients with coronary artery disease treated by percutaneous coronary intervention (PCI) with stent implantation. Its occurrence is expected to increase with the number of stent—in particular drug-eluting stent (DES)—implantation procedures done worldwide. Clinical consequences of ST are generally catastrophic, including short-term mortality rates of up to 20% to 25% and major myocardial infarction (MI) in 60% to 70% of cases and 6-month mortality rates, among survivors of ST, of up to 20% to 25% (1). The presentation of ST is very often an ST-segment elevation myocardial infarction (STEMI) (3,4). Thus, ST represents a new, although rare, cause of STEMI that seems to be associated with worse clinical outcomes than STEMI due to coronary thrombosis. Repeat PCI is the commonly adopted treatment in the ST setting. However, few scientific data are available on procedural and midterm comparison of

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STEMI due to ST versus de novo STEMI. We thus retrospectively analyzed clinical presentation and angiographic and clinical outcomes of 2 groups of consecutive patients with STEMI caused by ST versus de novo coronary thrombosis, all treated with primary PCI, to evaluate whether patients with STEMI due to ST have higher procedural risk and worse clinical outcome.

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Methods

Study population. From January 2004 to March 2007, 6,068 PCIs were performed with 3,645 bare-metal stents (BMS) and 5,457 DES implanted. During this period 115 (1.8%) STs were observed, of which 85 (2.3%) were DES thromboses, whereas 30 (1.2%) were BMS thromboses. Ninety-two (80%) of these STs presented as STEMI, and all were treated with primary PCI. We retrospectively compared this group of STs presenting with STEMI with a consecutive group of 98 patients with STEMI due to de novo coronary thrombosis treated with primary PCI from January to October 2004. Patients were identified in our database. Only patients fulfilling clinical criteria for STEMI diagnosis (i.e., chest pain persisting ≥30 min associated with ST-segment elevation ≥0.1 mV in ≥2 continuous electrocardiographic leads) and angiographic criteria for definite ST according to the Academic Research Consortium definition (5) were included in our study.

Procedure. Primary PCI was performed according to standard care. Unfractioned heparin was given as an initial bolus of 70 IU/kg, and additional boluses were administered during the procedure to achieve an activated clotting time of 250 to 300 s. All patients who had not taken aspirin before presentation with STEMI received chewable aspirin at a dose of 325 mg, followed by 100 mg/day by mouth indefinitely. Patients were loaded—if not previously taking clopidogrel—with 300 or 600 mg clopidogrel before or immediately at the end of the procedure, followed by 75 mg/day for at least 12 months. The use of glycoprotein IIb/IIIa inhibitors, thrombus removal, and embolic protection devices was left to the operator's discretion. Mechanical assistance devices (intra-aortic balloon pump and hemopump Impella Acute [Aachen, Germany]) were used when hemodynamic support was necessary (e.g., in the case of depressed systolic function and cardiogenic shock at presentation). Serial samples for determination of cardiac biomarkers were routinely collected in all patients 6, 12, and 24 h after the procedure.

Patients with ST at the time of the index procedure were recommended to take clopidogrel 75 mg/day in addition to aspirin for 1 month after BMS implantation, 12 months after DES implantation, and in case of acute coronary syndrome (ACS).

Angiographic analysis. All PCI angiograms have been analyzed to assess a series of key angiographic data: 1) pre- and post-procedural antegrade coronary flow according to the standard Thrombolysis In Myocardial Infarction (TIMI) criteria (6); 2) pre-procedural thrombus grade (TG) according to the TIMI study group (7) (and in patients presenting with TG 5, thrombus burden was also reclassified according to Sianos et al. [8]); 3) occurrence of angiographic distal embolization defined as occlusion with an abrupt cut-off appearance at angiography of a branch of the infarct related artery distal to the culprit lesion site; 4) corrected TIMI frame count according to Gibson et al. (9), calculated in patients with post-procedural TIMI flow grade ≥2; 5) post-procedural myocardial blush grade according to van't Hof et al. (10); and 6) post-procedural quantitative coronary angiography analysis performed, according to established methods (11) with a dedicated software (CMS-QCA 4, Medis, Leiden, the Netherlands), within the stented segment and the 5 mm proximal and distal to the stent (total analysis segment).

Clinical follow-up. Information regarding baseline clinical characteristics, procedural details, and in-hospital events was obtained from our database. At 6 months from the procedure, data regarding clinical status were obtained by follow-up visit or telephone interview.

