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Incidence and Correlates of Drug-Eluting Stent Thrombosis in Routine Clinical Practice

4-Year Results From a Large 2-Institutional Cohort Study

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Objectives We sought to determine the risk of late stent thrombosis (ST) during long-term follow-up beyond 3 years, searched for predictors, and assessed the impact of ST on overall mortality.

Background Late ST was reported to occur at an annual rate of 0.6% up to 3 years after drug-eluting stent (DES) implantation.

Methods A total of 8,146 patients underwent percutaneous coronary intervention with a sirolimus-eluting stent (SES) (n = 3,823) or paclitaxel-eluting stent (PES) (n = 4,323) and were followed up to 4 years after stent implantation. Dual antiplatelet treatment was prescribed for 6 to 12 months.

Results Definite ST occurred in 192 of 8,146 patients with an incidence density of 1.0/100 patient-years and a cumulative incidence of 3.3% at 4 years. The hazard of ST continued at a steady rate of 0.53% (95% confidence interval [CI]: 0.44 to 0.64) between 30 days and 4 years. Diabetes was an independent predictor of early ST (hazard ratio [HR]: 1.96; 95% CI: 1.18 to 3.28), and acute coronary syndrome (HR: 2.21; 95% CI: 1.39 to 3.51), younger age (HR: 0.97; 95% CI: 0.95 to 0.99), and use of PES (HR: 1.67; 95% CI: 1.08 to 2.56) were independent predictors of late ST. Rates of death and myocardial infarction at 4 years were 10.6% and 4.6%, respectively.

Conclusions Late ST occurs steadily at an annual rate of 0.4% to 0.6% for up to 4 years. Diabetes is an independent predictor of early ST, whereas acute coronary syndrome, younger age, and PES implantation are associated with late ST. (J Am Coll Cardiol 2008;52:1134–40) © 2008 by the American College of Cardiology Foundation

Drug-eluting stents (DES) reduce angiographic restenosis and the clinical need for repeat revascularization procedures (1,2). Recent systematic reviews and large-scale registries observed similar rates of death and myocardial infarction (MI) for patients treated with either a DES or bare-metal stent (BMS) during long-term 4-year follow-up (3–5). However, very late stent thrombosis (ST) has emerged as a distinct entity overshadowing the use of DES, and concerns persist as to whether this phenomenon might jeopardize the long-term outcome after DES implantation, particularly after discontinuation of dual antiplatelet therapy (6–11).

Drug-eluting stents delay healing and impair endothelialization as evidenced in necropsy studies and clinical investigations (12,13). Vessel remodeling (14) in concert with local drug release enhancing endothelial tissue factor expression (15,16) after DES implantation might result in a prothrombotic milieu predisposing to late ST. Previously, we reported on the frequency and timing of ST after the unrestricted use of DES implantation in a cohort of 8,146 consecutive patients treated at 2 academic institutions (10). Late and very late ST was encountered steadily at an annual rate of 0.6% with no evidence of diminution up to 3 years of follow-up. During extension of the follow-up period to 4 years in the current study, we investigated whether the risk of very late ST would change beyond 3 years, identified

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correlates of early as opposed to late ST, and assessed the impact of ST-related mortality after DES implantation on overall mortality in the entire cohort.

Methods

Study cohort, design, and follow-up. Between April 16, 2002, and December 31, 2005, a total of 8,146 consecutive patients underwent percutaneous coronary intervention with the 2 Food and Drug Administration–approved DES at 2 academic referral hospitals in Switzerland and the Netherlands, comprising 3,823 patients treated with sirolimus-eluting stents (SES) (Cypher, Cordis Corp., Johnson & Johnson, Warren, New Jersey) and 4,323 patients treated with paclitaxel-eluting stents (PES) (TAXUS Express2 or Liberté, Boston Scientific, Natick, Massachusetts). The use of the respective stent platforms at the 2 institutions has been reported previously (10). For the present extended 4-year follow-up, patients were again contacted 1 year after the last contact with specific questions addressing repeat hospital stay and major adverse cardiac events (MACE) with a health questionnaire. Patients who did not return the questionnaire were contacted by phone, at which time the questionnaire was completed. Moreover, survival data were obtained from municipal civil registries. If necessary, medical records and discharge summaries from other institutions were systematically reviewed and primary care physicians were contacted for additional or missing information. The median follow-up was 2.53 years/patient, and a complete clinical follow-up was achieved in 96.4% (n = 7,857). The common database was held and analyzed at the Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland. There was no industry involvement in the design, conduct, or analysis of the study.

