
One-Year Clinical Outcomes after Sirolimus-Eluting Coronary Stent Implantation for Acute Myocardial Infarction in the Worldwide e-SELECT Registry

STEPHEN G. WORTHLEY, M.D.,¹ ALEXANDRE ABIZAID, M.D.,² ADRIAN BANNING, M.D.,³ ANTONIO BARTORELLI, M.D.,⁴ VLADIMÍR DŽAVÍK, M.D.,⁵ STEPHEN ELLIS, M.D.,⁶ RUNLIN GAO, M.D.,⁷ VICTOR LEGRAND, M.D.,⁸ PHILIP URBAN, M.D.,⁹ CHRISTIAN SPAULDING, M.D., PH.D.,¹⁰ for the e-SELECT investigators¹¹

From the ¹Cardiovascular Investigation Unit, Royal Adelaide Hospital, Adelaide, Australia; ²Instituto Dante Pazzanese de Cardiologia, Sao Paulo, Brazil; ³John Radcliffe Hospital, Oxford, United Kingdom; ⁴Centro Cardiologico Monzino, IRCCS, University of Milan, Milan, Italy; ⁵Peter Munk Cardiac Centre, University Health Network, Toronto, Canada; ⁶Cleveland Clinic Foundation, Cleveland, Ohio, USA; ⁷Cardiovascular Institute and Fu Wai Hospital, Beijing, China; ⁸Centre Hospitalier Universitaire, Liège, Belgium; ⁹European Hospital Georges Pompidou, Assistance Publique-Hôpitaux de Paris, and INSERM U 970, Paris Descartes University, Paris, France; ¹⁰La Tour Hospital, Geneva, Switzerland, ¹¹List available as online-supplement

Background: The aim was to ascertain the 1-year clinical outcomes of 1,234 patients who underwent implantations of sirolimus-eluting stents (SES) for acute myocardial infarction (MI) in the multinational e-SELECT registry.

Methods: Fifteen thousand and one hundred and forty-seven patients treated with SES were entered in the e-SELECT registry, of whom 1,234 presented within <24 hours of onset of acute MI.

Results: At 1 year, the rates of major adverse cardiac events (MACE) (5.5% vs. 4.8%; $P = 0.28$) were similarly low in the acute and no acute MI groups. The rates of definite/probable stent thrombosis (ST) were higher in the acute MI group (2.1% vs. 0.88%, $P < 0.001$). ST was a strong independent predictor of death at 1 year (HR 13.4; 95% CI 5.0, 36.0; $P < 0.001$) and MI (HR 58.9; 95% CI 26.9, 129.1; $P < 0.001$). Dual antiplatelet therapy (DAPT) compliance at 6 months was 96.0% in the acute MI versus 94.5% in the no acute MI group ($P = 0.03$).

Conclusion: In selected patients presenting within <24 hours of acute MI onset and highly compliant with DAPT, SES implantation was associated with similar rates of MACE, though higher rates of ST, as compared to no acute MI patients.

Condensed abstract

In the e-SELECT registry which included 15,147 patients treated with sirolimus-eluting stent (SES), we ascertained the 1-year clinical outcomes of 1,234 patients who presented within <24 hours of acute MI onset. In acute MI patients SES implantation was associated with similar rates of MACE, though higher rates of ST, as compared to no acute MI patients (MACE: 5.5% vs. 4.8%; $P = 0.28$; ST: 2.1 vs. 0.88%, $P < 0.001$). (J Interven Cardiol 2012;25:253–261)

Introduction

Early percutaneous coronary intervention (PCI) with stent implantation is a widely accepted strategy for the management of acute myocardial infarction (MI) with or without ST segment elevation.^{1,2} Furthermore,

Address for reprints: Christian Spaulding, M.D., Ph.D., Cardiology Department, European Hospital Georges Pompidou and INSERM U 970, Paris Descartes University, 20 Rue Leblanc 75015 Paris, France. Fax: 33 1 56 09 21 19; e-mail: christian.spaulding@wanadoo.fr

in comparative trials, sirolimus-eluting stents (SES) were distinctly more effective than bare metal stents (BMS) in the prevention of coronary artery restenosis after primary PCI,³⁻⁵ whereas the performance of paclitaxel-eluting stents has been mixed.^{6,7} In contrast with their reliable estimates of angiographic endpoints, such as target lesion and target vessel restenosis, randomized trials have been weak at measuring clinical outcomes, because of their stringent inclusion and exclusion criteria, and the low incidence of adverse events observed in selected, relatively low-risk populations treated by highly experienced interventional cardiologists. Large, meticulously organized multicenter registries are a powerful means of studying the performance of new therapies broadly implemented in “real-world” practice, and of examining the incidence of infrequent, long-term clinical events, such as stent thrombosis (ST).

Using data from e-SELECT, a prospective observational registry of patients who underwent implantation of SES, we focused on the 1-year clinical outcomes of patients who underwent PCI within <24 hours after the onset of stent thrombosis-elevation myocardial infarction (STEMI) or non-STEMI.