End points and definitions. Primary end points identified for analysis in this study were the rate of optimal angiographic reperfusion defined, according to De Luca et al. (12), as the combination of post-procedural TIMI flow grade 3 and myocardial blush grade 2 or 3, and the rate of distal embolization. The occurrence of major adverse cardiovascular and cerebrovascular events (MACCE) (i.e., death, nonfatal myocardial reinfarction, target vessel revascularization [TVR], and cerebrovascular accident) was evaluated during hospital stay and at 6-month follow-up. Nonfatal reinfarction was defined as new clinical symptoms or electrocardiographic changes associated with an increase in the creatine kinase level more than twice the upper normal limit with an increased creatine kinase-myocardial band. In cases in which the creatine kinase level had not returned to normal values after the index event, a second peak was defined as repeat MI. Target vessel revascularization was defined as any repeat revascularization (with PCI or coronary artery bypass grafting) of the infarct-related artery. According to the Academic Research Consortium definition (5), ST was definite when there was angiographic confirmation of thrombus, with or without vessel occlusion, associated with the presence of an ACS and was classified into early (0 to 30 days, in particular acute if it occurred within 24 h after the index procedure and subacute if it occurred between 2 and 30 days), late (31 to 360 days), or very late (>360 days).

Statistical analysis. The SPSS version 12 software (SPSS Inc., Chicago, Illinois) was used for computations. Continuous data were expressed as mean ± SD and were compared with the Student *t* test. Categorical variables were expressed as percent (%) and were compared with either the chi-square or Fisher exact test when the expected cell number in

Abbreviations and Acronyms

ACS = acute coronary syndrome
BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
MACCE = major adverse cardiovascular and cerebrovascular events
MI = myocardial infarction
PCI = percutaneous coronary intervention
ST = stent thrombosis
STEMI = ST-segment elevation myocardial infarction
TG = thrombus grade
TIMI = Thrombolysis In Myocardial Infarction
TVR = target vessel revascularization

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a 2 × 2 table was <5. Because of inherent potential differences in baseline and clinical characteristics among the 2 study groups, a propensity score was built with a parsimonious approach and then forced into a multivariable logistic regression analysis (reported with odds ratios, 95% confidence intervals [CIs]) (13). Specifically, variables used in the generation of the propensity score were age, gender, hypertension, hypercholesterolemia, diabetes, smoking, family history of coronary artery disease, renal failure, previous MI, anterior STEMI, time from symptoms onset to intervention, shock at presentation, multivessel disease, left main disease, pre-procedural TIMI flow, pre-procedural TG, use of glycoprotein IIb/IIIa inhibitors, use of thrombus removal devices, and reference vessel diameter. A model also including left ventricular ejection fraction was specifically used as sensitivity analysis for in-hospital mortality predictors. The Kaplan-Meier method was used to construct survival curves. The log-rank test was used to compare survival distributions. In addition, a Cox proportional hazard analysis was performed for cumulative events at follow-up, with results expressed as hazard ratios (HR; 95% CI). For all tests, a 2-tailed $p < 0.05$ was considered significant.

Results

Patients' characteristics. Baseline clinical characteristics (Table 1) did not differ significantly between the 2 groups, except that patients in the ST group had higher rates of renal failure, prior MI, and prior stroke (15.7% vs. 4.1%, p = 0.008; 68.2% vs. 11.2%, p < 0.0001; 7.1% vs. 0%, p = 0.007, respectively) and fewer were smokers (26.5% vs. 48%, p = 0.003). All patients (n = 86) in the ST group reported at least 1 episode of ST presenting with STEMI (92 STEMI overall). Most ST (64.1%) occurred within 30 days from the index procedure, which was performed in most patients (88.4%) in the setting of an ACS; no difference in time from symptoms onset to intervention was found between patients with early and those with late or very late ST (179.0 ± 47.7 min vs. 181.1 ± 47.5 min, p = 0.83).