This study was approved by the local ethics committee in both hospitals and is in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Definitions. Definite ST was defined as follows:

1. Presence of Thrombolysis In Myocardial Infarction (TIMI) flow:
   a. Grade 0 with occlusion originating in the peri-stent region
   b. Grade 1, 2, or 3 in the presence of a thrombus originating in the peri-stent region. Angiographic evidence of thrombus was defined as a discrete, intraluminal filling defect with defined borders and separated from the vessel wall.

And at least 1 of the following criteria had to be met:

1. Acute ischemic symptoms (typical chest pain with duration >20 min)
2. Ischemic electrocardiographic changes
   a. ST-segment elevation in territory of implanted stent
   b. ST-segment depression or T-wave inversion in territory of implanted stent
3. Typical rise and fall in cardiac biomarkers (17).

All cases of definite ST were reviewed independently by 2 experienced interventional cardiologists, and in case of disagreement, a consensus was established between the 2 reviewers or a third interventional cardiologist was consulted. Moreover, ST was categorized into early (within 30 days), late (>30 days and ≤365 days), and very late (>365 days) depending on the timing of occurrence of the event. For the definition of probable ST, the Academic Research Consortium (ARC) criteria were applied (18).

Abbreviations and Acronyms

ACS = acute coronary syndrome
ARC = Academic Research Consortium
ASA = acetylsalicylic acid
BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
MACE = major adverse cardiac event
MI = myocardial infarction
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
ST = stent thrombosis
TIMI = Thrombolysis In Myocardial Infarction

The diagnosis of MI was based on the presence of new Q waves in at least 2 contiguous leads with an elevated creatine kinase-myocardial band fraction. In the absence of pathologic Q waves, the diagnosis of MI was based on an elevation in creatine kinase to more than twice the upper limit of normal with an elevated creatine kinase-myocardial band fraction of more than 3 times the upper limit of normal. Premature discontinuation of antiplatelet therapy was referred to as cessation of acetylsalicylic acid (ASA) or clopidogrel or both before the recommended duration of prescription. A creatinine value ≥150 μmol or chronic hemodialysis qualified as definition of renal impairment.

Interventional procedure and antiplatelet prescription. All interventions were performed according to current practice guidelines for percutaneous coronary intervention. The decision to choose a specific treatment strategy was left to the discretion of the operator. Patients were prescribed ASA 100 mg once daily plus clopidogrel 75 mg/day (after a loading dose of 300 or 600 mg) before or during baseline coronary interventions. After the procedure, all patients were advised to maintain ASA 100 mg once daily lifelong. In the Swiss institution, 12 months of clopidogrel therapy was prescribed irrespective of the stent type used. In the Dutch institution, PES-treated patients received at least 6 months of clopidogrel (75 mg/day), whereas patients treated with SES were prescribed clopidogrel for at least 3 months, unless 1 of the following was present (in which case clopidogrel was maintained for at least 6 months): ≥3 SES implantations, total stent length ≥36 mm, chronic total occlusion, and bifurcations. In a minority of patients under oral anticoagulation therapy, a shorter duration of clopidogrel (e.g.,

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3-month triple therapy with ASA, clopidogrel, and warfarin) was recommended.