Registry Sample and Methods

The e-SELECT worldwide registry has been described elsewhere in detail.⁸ In brief, baseline data were collected between May 2006 and April 2008 in consecutive recipients of ≥ 1 CYPHER Select[®] or CYPHER Select[®] Plus (Cordis Corporation, Bridgewater, NJ, USA), implanted at 320 medical centers in 56 countries. The protocol specified few inclusion or exclusion criteria. Off-label indications were not prohibited, and all post-procedural medical management, including antithrombotic therapy, was prescribed according to usual local practices. The patients were followed clinically at 30, 180, and 360 days after SES implantation. The protocol was approved by the ethics committee of each participating medical center and the patients granted their consent to participate in the registry after undergoing the index procedure.

Study Groups Definitions. This analysis compares the clinical, angiographic and procedural characteristics, and 1-year clinical outcomes of 1,234 patients who presented within <24 hours of the onset of MI (acute MI group) versus 13,913 patients who underwent SES implants for indications other than acute

MI (no acute MI group). MI was classified according to ST changes on the surface electrocardiogram (ECG) as non-STEMI or STEMI, and was diagnosed on the basis of elevated serum creatine kinase (CK) or CK-MB enzyme concentrations, in presence (Q-wave MI) or absence (non Q-wave MI) of new pathological Q waves in ≥ 2 contiguous leads of the surface ECG. MI was classified as undetermined if the pre- and postprocedural ECG was not available. Among the 1,234 patients who presented within <24 hours of MI onset, 589 (47.7%) presented within <12 hours.

Data Collection and Management. The data collected by the e-SELECT registry include demographic information, general health and cardiovascular history, assessment of angina status, co-morbidity,⁹ lesion and procedure characteristics, procedural outcomes, measurements of serum cardiac enzymes and creatinine, pre- and postprocedural ECG, cardiac medications and antithrombotic regimens, and postprocedural clinical observations up to 1 year of follow-up.

The data were collected electronically at each participating medical center, transferred to an independent data management organization (KICA Medical, Nancy, France), and analyzed by an independent clinical research organization (Cardialysis, Rotterdam, Netherlands). The overall consistency and accuracy of data collection was monitored by an independent organization (Covance, Princeton, NJ, USA) in a random selection of 20% of the overall sample at 100 enrolling centers.

End-points of the e-SELECT Registry. The primary end-point of the registry was a composite of definite and probable ST, as defined by the Academic Research Consortium (ARC)¹⁰ at 1 year of follow-up. The secondary end-points at 1 year included MB according to the Safety and Efficacy of Enoxaparin in PCI (STEEPLE) trial definition,¹¹ cardiac and noncardiac deaths, MI, and major adverse cardiac events (MACE), defined as any death, MI, or target lesion revascularization (TLR).

Study Organization and Supervision. A steering committee (Appendix A) planned the analysis of the registry, and presentations and publications of the results. A clinical event committee (Appendix A), composed of interventional cardiologists not associated with the sponsor and not participants in the registry, adjudicated all MACE, MB and acute, subacute, and late ST by a systematic review of the data collection forms and by review of the source documents, ECG, and angiograms, when necessary.

Statistical Analysis. For all patients, standard descriptive statistics were used for baseline, lesion, and procedural characteristics and for clinical results. Continuous variables are presented as means \pm standard deviation (SD), or median and range, and categorical variables are presented as counts and percentages. Cumulative rates of adverse clinical events were calculated with event-specific adjusted denominators, such that all patients experiencing an adverse event within 360 days or followed for ≥ 330 days after the index procedure contribute to the denominator. Comparisons of continuous variables between both groups were made using one-way analysis of variance. Fisher's exact test was used to compare dichotomous variables and cumulative event rates. Because the cumulative rates of adverse clinical events did not correct for censoring within 330 days after the index procedure, Kaplan-Meier curves and time-to-event summaries were constructed, and the life-table method was used to examine the long-term incidence of clinical and safety end-points, correcting for all censoring, though the results were similar. Predictors of major clinical safety end-points were identified with the Cox proportional hazards, single and multiple variable analyses. For each outcome end-point, baseline covariates identified by the single variable analysis ($P < 0.005$) by a non-significant proportional hazards assumption test ($P > 0.05$ combined with graphic assessment), and by clinical relevance, were included in the multiple variable model stepwise selection procedure. An entry criterion probability value of 0.10 and a stay criterion of 0.15 were used, and baseline covariates with $>15\%$ missing values were excluded from the analysis. Missing values were not imputed. P values <0.05 were considered statistically significant. All statistical analyses were performed with the SAS software, version 8.2 (SAS Institute, Cary, NC, USA).