Table 1 Baseline Clinical Characteristics

	STEMI (n = 98)	STEMI With ST (n = 86)	p Value
Age (yrs)	62.9 ± 10.3	66.0 ± 11.9	0.06
Male	81 (82.7%)	68 (79.1%)	0.5
Cardiac risk factors			
Hypertension	45 (45.9%)	44 (51.8%)	0.4
Diabetes mellitus	14 (14.3%)	21 (25.3%)	0.06
Hypercholesterolemia	34 (34.7%)	37 (43.4%)	0.2
Current smoker	47 (48.0%)	23 (26.5%)	0.003
Family history of CAD	35 (35.7%)	23 (26.5%)	0.2
Creatine ≥1.5 mg/dl	4 (4.1%)	13 (15.7%)	0.008
COPD	3 (3.1%)	8 (9.5%)	0.07
Prior MI	11 (11.2%)	59 (68.2%)	<0.0001
Prior stroke	0 (0%)	6 (7.1%)	0.007

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; ST = stent thrombosis; STEMI = ST-segment elevation myocardial infarction.

Table 2 ST Characteristics (n = 92)

Definite ST (ARC definition)	92 (100%)
Thrombosis timing (ARC definition)	
Early (<30 days)	59 (64.1%)
Late (30–360 days)	14 (15.2%)
Very late (>360 days)	19 (20.7%)
Clinical presentation at the index procedure	43 (46.5%)
MI (acute or sub-acute)	38 (41.9%)
UA/NSTEMI stable angina or silent ischemia	11 (11.6%)
Double antiplatelet therapy at the moment of stent thrombosis	62 (67.4%)
Early discontinuation of double antiplatelet therapy	6 (6.9%)
Stent	
BMS	22 (23.9%)
DES	70 (76.1%)
Stent length	25.2 ± 12.7
Stent diameter	2.8 ± 0.3

ARC = Academic Research Consortium; BMS = bare-metal stent; DES = drug-eluting stent; MI = myocardial infarction; ST = stent thrombosis; UA/NSTEMI = unstable angina/non–ST-segment elevation myocardial infarction.

Seventy events (76.1%) were STs in patients with DES, whereas 22 (23.9%) were STs in patients with BMS; 62.7% of patients were on double antiplatelet therapy at the moment of ST, whereas 6.9% of patients reported an early discontinuation of the double antiplatelet therapy (owing to the occurrence of bleeding, the diagnosis of cancer unknown at the time of the first PCI, and the lack of compliance to the therapy). A detailed description of this group of patients is given in Table 2.

Clinical, angiographic, and procedural characteristics. As shown in Table 3, patients in the ST group had a higher albeit statistically nonsignificant rate of cardiogenic shock at presentation in comparison with patients in the other group (15.2% vs. 7.1%, p = 0.07). Multivessel disease was significantly more common in the ST group (72.8% vs. 48%, p < 0.0001), whereas there were no differences in MI location, time from onset of symptoms to PCI, and creatine phosphokinase values between the 2 groups. Procedural characteristics, in particular use of glycoprotein IIb/IIIa inhibitors, embolic protection, thrombus removal, and mechanical assistance devices, did not differ between the 2 groups (only use of angiojet was significantly higher in the ST group: 6.5% vs. 0%, p = 0.03).

Angiographic analysis. A lower successful reperfusion rate and a higher distal embolization rate were observed in patients with ST (80.4% vs. 96.9%, p < 0.0001; 6.5% vs. 0%, p = 0.01, respectively) (Table 4, Fig. 1). Indeed, ST proved to be the only significant independent predictor of unsuccessful reperfusion (odds ratio 6.8, 95% CI 1.8 to 25.2, p = 0.004) at propensity-adjusted binary logistic regression. In the ST group, shock at presentation was the only independent predictor of unsuccessful reperfusion (p = 0.01). Among patients with ST, reperfusion and distal embolization rates did not differ between patients with DES and those with BMS thromboses (77.3% vs. 90%, p = 0.2 and 7.6% vs. 5%, p = 0.7, respectively). The angiographic