Statistical analysis. Continuous variables are expressed as mean ± SD or median values with the corresponding interquartile range. Dichotomous variables are expressed as counts and percentages. For comparison of continuous variables between SES and PES as well as early and late thrombosis, a Student *t* test for continuous variables was used.

The incidence of ST was calculated in 2 different ways: 1) incidence density, defined as the number of patients with ST divided by the total number of patient-years under observation (expressed as a number of events/100 patient-years); and 2) cumulative incidence, estimated according to the Kaplan-Meier method and the log-rank test for the differences in survival curve. Univariable and multivariable Cox proportional hazards models were used to assess predictors of ST, with the following variables: age, gender, family history of cardiovascular disease, diabetes, hypertension, current smoking, dyslipidemia, renal impairment, left ventricular ejection fraction, acute coronary syndrome (ACS) at presentation, stent type, number of stents, total stent length, average stent diameter, bifurcation treatment, and prescribed duration of clopidogrel. Statistical analyses were performed with Stata version 9 for Windows (Stata Corp., College Station, Texas). All p values were 2-sided and values <0.05 were considered statistically significant.

Results

Baseline clinical and procedural characteristics of patients with and without ST are summarized in Table 1. Compared with patients without ST, those suffering from definite ST were younger (59.4 ± 12.1 years vs. 62.9 ± 11.5 years, p < 0.001), had a lower left ventricular ejection fraction (52 ± 12% vs. 55 ± 12%, p = 0.035) and more often an ACS (67.7% vs. 54.9%, p < 0.001) at the time of stent implantation, and had received longer (total stent length: 44.0 ± 38.8 mm vs. 36.1 ± 25.5 mm, p < 0.001) and more stents (number of stents: 2.33 ± 1.71 vs. 1.95 ± 1.21, p < 0.001), which were smaller in diameter (2.88 ± 0.32 mm vs. 2.94 ± 0.38 mm, p = 0.048). The status of antiplatelet therapy as recorded during early and late and very late ST is summarized in Figure 1.

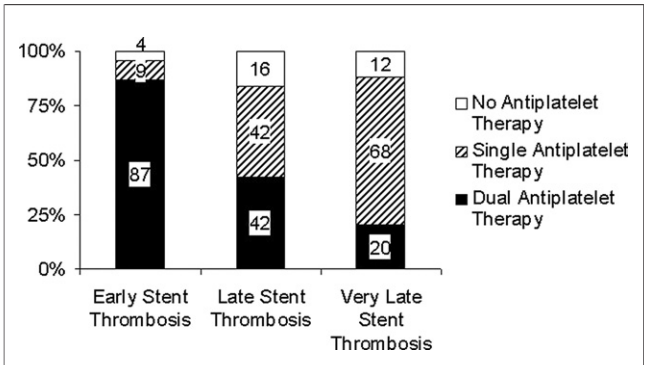


Figure 1 Status of Antiplatelet Treatment at Time of Definite Stent Thrombosis

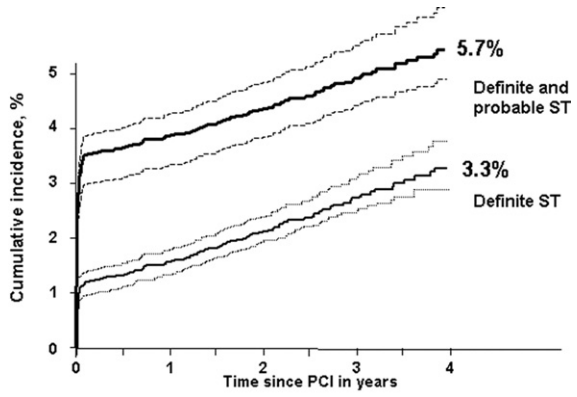
Proportion of patients with early and late stent thrombosis treated with dual, single, or no antiplatelet therapy.