Results

Registry Sample and Clinical Characteristics of the Study Subgroups. The e-SELECT sample comprised 15,147 patients who fulfilled the inclusion and exclusion criteria specified in the protocol. Follow-up data were available in 14,905 patients at 30 days, 14,430 at 6 months, and 13,693 at 1 year, representing 99%, 96%, and 92% of survivors, respectively. This subgroup analysis compares the baseline clinical and

angiographic characteristics, and the procedural and 1-year clinical outcomes of 1,234 patients (8.1%) with 1,507 treated lesions, who presented within 24 hours of onset of acute MI (acute MI group), versus those of 13,913 patients (91.8%) with 18,481 lesions, who underwent SES for other indications (no acute MI group). The clinical characteristics of the 2 groups are shown in Table 1. The prevalence of (a) prior percutaneous or surgical revascularization, (b) risk factors for coronary artery disease (except for smoking), and (c) renal insufficiency was significantly higher in the no acute MI than in the acute MI group. Patients in the no acute MI group were also significantly more likely to present with multiple vessel disease.

Subgroups and Index Procedural and Angiographic Characteristics. The lesion and procedural characteristics of the patient subgroups are shown in Table 2. The mean reference vessel diameter was significantly smaller, and mean preprocedural percent vessel stenosis significantly greater in the acute MI than in the no acute MI group. However, the proportion of restenotic lesions and the overall lesion complexity were significantly greater in the no acute MI group. Accordingly, the mean numbers of lesions and vessels treated, and the mean number of stents implanted per patient were greater in the no acute MI than in the acute MI group (Table 2). Finally, approximately 60% and one-third of patients were treated with aspirin and clopidogrel, respectively, before undergoing the index SES implant procedure in the MI group, versus nearly 90% and one-third of patients, respectively, in the no acute MI group ($P < 0.001$ for both comparisons).

Long-Term Antithrombotic Therapy. The compliance with dual antiplatelet therapy (DAPT) was high in both patient subgroups (Table 3). At 30-day follow-up, 98.0% and 98.1% of patients in the acute MI and no acute MI groups, respectively, were treated with aspirin and clopidogrel or ticlopidine, while 81.7% and 79.2% of patients, respectively, remained on DAPT at 12 months.

Stent Thrombosis, Major Bleeding, and Other Major Adverse Clinical Events. The rates of ST, MB, and MACE at 1 year are presented in Table 4. The 1-year rates of ST were significantly higher in the acute MI than in the no acute MI group, due to a significantly higher incidence of acute and subacute ST. In the first 30 days, the rate of MB was 0.74% in the acute MI versus 0.35% in the no acute MI group ($P = 0.47$). Between 31 and 180 days, the rate of MB was

Table 1. Baseline Characteristics of Patients Presenting within 24 h of Onset of Acute MI (Acute MI), versus the Remainder (No Acute MI) of the e-SELECT Registry Sample

	Acute MI (n = 1,234)	No Acute MI (n = 13,913)	P Value
Age, y	60.3 ± 11.8	62.3 ± 10.7	<0.001
Men	77.7 (959/1,234)	75.2 (10,464/13,913)	0.053
Body mass index ≥30	20.5 (253/1,232)	24.7 (3,420/13,829)	<0.001
<i>History of:</i>			
Earlier myocardial infarction	34.8 (429/1,234)	32.0 (4425/13,849)	<0.045
PCI	13.8 (170/1,234)	33.8 (4,680/13,849)	<0.001
Coronary artery bypass graft surgery	4.9 (60/1,234)	9.5 (1,310/13,849)	<0.001
Diabetes	28.2 (348/1,234)	30.5 (4,229/13,849)	0.09
Insulin-dependent diabetes	21.3 (74/348)	27.5 (1,164/4,229)	0.012
Hypertension	55.4 (684/1,234)	68.5 (9,487/13,849)	<0.001
Hyperlipidemia	56.1 (692/1,234)	69.3 (9,597/13,849)	<0.001
Current and past smoking	59.9 (739/1,234)	52.9 (7,321/13,849)	<0.001
Peripheral vascular disease	4.0 (49/1,234)	6.4 (892/13,849)	<0.001
Cerebral vascular disease	3.6 (44/1,234)	4.3 (599/13,849)	0.24
Serum creatinine >2.0 mg/dL	1.7 (19/1,101)	2.7 (332/12,306)	0.06
Chronic lung disease	3.9 (48/1,234)	4.0 (549/13,849)	1.00
Mean Charlson index score	1.0 ± 1.2	1.1 ± 1.3	0.018
Charlson index score ≥3	8.7 (107/1,234)	10.4 (1,439/13,849)	0.056
<i>Coronary arteries with >50%stenoses</i>			
0	8.6 (106/1,234)	8.6 (1,201/13,913)	1.00
1	82.7 (1,021/1,234)	76.6 (10,646/13,913)	<0.001
2	7.9 (97/1,234)	13.5 (1,878/13,913)	<0.001
3	0.7 (9/1,234)	1.3 (184/13,913)	0.08
<i>Target vessel</i>			
Left main coronary artery	1.7 (25/1,477)	2.3 (424/18,087)	0.12
Left anterior descending artery	53.7 (793/1,477)	50.8 (9,188/18,087)	0.035
Circumflex artery	18.8 (278/1,477)	22.2 (4,013/18,087)	0.003
Right coronary artery	26.8 (396/1,477)	25.9 (4,680/18,087)	0.44
Bypass graft	1.6 (24/1,501)	1.9 (347/18,434)	0.49