Table 3 Clinical, Angiographic, and Procedural Characteristics

	STEMI (n = 98)	STEMI With ST (n = 92)	p Value
Anterior STEMI	55 (56.1%)	54 (58.7%)	0.7
Shock at presentation	7 (7.1%)	14 (15.2%)	0.07
Creatine phosphokinase max (U/l)	2,936.1 ± 2,629.8	2,285.1 ± 3,905.9	0.2
CK-MB max (ng/ml)	337.1 ± 279.4	226.6 ± 409.9	0.08
Time from symptoms onset to intervention (min)	172.6 ± 87.4	179.7 ± 47.1	0.5
Multivessel disease	47 (48%)	67 (72.8%)	<0.0001
Left main coronary artery	0 (0%)	1 (1.1%)	0.7
Left anterior descending artery	53 (54.1%)	52 (56.5%)	
Left circumflex artery	15 (15.3%)	18 (19.5%)*	
Right coronary artery	30 (30.6%)	24 (26.1%)	
Mechanical assistance devices	19 (19.4%)	25 (27.2%)	0.2
IABP	19 (19.4%)	25 (27.2%)	0.2
Hemopump Impella Acute	0 (0%)	3 (3.3%)†	0.07
Thrombus aspiration	61 (62.2%)	64 (69.6%)	0.3
AngioJet	0 (0%)	6 (6.5%)	0.03
Export or Pronto devices	61 (62.2%)	58 (63.1%)	0.9
Distal protection	0 (0%)	0 (0%)	—
Glycoprotein antagonist	89 (90.8%)	76 (82.8%)	0.1

*In 3 patients the contemporary stent thrombosis within the left anterior descending artery and left circumflex artery has been documented. †In these 3 patients either intra-aortic balloon pump (IABP) or Hemopump Impella Acute were implanted.

CK-MB = creatine kinase–myocardial band; ST = stent thrombosis; STEMI = ST-elevation myocardial infarction.

analysis revealed in patients with ST a more complex PCI (Table 4) with a higher rate of residual dissections (16.3% vs. 1%, p < 0.0001) and a larger thrombus burden (TG ≥3 was present in 100% of patients in the ST group vs. 93.9% of patients in the other group, p = 0.01; even after reclassification of the TG 5 after flow achievement, a higher thrombus burden was still observed in the ST group: TG ≥3 was present in 95.6% of patients in the ST group vs. 86.7% of patients in the other group, p = 0.03). However, when an acceptable antegrade flow (TIMI ≥2) was achieved, corrected TIMI frame count did not differ between the 2 groups (21.2 ± 9.4 in the ST group vs. 24.2 ± 12.6 in the other group, p = NS). The post-procedural quantitative coronary angiography analysis showed in patients with ST a smaller diameter of the infarct-related artery (2.9 ± 0.3 mm vs. 3.2 ± 0.4 mm, p < 0.0001) and a worse angiographic result expressed by a smaller minimal lumen diameter, a larger residual diameter stenosis, and a longer residual lesion length (2.0 ± 0.7 mm vs. 2.9 ± 0.4 mm, 31.8 ± 24.9 mm vs. 8.1 ± 6.6 mm, 7.0 ± 4.7

Table 4 Angiographic Analysis

	STEMI (n = 98)	STEMI With ST (n = 92)	p Value
Pre-procedural TIMI flow ≤1	77 (78.6%)	69 (80%)	0.8
Post-procedural TIMI flow = 3	95 (96.9%)	74 (80.4)	<0.0001
Pre-procedural TG ≥3	92 (93.9%)	92 (100%)	0.01
Post-procedural myocardial blush ≤1	1 (1.0%)	12 (13.0%)	0.001
Post-procedural cTFC*	24.2 ± 12.6	21.2 ± 9.4	0.1
Successful reperfusion	95 (96.9%)	74 (80.4%)	<0.0001
Distal embolization	0 (0%)	6 (6.5%)	0.01
Residual dissection	1 (1.0%)	15 (16.3%)	<0.0001
Post-procedural QCA analysis			
RVD (mm)	3.2 ± 0.4	2.9 ± 0.3	<0.0001
Lesion length (mm)	2.9 ± 2.6	7.0 ± 4.7	<0.0001
MLD (mm)	2.9 ± 0.4	2.0 ± 0.7	<0.0001
Diameter stenosis (%)	8.1 ± 6.6	31.8 ± 24.9	<0.0001

*Calculated in patients with post-procedural TIMI flow ≥2.

cTFC = corrected TIMI frame count; MLD = minimal lumen diameter; QCA = quantitative coronary angiography; RVD = reference vessel diameter; ST = stent thrombosis; STEMI = ST-segment elevation myocardial infarction; TG = thrombus grade; TIMI = Thrombolysis In Myocardial Infarction.