Incidence and time course of ST. During a follow-up period of 4 years, definite ST was encountered in 192 of 8,146 patients after a median of 56 (interquartile range 4 to 593) days (Fig. 2). Early ST was observed in 92 (48%), late ST in 31 (16%), and very late ST in 69 (36%) of 192 patients. Definite ST occurred with an incidence density of 1.0/100 patient-years and a cumulative incidence of 3.3% at 4 years of follow-up. The hazard of late ST (between 30 days and 1 year) amounted to 0.46% (95% confidence interval [CI]: 0.32% to 0.65%), the hazard of very late ST (between 1 and 4 years) to 0.57% (95% CI: 0.45% to

Table 1 Clinical and Procedural Characteristics of Patients With and Without Definite ST

	Overall Population (n = 8,146)	ST (n = 192)	No ST (n = 7,954)	p Value
Age (yrs), mean ± SD	62.8 ± 11.5	59.4 ± 12.1	62.9 ± 11.5	<0.001
Male gender, %	74.5	75.0	74.5	0.88
Hypertension, %	46.5	42.2	46.6	0.23
Current smoking, %	36.8	41.7	36.7	0.16
Family history of CAD, %	28.1	29.2	28.1	0.75
Dyslipidemia, %	50.9	50.0	50.9	0.81
Diabetes, %	16.3	20.8	16.2	0.09
Left ventricular ejection fraction (%), mean ± SD	55 ± 12	52 ± 12	55 ± 12	0.035
Renal impairment, %	4.1	2.6	4.2	0.48
ACS at presentation, %	55.2	67.7	54.9	<0.001
Bifurcation treatment, %	11.8	17.9	11.6	0.06
Sirolimus-eluting stent, %	47.9	43.2	48.0	0.19
Total stent length/patient (mm), mean ± SD	36.3 ± 25.9	44.0 ± 38.8	36.1 ± 25.5	<0.001
Number of stents/patient, mean ± SD	1.96 ± 1.23	2.33 ± 1.71	1.95 ± 1.21	<0.001
Average stent diameter/patient (mm), mean ± SD	2.94 ± 0.38	2.88 ± 0.32	2.94 ± 0.38	0.048

ACS = acute coronary syndrome; CAD = coronary artery disease; ST = stent thrombosis.



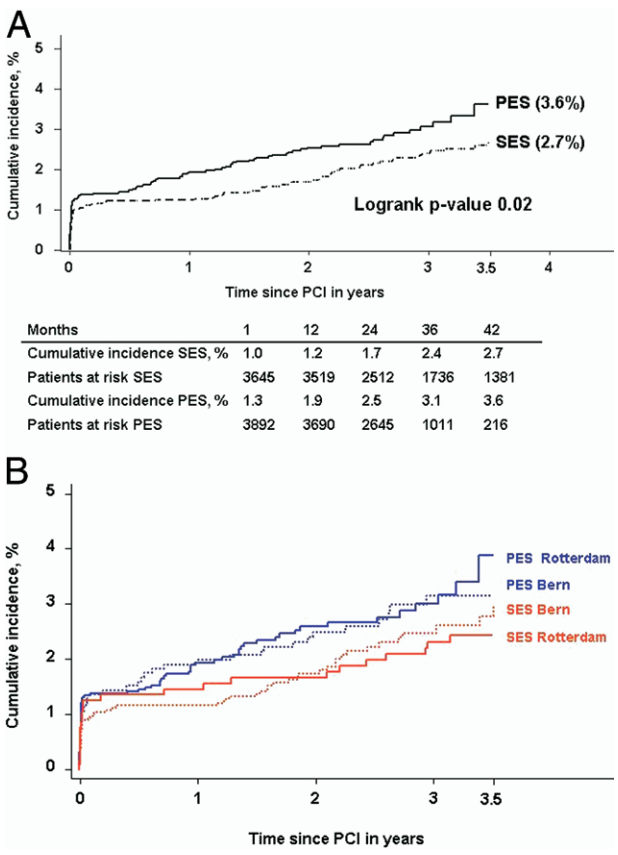
Months	1	12	24	36	48
Cumulative incidence definite ST, %	1.2	1.6	2.1	2.7	3.3
Cumulative incidence probable and definite ST, %	3.7	4.1	4.6	5.2	5.7
Patients at risk	7537	7209	5157	2747	1051

Figure 2 **Cumulative Incidence of Definite ST in 8,146 Patients During a 4-Year Follow-Up Period**

PCI = percutaneous coronary intervention; ST = stent thrombosis.