Values are means ± SD, or % (numbers) of observations.

significantly higher in the acute MI than in the no acute MI group (0.46% vs. 0.24%, $P = 0.04$). Between 181 and 360 days the rates of MB were similar in both groups (0.20% vs. 0.27%, $P = 0.1$). At 1 year, the rates of deaths from all causes, cardiac deaths, MI, TLR, and MB were similarly low in both groups (Table 4). Figure 1 illustrates the significant difference between the 2 study groups in cumulative rates of definite and probable ST within the first month of follow-up and low incidence of ST in both groups thereafter.

Predictors of Adverse Clinical Events. The independent predictors of death, MI, ST, and MB in the acute MI group by multiple variable analysis are shown in Table 5. ARC-defined definite or probable ST related to the index procedure was a strong independent predictor of death and recurrent MI. Total or partial temporary interruption of DAPT within 30 days after the index procedure was a strong independent predictor of ST.

Discussion

In this subgroup analysis of the e-SELECT registry, the rates of death, MI, and TLR among patients presenting within <24 hours of acute MI onset were low. The incidence of acute and subacute ST in the acute MI group was higher than in the no acute MI group. Discontinuation of DAPT before 30 days was an independent predictor of ST. Interestingly, the increased rate of ST in the acute MI group was driven by a higher incidence of early (0 to 30 days) thrombotic events.

Several randomized trials and meta-analyses have compared the use of DES and BMS in the setting of primary PCI for acute MI. A lower rate of repeat revascularization was regularly observed with DES, without increase in the rates of death, recurrent MI or ST at 1 year.¹² Long-term follow-up was reported in 3 studies.^{13–15} No difference in the rate of late ST was observed between DES and BMS, although these

SIROLIMUS-ELUTING STENTS IN ACUTE MI

Table 2. Lesion and Procedure Characteristics in 1,234 Patients Presenting within 24 h of Onset of Acute MI (Acute MI), versus the Remainder (No Acute MI) of the e-SELECT Registry Sample

	Acute MI (n = 1,234 patients, 1,507 lesions, 1,769 stents)	No Acute MI (n = 13,913 patients, 18,481 lesions, 21,723 stents)	P Value*
Reference vessel diameter, mm*	2.8 ± 0.45	2.92 ± 0.45	<0.013
Preprocedural percent stenosis	89.9 ± 13.7	84.1 ± 12.1	<0.001
Lesion length, mm*	20.02 ± 10.72	20.25 ± 11.65	0.45
<i>Target lesion types</i>			
Restenotic†	6.1 (90/1,486)	12.2 (2,224/18,165)	0.001
In-stent restenosis†	5.2 (78/1,486)	11.6 (2,103/18,165)	0.005
Length ≥30 mm††	11.3 (139/1,225)	13.7 (1,874/13,710)	0.023
Reference vessel diameter <2.25 mm††	6.4 (79/1,226)	3.7 (506/13,721)	<0.001
Ostial†	11.2 (166/1,486)	12.7 (2,310/18,165)	0.09
Moderately or severely calcified†	18.0 (245/1,362)	24.2 (2,766/16,418)	<0.001
<i>Procedural characteristics</i>			
Numbers per patient			
Vessels treated	1.1 ± 0.35	1.18 ± 0.43	<0.001
Lesions treated	1.2 ± 0.51	1.33 ± 0.62	<0.001
Stents implanted	1.4 ± 0.73	1.56 ± 0.88	<0.001
Overlapping stents††	13.2 (164/1,234)	14.8 (2,054/13,913)	0.002
Total stent length, mm			
Per lesion	25.8 ± 11.90	25.32 ± 13.29	0.18
Per patient	31.5 ± 16.95	33.65 ± 21.28	0.001
Direct stenting	33.6 (500/1,486)	35.8 (6,512/18,165)	0.09
Postdilatation	33.0 (546/1,654)	36.3 (7,510/20,671)	<0.007
Maximum pressure per stent, atm	15.6 ± 3.1	15.5 ± 3.3	0.25
Intravascular ultrasound imaging	1.8 (26/1,447)	3.8 (687/17,847)	<0.001
<i>Preprocedural antithrombotic regimens</i>			
Aspirin	59.7 (717/1,201)	88.1 (12,006/13,630)	<0.001
Clopidogrel	36.7 (441/1,201)	62.5 (8,516/13,623)	<0.001
Ticlopidine	0.3 (4/1,198)	2.0 (277/13,591)	<0.001

Values are means ± SD, or % (numbers) of observations. *Visual estimate; †calculated per lesion; ††calculated per patient.