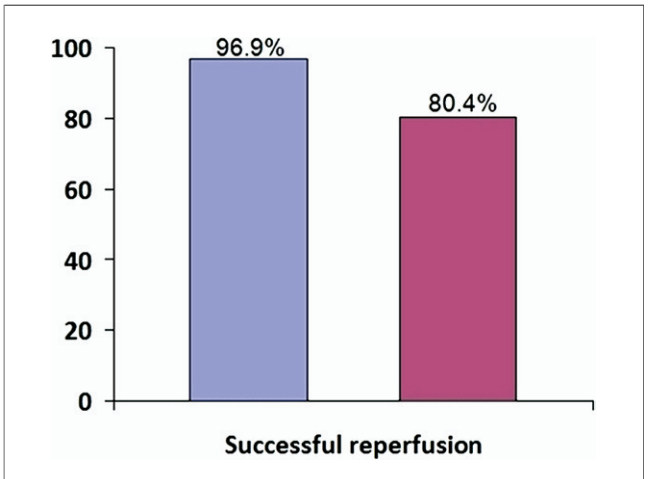

Figure 1 Successful Reperfusion

Comparison of successful reperfusion rate between patients with ST-segment elevation myocardial infarction (STEMI) due to de novo thromboses versus stent thromboses. p < 0.0001. **Blue bar** = STEMI without stent thrombosis (ST); **purple bar** = STEMI with ST.

Table 5 In-Hospital and 6-Month Follow-Up Outcomes

	In-Hospital Outcomes			Hospital Survivors 6-Month Outcomes			Cumulative 6-Month Outcomes		
	STEMI (n = 98)	STEMI With ST (n = 86)	p Value	STEMI (n = 91)	STEMI With ST (n = 71)	p Value	STEMI (n = 98)	STEMI With ST (n = 86)	p Value
Death	7 (7.1%)	15 (17.4%)	0.03	3 (3.3%)	3 (4.2%)	0.7	10 (10.2%)	18 (20.9%)	0.04
MI	1 (1%)	7 (8.1%)	0.02	0 (0%)	3 (4.2%)	0.04	1 (1%)	6 (6.9%)	0.03
TVR (PCI or CABG)	2 (2%)	8 (9.3%)	0.009	6 (6.6%)	7 (9.8%)	0.4	7 (7.1%)	12 (13.9%)	0.1
Stroke	1 (1%)	0 (0%)	0.3	0 (0%)	0 (0%)	—	1 (1%)	0 (0%)	0.3
MACCE	9 (9.2%)	22 (25.6%)	0.003	9 (9.9%)	8 (11.3%)	0.7	17 (17.3%)	27 (31.4%)	0.02
Stent thrombosis	1 (1%)*	7 (8.1%)*	0.02	0 (0%)†	2 (2.8%)†	0.1	1 (1%)	9 (10.4%)	0.01

*Subacute stent thrombosis. †Late stent thrombosis.
CABG = coronary artery bypass graft; MACCE = major adverse cardiovascular and cerebrovascular events; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; TVR = target vessel revascularization; other abbreviations as in Table 1.

mm vs. 2.9 ± 2.6 mm, respectively, with $p < 0.0001$ for all) (Table 4).

In-hospital and 6-month follow-up outcomes. Complete follow-up information was obtained in 100% of patients. In-hospital and 6-month follow-up MACCE are presented in Table 5. Patients in the ST group had a higher in-hospital MACCE rate (25.6% vs. 9.2%, $p = 0.003$), with higher mortality, reinfarction, and TVR rates but not stroke rate, which was similar between the 2 groups (17.4% vs. 7.1%, $p = 0.03$; 8.1% vs. 1%, $p = 0.02$; 9.3% vs. 2%, $p = 0.009$; 0% vs. 1%, $p = 0.3$, respectively). The rate of subacute ST was higher in patients with a previous ST (8.1% vs. 1%, $p = 0.02$); in particular, all of these STs presented with myocardial reinfarction. Stent thrombosis did not prove to be an independent predictor of in-hospital mortality (odds ratio 2.9, 95% CI 0.5 to 15.6, $p = 0.2$) at propensity-adjusted binary logistic regression. Similar findings were obtained at sensitivity analysis when forcing post-procedural left ventricular ejection fraction in the multivariable propensity-adjusted model ($p = 0.2$).

Among hospital survivors MACCE rate at 6-month follow-up did not differ between the 2 groups (11.3% in the ST group vs. 9.9% in the other group, $p = 0.7$). Only myocardial reinfarction rate was higher in patients with ST (4.2% vs. 0%, $p = 0.04$); 2 of these new MIs were subsequent to late ST, whereas 1 was subsequent to diffuse intrastent restenosis.