0.72%), and the hazard of the combined rate for late and very late ST (between 30 days and 4 years) was 0.53% (95% CI: 0.44% to 0.64%)/year. The rate of definite and probable ST after 4 years amounted to 5.7% (95% CI: 5.15% to 6.39%) with an incidence of 3.68% (95% CI: 3.29% to 4.12%) after 30 days and 4.09% (95% CI: 3.67% to 4.55%) after 1 year (Fig. 2).

Baseline demographic data for SES- and PES-treated patients differed widely (Table 2). The cumulative incidence of ST up to 3.5 years amounted to 2.7% for SES-treated and 3.6% for PES-treated patients (HR: 0.7; 95% CI: 0.53 to 0.95, p = 0.02) (Fig. 3A). Whereas early ST occurred with similar frequency in SES- (1.0%) and PES-treated



Months	1	12	24	36	42
Cumulative incidence SES, %	1.0	1.2	1.7	2.4	2.7
Patients at risk SES	3645	3519	2512	1736	1381
Cumulative incidence PES, %	1.3	1.9	2.5	3.1	3.6
Patients at risk PES	3892	3690	2645	1011	216

Figure 3 **Cumulative Incidence of Definite ST Stratification**

(A) Cumulative incidence of definite stent thrombosis (ST) stratified by stent type. **(B)** Cumulative incidence of definite ST stratified by stent type and treatment site. PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s).

Table 2 **Clinical and Procedural Characteristics of Patients Stratified by Stent Type**

	SES (n = 3,823)	PES (n = 4,323)	p Value
Age (yrs), mean ± SD	62.6 ± 11.4	63.0 ± 11.5	0.31
Male gender, %	74.9	74.2	0.51
Hypertension, %	41.9	51.6	<0.0001
Current smoking, %	44.9	29.5	<0.0001
Family history of CAD, %	29.0	27.3	0.09
Dyslipidemia, %	55.8	47.3	<0.0001
Diabetes, %	18.3	14.6	<0.0001
Left ventricular ejection fraction (%), mean ± SD	54 ± 12	55 ± 12	0.01
Renal impairment, %	4.3	3.9	0.58
ACS at presentation, %	52.1	58.0	<0.0001
Bifurcation treatment, %	10.3	12.3	0.09
Total stent length/patient (mm), mean ± SD	33.8 ± 23.0	38.6 ± 28.1	<0.0001
Number of stents/patient, mean ± SD	1.87 ± 1.14	2.03 ± 1.30	<0.0001
Average stent diameter/patient (mm), mean ± SD	2.86 ± 0.32	3.00 ± 0.40	<0.0001
Duration of clopidogrel prescription (days), mean ± SD	144 ± 120	194 ± 80	<0.0001

PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s); other abbreviations as in Table 1.

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(1.3%) patients (HR: 0.76; 95% CI: 0.50 to 1.15, p = 0.19), late and very late ST occurred with an annual rate of 0.44% (95% CI: 0.33% to 0.59%) after SES and 0.63% (95% CI: 0.49% to 0.83%) after PES implantation (HR: 0.66; 95% CI: 0.44 to 0.99, p = 0.047). A stratified analysis according to treatment site revealed a similar frequency and time course of definite ST after SES (Bern: 2.9% vs. Rotterdam: 2.4%, p = 0.49) and PES (Bern: 3.1% vs. Rotterdam: 3.9%, p = 0.83) implantation at both institutions (Fig. 3B).