studies were underpowered to assess this safety endpoint. Registries have generated conflicting data. In a large US state-based registry, Mauri et al. noted a significant difference in the rate of repeat revascularization and a decrease in all-cause mortality favoring DES.¹⁶ In contrast, Steg et al. reported a higher rate of death at 2 years in patients presenting with acute MI who received a DES during the initial hospitalization.¹⁷

The reported incidence of late ST after DES implantation varies between 0.2 and 0.6% per year.^{18–20} Pathological studies have shown that lack of complete endothelialization may be a leading cause of late DES thrombosis.^{21,22} Furthermore Nakazawa et al. observed considerably less vascular healing at plaque ruptures of culprit lesions than in stable culprit lesions.²³ Screening acute MI patients undergoing primary PCI for potential contraindications to prolonged DAPT may be difficult. In the PREMIER registry, nearly 1 in 7 pa-

tients who received a DES during primary PCI were no longer treated with a thienopyridine 30 days after the procedure. Prematurely stopping thienopyridine therapy was strongly associated with subsequent mortality.²⁴

Our subgroup analysis confirmed a high compliance with DAPT, similar to that observed among the stable patients enrolled in the e-SELECT registry. Moreover, the issues regarding the prescription of prolonged DAPT after implantation of a DES during primary PCI are overshadowed by the benefits it confers to patients presenting with an acute coronary syndrome (ACS). Given these demonstrated benefits, current guidelines on the management of STEMI recommend DAPT for 1 year after primary PCI, regardless of the type of stent implanted.^{1,25} Therefore, in acute MI treated by primary PCI, patient education should emphasize the importance of complying with long-term DAPT, whether or not a DES has been implanted. Careful patient

Table 3. Antithrombotic Regimens up to 360 Days of Follow-Up in Each Study Group

Regimen	Acute MI (n = 1,234 Patients)	No Acute MI (n = 13,913 Patients)	P Value
<i>Discharge</i>			
Aspirin	99.6 (1,226/1231)	98.6 (13,597/13,782)	0.003
Clopidogrel	99.5 (1,225/1231)	98.5 (13,588/13,788)	0.003
Ticlopidine	0.5 (6/1225)	1.4 (188/13,645)	0.005
DAPT	99.4 (1,218/1225)	98.5 (13,430/13,624)	0.009
<i>1 month</i>			
Aspirin	99.0 (1,146/1,158)	98.4 (12,997/13,207)	0.17
Clopidogrel	99.0 (1,147/1,158)	98.0 (12,948/13,207)	0.013
Ticlopidine	0.9 (11/1,158)	1.7 (221/13,207)	0.07
Dual antiplatelet therapy	98.1 (1,136/1,158)	98.0 (12,940/13,207)	0.91
<i>6 months</i>			
Aspirin	98.2 (1,070/1,090)	97.4 (12,387/12,719)	0.13
Clopidogrel	97.2 (1,060/1,090)	95.2 (12,107/12,719)	0.001
Ticlopidine	0.5 (5/1,090)	1.5 (186/12,719)	0.004
Dual antiplatelet therapy	96.0 (1,047/1,090)	94.5 (12,022/12,719)	0.030
<i>1 year</i>			
Aspirin	97.0 (1,080/1,113)	95.9 (11,907/12,420)	0.07
Clopidogrel	83.1 (925/1,113)	80.9 (10,052/12,420)	0.08
Ticlopidine	0.4 (4/1,113)	1.3 (161/12,420)	0.004
Dual antiplatelet therapy	81.7 (909/1,113)	79.2 (9,835/12,420)	0.053

Values are % (numbers) of observations; different denominators are due to missing data and deaths during follow-up.

Table 4. Cumulative Rates of Adverse Clinical Events at 1 Year of Follow-Up in Each Study Group

	Acute MI (n = 1,234)	No Acute MI (n = 13,913)	P Value
<i>Definite or probable stent thrombosis</i>	2.12 (24/1,131)	0.88 (111/12,618)	<0.001
Acute (0–1 day)	0.24 (3/1,233)	0.05 (7/13,849)	0.042
Subacute (2–30 days)	1.32 (16/1,215)	0.44 (61/13,724)	<0.001
Early (0–30 days)	1.56 (19/1,215)	0.49 (68/13,724)	<0.001
Late (31–360 days)	0.44 (5/1,125)	0.34 (43/12,579)	0.59
<i>Any ARC stent thrombosis</i>	2.72 (31/1,137)	1.26 (160/12,661)	<0.001
Definite	1.56 (18/1,127)	0.55 (70/12,588)	<0.001
Probable	0.53 (6/1,129)	0.32 (41/12,598)	0.28
Possible	0.71 (8/1,132)	0.39 (50/12,612)	0.14
Death	2.18 (25/1,147)	1.65 (211/12,764)	0.19
Myocardial infarction	2.57 (29/1,127)	1.86 (235/12,612)	0.11
TLR	2.13 (24/1,127)	2.14 (269/12,601)	1.00
<i>Major adverse cardiac events</i>	5.48 (63/1,149)	4.76 (608/12,783)	0.28
In-hospital	1.14 (14/1,234)	0.88 (122/13,913)	0.34
Out-of-hospital	4.45 (51/1,147)	3.89 (497/12,767)	0.34
Target vessel revascularization	2.57 (29/1,127)	2.31 (291/12,602)	0.54
Major bleeding	1.42 (16/1,126)	0.99 (124/12,582)	0.11

Values are % (numbers) of observations; different denominators are due to missing data and deaths during follow-up; ARC = Academic Research Consortium.

selection and a high compliance may explain the low rates of MACE noted in our registry.