Kaplan-Meier survival curves show—considering the unadjusted cumulative mortality and MACCE rate at 6 months—significantly better survival and lower MACCE rate in patients with STEMI due to de novo coronary thromboses ($p = 0.04$ and $p = 0.02$, respectively) (Fig. 2). However, these comparisons were no longer significant at propensity-adjusted Cox analysis (HR for death = 1.64, 95% CI 0.62 to 4.28, $p = 0.3$; HR for MACCE = 1.29, 95% CI 0.62 to 2.67, $p = 0.4$).

Mortality and cumulative MACCE rates during hospital stay and at 6-month follow-up were not different between patients with DES and BMS thromboses (p = NS for all).

Discussion

Clinical consequences of ST are generally severe, including short-term mortality rates of up to 20% to 25% and MI in

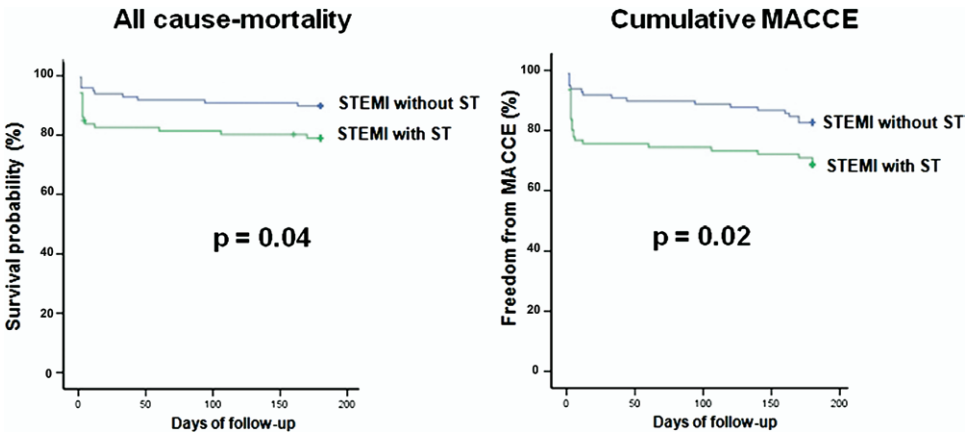

Figure 2 All-Cause Mortality and Cumulative MACCE Rate

Kaplan-Meier curve (6-month follow-up) for all-cause mortality and for cumulative major adverse cardiovascular and cerebrovascular event (MACCE) rate of patients with ST-segment elevation myocardial infarction (STEMI) due to de novo thromboses versus stent thromboses (STs).

60% to 70% of cases (1). The poor clinical outcomes associated with ST could be related to the angiographic suboptimal results often recorded after PCI for ST (4). The main finding of our study is consistent with this hypothesis. Actually, we observed a significantly lower rate of successful reperfusion and a higher rate of distal embolization in patients with ST. We performed a binary logistic regression analysis with a propensity score adjustment to reduce the disadvantage caused by the higher risk profile of patients with ST; ST itself resulted as an independent predictor of unsuccessful reperfusion. Several issues could explain this finding. The presence of a larger thrombus burden, recorded in our study in patients with ST, is probably one of the most important causes of poor procedural results, with worst reperfusion indexes (i.e., higher rate of post-procedural TIMI flow ≤2 and myocardial blush grade ≤1) and higher rate of distal embolization. Moreover, the presence of stent underexpansion, malapposition, residual dissection, and in-flow/outflow disease that have just been well established by intravascular ultrasound as mechanical causes related to ST both for BMS and DES (1,14–16) might lead to a more complex PCI with consequently poor angiographic results. Accordingly, we found more residual dissections and worse angiographic results at quantitative coronary angiography analysis in patients with ST. Unfortunately, because we did not perform intravascular ultrasound analysis in every patient presenting with ST, data regarding stent malapposition—one of the recognized causes of ST (14,16), in particular late and very late ST—are not available.