Predictors of ST. The results of multivariate analyses to identify overall, early, and late definite ST are summarized in Table 3. Acute coronary syndrome at the time of stent implantation (HR: 1.81; 95% CI: 1.32 to 2.49), diabetes (HR: 1.61; 95% CI: 1.11 to 2.33), younger age (HR: 0.98; 95% CI: 0.96 to 0.99), and use of PES (HR: 1.51; 95% CI: 1.10 to 2.04) were independent predictors of overall ST. Diabetes (HR: 1.96; 95% CI: 1.18 to 3.28) was the only predictor of early ST, whereas ACS at time of stent implantation (HR: 2.21; 95% CI: 1.39 to 3.51), younger age (HR: 0.97; 95% CI: 0.95 to 0.99), and use of PES (HR: 1.67; 95% CI: 1.08 to 2.56) were independently associated with an increased risk of late ST.

Long-term clinical outcome. Mortality after definite ST amounted to 15.6% at 2 years and tended to be higher in patients suffering from early (20.3%) as opposed to late and very late ST (10.4%) (Fig. 4). At 4 years of follow-up, rates of death, MI, and the composite of death or MI were 10.6%, 4.6%, and 14.6%, respectively, in the overall population (Fig. 5). During the entire observation period of 4 years, 27 patients suffering from definite ST subsequently died. Death after the diagnosis of definite ST occurred in 0.4% of the entire population and accounted for 3.9% of all 702 deaths.

Discussion

The results of the present study indicate a continuous hazard of late and very late ST at an annual rate of 0.4% to 0.6% extending to 4 years after DES implantation. The only independent predictor of early ST was diabetes, whereas ACS, younger age, and use of PES were independently associated with an increased risk of late ST. Mortality due to definite ST accounted for only a small fraction of overall mortality.

Autopsy studies and clinical investigations using angioscopy and assessment of endothelial function indicate that DES delay healing and impair endothelialization (12,13,19–22). Intravascular ultrasound studies demonstrate a higher incidence of stent malapposition and evidence of vessel remodeling after DES implantation in patients with very late ST (14). Furthermore, drugs released from the drug-polymer combination might be thrombogenic on their own, because both sirolimus and paclitaxel enhance endothelial tissue factor expression, the principal activator of the coagulation cascade that activates factors IX and X (15,16). Therefore, it has been suggested that DES might create a prothrombotic milieu predisposing to thrombotic stent occlusion.

Previously, we reported the phenomenon of late ST after DES implantation occurring continuously without diminu-

Table 3 Hazard Ratio and 95% CI for Risk Factors Associated With Definite ST During the Entire Follow-Up Period From Multivariable Cox Regression

Variables	Hazard Ratio	95% CI
ACS at presentation	1.8	1.3–2.5
Diabetes	1.6	1.1–2.3
Number of stents/patient	1.2	0.95–1.4
Current smoking	1.1	0.78–1.5
Family history of CAD	1.0	0.73–1.4
Total stented length/patient	1.0	1.00–1.01
Age	0.98	0.96–0.99
Dyslipidemia	0.95	0.70–1.28
Female	0.89	0.63–1.25
Hypertension	0.85	0.62–1.16
Use of PES	1.67	1.08–2.56

CI = confidence interval; other abbreviations as in Tables 1 and 2.

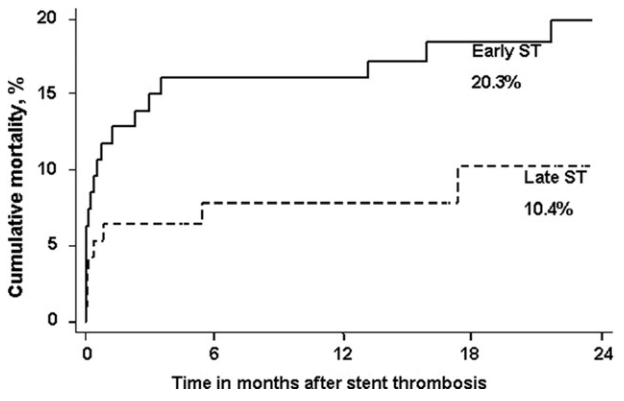

Figure 4 Cumulative Incidence of Death in Patients With Definite ST Stratified According to Early and Late ST

ST = stent thrombosis.