Despite the high compliance with DAPT, the rate of ST was higher in the acute MI than in the no acute MI

group. Indeed, an ACS was a predictor of ST²⁶ also in the e-Cypher registry. The TRITON TIMI 38 study randomly assigned 12,844 moderate to high risk ACS patients scheduled for PCI to receive clopidogrel or

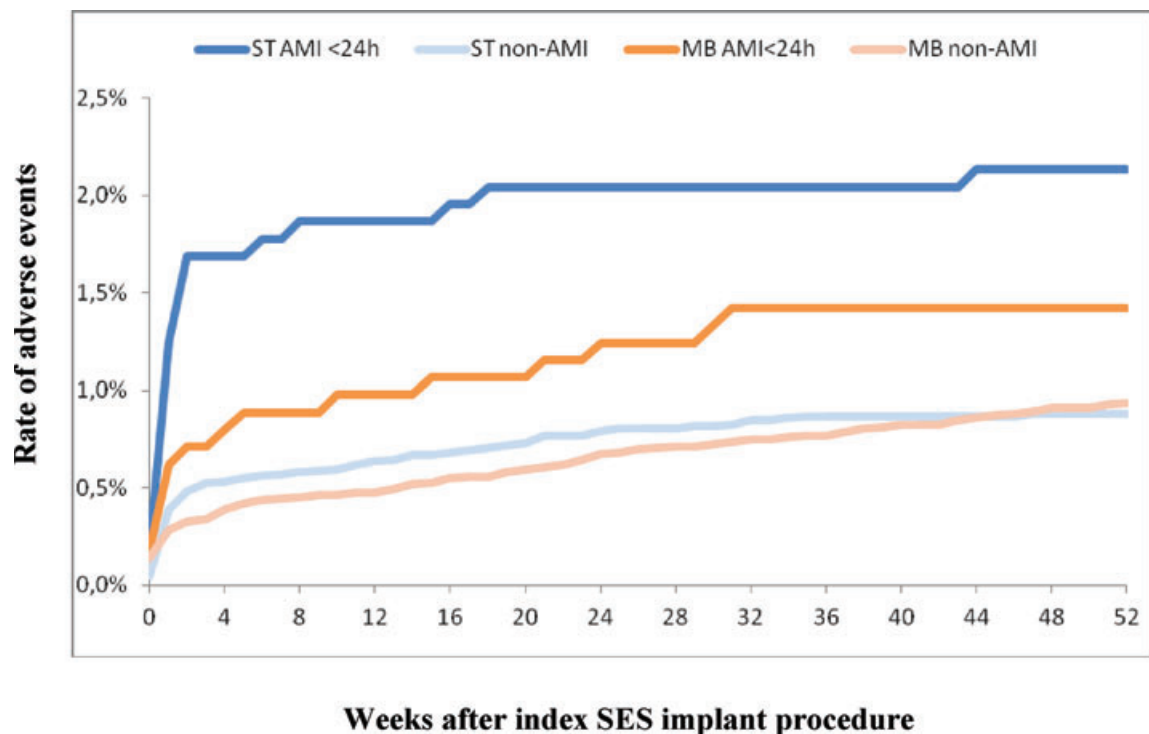


Figure 1. Cumulative incidence of stent thromboses and major bleeding events up to 1 year in each study group.

prasugrel.^{27,28} The rates of ST increased depending on the risk profile, reaching 2.8% in the STEMI group treated with clopidogrel, after a median of 14.5 months. No difference in rates of ST was noted between DES and BMS recipients. The administration of prasugrel lowered the rate of ST by 21%. Therefore, ST is a concern in all acute MI patients undergoing primary PCI, regardless of stent type. The causes of ST in the setting of acute MI are multi-factorial. Clinical evidence for a relationship between underlying vascular inflammation and ST has been found in patients with ruptured plaque. Risk of ST is directly related to the acuity of the index clinical syndrome preceding stenting. Patients presenting with an ACS have a several-fold increased risk for ST regardless of stent type compared with patients with stable symptoms.^{29,30} Possible histopathologic mechanisms include the thin fibrous cap that characterizes vulnerable plaque, abundant inflammatory cells, and a necrotic lipid core.³¹ Implantation of undersized stents has been recognized as a cause of ST. In acute MI, vasoconstriction and underlying thrombus may lead to underestimation of the reference vessel size and positioning of an under-sized stent.^{32,33}

Despite the use of thromboaspiration, residual thrombosis between the struts and the vessel wall has been demonstrated and could potentially be a cause of early ST.³⁴ Of interest, the rate of late thrombosis, which was the main concern for the use of DES in acute MI was low in both groups.