Patients with ST showed higher in-hospital mortality than the other patients. However, ST was not found to be an independent predictor of in-hospital mortality. The higher in-hospital mortality observed in patients with ST could be related not only to the lower rate of successful reperfusion but also to the worse baseline clinical characteristics at the time of ST. In particular, we found that patients with ST had a higher albeit statistically nonsignificant rate of cardiogenic shock at presentation. This finding could in part explain the higher in-hospital mortality, because the development of cardiogenic shock during MI is characterized by a poor prognosis with an early mortality up to 50% (17) despite reperfusion therapy. Moreover, patients with ST had a high baseline risk profile due to a higher rate of renal failure, prior stroke, prior MI, and multivessel disease, which could explain the higher rate of adverse outcome. These severe baseline characteristics are probably related to the use of DES in an off-label setting. Most of the ST observed in our study (76.1%) were on DES, and in 87.5% of cases DES were implanted in an off-label setting, which seems to be associated with an increased risk of death as well as of MI (18). In particular, the high rate of prior MI in the ST group is due to the high percentage (88.4%) of patients treated with stent implantation at the index procedure for an ACS and for STEMI in 46.5% of the cases. Acute coronary syndromes have been associated with increased rates of ST. Real-world registries, which included patients with ACS and STEMI treated either with BMS or DES (4,19), reported higher rates of ST than the ones observed after elective stent implantation.

Patients with ST had a higher rate of nonfatal myocardial reinfarction either during hospital stay or at 6-month follow-up. All myocardial reinfarctions occurred after an ST except 1 that was due to a diffuse intrastent restenosis that occurred after 3 months. It has been reported that ST recurs in 12% of patients with a previous ST (4). Sianos et al. (8) demonstrated that a large thrombus burden recorded during STEMI is the strongest predictor of ST and that patients with a large thrombus burden experienced an extremely high infarct-related artery ST rate of 8.2%. Moreover, the suboptimal angiographic results demonstrated by the high residual stenosis observed at the post-procedural quantitative coronary angiography analysis could be explained by some residual thrombus burden or stent underexpansion, which are both identified as factors predisposing to ST (8,15). In particular, residual thrombus is an independent predictor of early repeat MI in the PAMI (Primary Angioplasty in Myocardial Infarction) trial (20). Furthermore, ST has been associated with an impaired response to antiplatelet therapy, particularly in patients with ACS (21). Patients who experienced an ST are likely to be nonresponders to antiplatelet therapy, and this might lead to another thrombotic event.

Among hospital survivors at 6-month follow-up, we found no difference in MACCE rate between the 2 groups. Moreover, no difference in the cumulative mortality and MACCE rates was observed among patients with DES and BMS thromboses, although the small number of patients does not permit us to draw any definite conclusion.

All of these observations suggest that the management of patients with ST might be improved in order to improve clinical outcomes. In recent years, a series of adjunctive devices with the theoretical property of reducing distal embolization of thrombotic material have been conceived and entered the clinical practice. The negative or inconclusive trials performed to date in the field of thrombotic protection/extraction devices in an acute MI setting might be due to the selective enrollment of low-risk patients with limited coronary thrombus (22,23). Therefore, the large thrombus burden and the high risk of distal embolization associated with ST makes it a promising field of application for adjunctive devices. The preliminary results of the OPTIMIST (The Outcome of PCI for stent-ThrombosIs MultIcentre Study) trial have shown that patients without unstable conditions (absence of shock) treated with thrombectomy devices had no excess of adverse clinical events and had a 5-fold improved rate of optimal coronary flow restoration, thus supporting the safety and the efficacy of such devices in this high-risk scenario (24). Probably the use of such devices in combination with an extensive use of glycoprotein IIb/IIIa inhibitors might improve angiographic results. Moreover, extensive use of mechanical assistance devices might be helpful in the treatment of slow or

no-reflow often recorded during PCI in the presence of a large thrombus burden as well as for hemodynamic support, which is needed for the higher rate of cardiogenic shock present in ST setting. Finally, procedural and clinical outcomes after ST could be improved by identification and correction of procedural issues leading to ST in order to avoid its recurrence. Therefore, intravascular ultrasound analysis, performed either during or—even better—after the acute phase of ST, should be considered to assess the optimal stent deployment and the presence of residual dissection.

Study limitations. This is an observational study. We strived to minimize confounding by means of propensity analysis, but this approach cannot completely remove the risk of selection bias. In addition, intravascular ultrasound data are not available, thus limiting the ability to appraise the role of stent expansion, residual dissections, and malapposition that seem to be predictors of ST according to the published scientific data. Moreover, we did not analyze the prevalence of antiplatelet resistance, another major pathogenetic mechanism leading to thrombosis and adverse cardiac events after PCI.

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