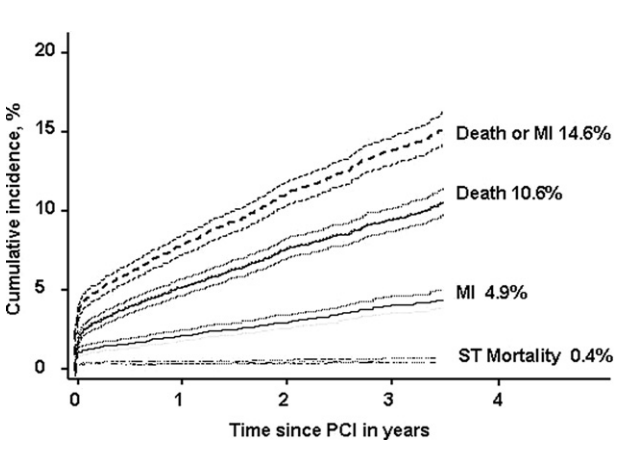

Figure 5 Cumulative Incidence of Ischemic Adverse Events in 8,146 Patients During 4 Years of Follow-Up

MI = myocardial infarction; PCI = percutaneous coronary intervention; ST = stent thrombosis.

tion up to 3 years of follow-up in a large cohort of consecutive patients treated with the unrestricted use of DES (10). The present study extends these findings to a longer-term follow-up and shows that the steady annual rate of 0.4% to 0.6% remains unchanged between 3 and 4 years of follow-up. A continuous linear hazard of late ST comparable to the present study has been corroborated more recently in the extended follow-up of 21,717 DES-treated patients included in the SCAAR (Swedish Coronary Angiography and Angioplasty Registry) with an annual rate of ST of 0.5% during a follow-up of 2 years (23,24). Moreover, several systematic reviews reported a significantly higher rate of very late ST in disfavor of both SES and PES compared with BMS, although the overall rate of ST was not different between the different stent types (3,4,25). Accordingly, very late ST is a distinct entity complicating the use of DES, and arterial healing remains incomplete up to 4 years after DES implantation in humans.

Although late and very late ST complicated the clinical course of both DES types, it was more frequent with PES than SES, and use of PES emerged as independent of late ST. Of note, PES was implanted in more complex lesions in this cohort, whereas SES had been used earlier than PES, and subsequently the length of follow-up was different between the 2 devices, which might have biased the results in disfavor of PES. Yet, Bavry et al. (7) made a similar observation and found the risk of very late ST more pronounced with PES (5.9 of 1,000 patient-years) than SES (3.6 of 1,000 patient-years) in a meta-analysis of 14 trials with 6,675 patients. A meta-analysis directly comparing SES (4,391 patients) with PES (4,304 patients) also reported a higher risk of protocol-defined ST with PES (1.9%) than SES (1.2%; HR: 0.66, 95% CI: 0.46 to 0.94, $p = 0.02$) (26). Finally, a network meta-analysis of 38 trials comparing BMS, SES, and PES reported an increased risk of late ST with PES compared with BMS (HR: 2.11; 95% credibility interval: 1.2 to 4.2, $p = 0.02$), whereas the risk was less pronounced with SES (HR 1.1; 95% credibility interval: 0.6 to 2.3, $p = 0.71$) (5). It can only be speculated whether the different drug-release kinetics, distribution within the vessel wall, mechanisms of action, inhomogeneity of strut coverage, or design of the stent platforms impact on the incidence and time course of late ST.