Limitations of the Study. The source data were verified in a random sample representing 20% of the patients enrolled in e-SELECT. While this compares favorably with other recent stent registries,^{26,35,36} the underreporting of adverse events remains a potential limitation. However, the monitored sample confirmed that the data collection was reliable. Moreover, the 1.5% rate of definite ST at 1 year among our patients presenting with acute MI was close to the 2.0% reported by the fully monitored randomized TYPHOON trial that used the same DES.⁴ Another limitation is the fact that patients enrolled were evidently selected, since they were included in the registry only after having undergone successful implantation of a SES, and had no contraindication to prolonged DAPT. Finally, the CYPHER Select[®] or CYPHER Select[®] Plus SES stents will no longer be available for use after 2012.

Table 5. Predictors of Adverse Events for Patients with Acute MI Multiple Variable Regression Analysis at 360 Days

Predictors of	Hazard Ratio [95% CI]	P Value
Death		
Index procedure-related stent thrombosis	13.4 [5.0, 36.0]	<0.001
History of coronary artery bypass graft surgery	5.7 [2.3, 14.4]	<0.001
Myocardial infarction		
Index procedure-related stent thrombosis	58.9 [26.9, 129.1]	<0.001
History of coronary artery bypass graft surgery	3.0 [1.2, 7.9]	0.022
Stent thrombosis		
Charlson comorbidity index	1.3 [1.1, 1.6]	<0.001
Total or partial temporary interruption of DAPT within 1st 30 days	10.1 [2.2, 46.9]	0.003
History of coronary artery bypass graft surgery	3.4 [1.3, 9.2]	0.015
Major bleeding		
Glycoprotein IIb/IIIa inhibitor	2.6 [0.9, 7.9]	0.08
Female gender	2.5 [0.9, 7.1]	0.08

CI = confidence interval; DAPT = dual antiplatelet therapy.

Conclusions

In selected patients presenting within <24 hours of acute MI onset and highly compliant with DAPT, the implantation of SES was associated with low MACE rates, similar to those observed in more stable patients. The rate of ST was higher in patients presenting with than without acute MI.

Acknowledgment: Rodolphe Ruffy, MD contributed to the preparation of this manuscript.

References

- Antman EM, Hand M, Armstrong PW, et al. 2004 Writing Committee Members, Anbe DT, Kushner FG, Ornato JP, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Halperin JL, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B, Tarkington LG, Yancy CW. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee. *Circulation* 2008;117:296–329.
- Anderson JL, Adams CD, Antman EM, et al. American College of Cardiology; American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction); American College of Emergency Physicians; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; American Association of Cardiovascular and Pulmonary Rehabilitation; Society for Academic Emergency Medicine. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *Circulation* 2007;116:e148–304.
- Valgimigli M, Percoco G, Malagutti P, et al. STRATEGY Investigators. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: A randomized trial. *JAMA* 2005;293:2109–2117.
- Spaulding C, Henry P, Teiger E, et al. TYPHOON Investigators. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. *N Engl J Med* 2006;355:1093–1104.
- Menichelli M, Parma A, Pucci E, et al. Randomized trial of sirolimus-eluting stent versus bare-metal stent in acute myocardial infarction (SESAMI). *J Am Coll Cardiol* 2007;49:1924–1930.
- Laarman GJ, Suttorp MJ, Dirksen MT, et al. Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. *N Engl J Med* 2006;355:1105–1113.
- Stone GW, Lansky AJ, Pocock SJ, et al. HORIZONS-AMI Trial Investigators. Paclitaxel-eluting stents versus bare metal stents in acute myocardial infarction. *N Engl J Med* 2009;360:1946–1959.
- Urban P, Abizaid A, Banning A, et al. for the e-SELECT investigators. Stent thrombosis and bleeding complications after implantation of sirolimus-eluting coronary stents in an unselected worldwide population. A report from the e-SELECT registry. *J Am Coll Cardiol* 2011;57:1445–1454.
- Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987;40:373–383.
- Cutlip DE, Windecker S, Mehran R, et al. Academic Research Consortium. Clinical end points in coronary stent trials: A case for standardized definitions. *Circulation* 2007;115:2344–2351.
- Montalescot G, Gallo R, White HD, et al. STEEPLE Investigators. Enoxaparin versus unfractionated heparin in elective percutaneous coronary intervention. *N Engl J Med* 2006;355:1006–1017.
- Kastrati A, Dibra A, Spaulding C, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. *Eur Heart J* 2007;28:2706–2713.

13. Valgimigli M, Percoco G, Malagutti P, et al. STRATEGY Investigators. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: A randomized trial. *JAMA* 2005;293:2109–2117.
14. Di Lorenzo E, Sauro R, Varricchio A, et al. Benefits of drug-eluting stents as compared to bare metal stent in ST-segment elevation myocardial infarction: Four year results of the Paclitaxel or sirolimus-eluting stent vs bare metal stent in primary angioplasty (PASEO) randomized trial. *Am Heart J* 2009;158:e43–50.
15. Spaulding C, Teiger E, Commeau P, et al. Four-year follow-up of TYPHOON (trial to assess the use of the CYPHER sirolimus-eluting coronary stent in acute myocardial infarction treated with BALLOON angioplasty). *JACC Cardiovasc Interv* 2011;4:14–23.
16. Mauri L, Silbaugh TS, Garg P, et al. Drug-eluting or bare-metal stents for acute myocardial infarction. *N Engl J Med* 2008;359:1330–1342.
17. Steg PG, Fox KA, Eagle KA, et al. Global Registry of Acute Coronary Events (GRACE) Investigators. Mortality following placement of drug-eluting and bare-metal stents for ST-segment elevation acute myocardial infarction in the Global Registry of Acute Coronary Events. *Eur Heart J* 2009;30:321–329.
18. Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: Data from a large two-institutional cohort study. *Lancet* 2007;369(9562):667–678.
19. Mauri L, Hsieh WH, Massaro JM, et al. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med* 2007;356:1020–1029.
20. Schulz S, Schuster T, Mehilli J, et al. Stent thrombosis after drug-eluting stent implantation: Incidence, timing, and relation to discontinuation of clopidogrel therapy over a 4-year period. *Eur Heart J* 2009;30:2714–2721.
21. Finn AV, Joner M, Nakazawa G, et al. Pathological correlates of late drug-eluting stent thrombosis: Strut coverage as a marker of endothelialization. *Circulation* 2007;115:2435–2441.
22. Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug eluting stents: Importance of delayed healing. *Arterioscler Thromb Vasc Biol* 2007;27:1500–1510.
23. Nakazawa G, Finn AV, Joner M, et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: An autopsy study. *Circulation* 2008;118:1138–1145.
24. Spertus JA, Kettelkamp R, Vance C, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: Results from the PREMIER registry. *Circulation* 2006;113:2803–2809.
25. Van de Werf F, Bax J, Betriu A, et al. ESC Committee for Practice Guidelines (CPG). Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: The Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J* 2008;29:2909–2945.
26. Urban P, Gershlick AH, Guagliumi G, et al. e-Cypher Investigators. Safety of coronary sirolimus-eluting stents in daily clinical practice: One-year follow-up of the e-Cypher registry. *Circulation* 2006;113:1434–1441.
27. Montalescot G, Wiviott SD, Braunwald E, et al. TRITON-TIMI 38 investigators. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): Double-blind, randomised controlled trial. *Lancet* 2009;373(9665):723–731.
28. Wiviott SD, Braunwald E, McCabe CH, et al. TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007;357:2001–2015.
29. Leibundgut G, Nietlispach F, Pittl U, et al. Stent thrombosis up to 3 years after stenting for ST-segment elevation myocardial infarction versus for stable angina-comparison of the effects of drug-eluting versus bare-metal stents. *Am Heart J* 2009;158:271–276.
30. Kukreja N, Onuma Y, Garcia-Garcia HM, et al. The risk of stent thrombosis in patients with acute coronary syndromes treated with bare-metal and drug-eluting stents. *J Am Coll Cardiol Interv* 2009;2: 534–541.
31. Holmes D, Kereiakes D, Garg S, et al. Stent thrombosis. *J Am Coll Cardiol* 2010;56:1357–1313.
32. Cook S, Windecker S. Early stent thrombosis: Past, present and future. *Circulation* 2009;119:657–659.
33. Van Werkum JW, Heestermaans AA, Zomer AC. Predictors of coronary stent thrombosis. *J Am Coll Cardiol* 2009;53:1399–1409.
34. Amoroso G, van Geuns RJ, Spaulding C, et al. Assessment of the safety and performance of the STENTYS self-expanding coronary stent in acute myocardial infarction: Results from the APPOSITION I study. *EuroIntervention* 2011;7:428–436.
35. Lotan C, Meredith IT, Mauri L, et al. E-Five Investigators. Safety and effectiveness of the Endeavor zotarolimus-eluting stent in real-world clinical practice: 12-month data from the E-Five registry. *JACC Cardiovasc Interv* 2009;2:1227–1235.
36. Lasala JM, Cox DA, Dobies D, et al. ARRIVE 1 and ARRIVE 2 Participating Physicians. Drug-eluting stent thrombosis in routine clinical practice: Two-year outcomes and predictors from the TAXUS ARRIVE registries. *Circ Cardiovasc Interv* 2009;2:285–293.

Supporting Information

Additional supporting information may be found in the online version of this article:

Appendix A: Steering committee and Clinical event committee.

Please note: Wiley-Blackwell is not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.