Previous studies identified clinical characteristics such as premature discontinuation of antiplatelet therapy (27–29), ACS (10,30), diabetes (10,27,30), and renal failure (27,28) as independent risk factors of DES-associated ST. In addition, lesion characteristics including smaller reference vessel diameter, stent length (29), thrombus burden (31), and bifurcation lesions (27,28) were identified as predictive of ST. The present study not only confirms the hazard related to diabetes and ACS in the largest cohort of patients with definite ST to date but also identifies diabetes as a predictor of early ST and ACS as a predictor of late ST. The reasons for a predisposition of diabetic patients to early ST might be related to smaller vessel size (32), longer lesion length, a higher rate of residual dissections, and an increased platelet aggregation (11,33). Conversely, patients with ACS might be predisposed to late and very late ST due to a higher thrombus burden at the time of stent implantation (31), which upon dissolution might result in late acquired stent malapposition and altered flow dynamics around stent struts (14).

The contribution of definite ST to overall mortality was small in the present study (<5%). A similar observation has been made in a pooled analysis of pivotal trials comparing DES with BMS (25), where mortality due to ST accounted for <10% of overall mortality. It might be speculated that the overall outcome regarding death or MI of patients treated by percutaneous coronary interventions might be determined in large part by causes other than target lesion revascularization or ST. Along this line, a pooled analysis of 4 randomized trials comparing SES with BMS in 1,748 patients found that the majority of death or MI in both stent groups was unrelated to either target lesion revascularization or ST, suggesting another etiology, such as disease progression (34). However, it is important to note that the definition of definite ST requiring angiographic or autopsy confirmation of thrombotic stent occlusion leads to a considerable underestimation of the true incidence of ST-related mortality. Because only those patients reaching the catheterization laboratory alive qualify for the diagnosis of definite ST, all deaths before angiographic or autopsy confirmation are missed and not classified as "definite ST"–related. In other words, the presented data only reflect the mortality toll of definite ST after initial survival.

Study limitations. The findings of this study have to be interpreted in light of several limitations. First, the study was nonrandomized, with the decision regarding stent type and antiplatelet therapy largely determined by local institutional practice. The principal purpose was to investigate the incidence and time course of definite ST in unselected patients treated with DES during long-term follow-up rather than a comparison of ST as encountered after BMS implantation. This is an observational study, which suffers from confounding by indication. The SES and PES were used in both centers during different time periods, and PES was available for commercial use 1 year later than SES. This might have resulted in bias due to differences in follow-up. Due to the continuous enrollment of patients into this registry between 2002 and 2005, not all patients had completed the 4-year follow-up. Accordingly, estimates of the risk of ST are less precise during later time points, and the data should be carefully interpreted by considering the corresponding CIs. Second, the data were obtained from a patient population at 2 tertiary care centers with a high number of stents/patient, a small average stent diameter, and an overall long total stent length, which might not apply to institutions with a more restricted DES use. Third, it is possible that some ST went undetected in our study despite our attempts at an active surveillance of harms. In addition, the focus of the present study was on definite ST, which might have led to an underestimation of the actual incidence

of ST as well as mortality related to definite ST. The latter requires angiographic or autopsy confirmation of thrombotic stent occlusion and therefore ignores any death without these prerequisites. However, the definition is in line with previous reports from our group on ST either after DES or BMS implantation and allows for appropriate comparisons. Moreover, the composite of definite and probable ST, suggested as a useful parameter to avoid underestimation and overestimation of ST, is provided in the present study as are the ischemic end points of death and MI. Finally, only the prescribed duration of antiplatelet therapy was available in the present study, whereas the exact duration of dual antiplatelet therapy could not reliably be ascertained in the whole patient population. Therefore, it cannot be excluded that we missed an important relation between the actual duration of thienopyridine therapy and ST.

Conclusions

Late ST is a distinct entity complicating the use of DES and occurs steadily at an annual rate of 0.4% to 0.6% for up to 4 years of follow-up. Diabetes is an independent predictor of early ST, whereas ACS, younger age, and use of PES are associated with late ST.

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