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Original article

Incidence of cardiac death and recurrent stent thrombosis after treatment for angiographically confirmed stent thrombosis

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ABSTRACT

Background: Although many studies showed the predictive factors of stent thrombosis (ST) occurrence, there are few data about clinical outcomes and recurrent ST after percutaneous coronary intervention (PCI) for ST. Furthermore, it is uncertain which factors can cause adverse clinical events including recurrent ST.

Methods: This study examined the clinical outcomes after treatment for definite ST. Among 18,739 patients between June 2003 and December 2016 who underwent PCI using a drug-eluting stent (DES) or bare-metal stent (BMS), 243 consecutive patients who suffered definite ST were enrolled in this study. The overall incidence of ST was 1.3% (DES 1.4% and BMS 0.8%). The study endpoint was 1-year cardiac death or recurrent definite ST after the initial ST.

Results: Study endpoint occurred in 57 patients (23.5%) during the 1-year follow-up after the initial ST. In multivariate analysis, the factors predicting 1-year endpoint were early ST [adjusted hazard ratio (HR): 2.23, 95% confidence interval (CI): 1.26–4.08, $p = 0.006$], BMS ST (HR: 2.42, 95% CI: 1.27–4.81, $p = 0.045$), serum level of glucose (HR: 1.03, 95% CI: 1.01–1.05, $p = 0.048$), and ST-segment elevation myocardial infarction (STEMI) at the initial ST (HR: 3.73, 95% CI: 1.82–7.65, $p < 0.001$).

Conclusions: Recurrent ST or cardiac death during the first year after the initial ST event occurred in ~25% of patients treated for definite ST. BMS ST, serum level of glucose, STEMI, and early ST at the initial ST were associated with adverse cardiac events.

Introduction

Stent thrombosis (ST) is a serious complication after percutaneous coronary intervention (PCI), with most of these patients presenting with acute myocardial infarction (AMI) [1,2]. Although the use of drug-eluting stents (DES) markedly reduced in-stent restenosis, patients with first-generation DES were much more prone to ST, especially very late stent thrombosis (VLST), than patients treated with a bare-metal stent (BMS), because of the thick struts, the high drug doses used, and the high polymer load [3,4]. However, newer-generation DES have a similar or reduced incidence of ST compared to BMS and thus have been recommended for the treatment of coronary artery disease [5–7]. Use of the potent inhibitor P2Y12 has also resulted in fewer cases of ST events, irrespective of stent type [8]. The correct management of ST and the achievement of a favorable long-term prognosis are critical to avoiding the unfavorable clinical outcomes associated with ST. However, few studies have evaluated long-term results after ST. Therefore, in this study, we evaluated the 1-year clinical outcomes of 18,739 patients who underwent PCI using coronary stents at a large tertiary center during a 14-year period. Our focus was the group of patients with cardiac death or recurrent ST suffered after an angiographically confirmed ST.

Methods

Study population and data collection

Among the 18,739 patients who underwent PCI with a DES ($n = 14,821$) or BMS ($n = 3918$) at Chonnam National University

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Hospital from June 2003 to December 2016, 243 consecutive patients who suffered from a definite ST after the index PCI (210 patients with DES ST and 33 patients with BMS ST) were retrospectively analyzed. Only patients who had angiographically confirmed ST corresponding to a definite ST as defined by the Academic Research Consortium classification [9] were included. The study protocols were approved by the Chonnam National University Hospital Institutional Review Board and adhered to the principles of the Declaration of Helsinki (IRB approval number: CNUH-2018-265). A waiver for informed consent was obtained from the Board.

Baseline characteristics, including demographics, medical history, antiplatelet status, echocardiographic data, and laboratory findings were assessed by reviewing medical charts. Laboratory data were obtained on admission for the ST event. AMI was defined as an increase in cardiac biomarkers with at least one of the following: symptoms of ischemia or an electrocardiogram with new significant ST-T changes or left bundle branch block, or pathologic Q-wave. AMI was assessed as ST-segment (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI). All quantitative coronary analyses were conducted using software. Cine coronary angiograms were reviewed by four interventional cardiologists at Chonnam National University Hospital. ST was classified as early (EST, 0–30 days), late (LST, 30 days–1 year), and VLST (>1 year after stent implantation) based on the timing of ST occurrence [9].

Study endpoints and statistical analysis

The study endpoint was a composite of cardiac death or recurrent ST within 1-year after the initial ST event, as registered by chart review or telephone contact. Recurrent ST was also defined as definite ST. In-hospital mortality was investigated and a landmark analysis for each cardiac death and recurrent ST at 30 days and 1 year was performed. Baseline and procedural characteristics at both the index PCI and initial ST event were compared between patients with and without the study endpoint at 1 year.

Continuous variables are presented as the mean ± standard deviation or as the median and interquartile range and were compared using an unpaired *t*-test or the Mann–Whitney rank-sum test. Discrete variables are expressed as counts and percentages and were analyzed using Pearson's chi-square or Fisher's exact test. Cox proportional hazards regression analyses with adjustment for covariates were used to evaluate independent predictors of the study endpoint; variables with a $p \leq 1.0$ in univariate analyses were included in multivariate analyses. Kaplan–Meier curves were constructed to compare groups (BMS ST versus DES ST; EST versus LST or VLST; STEMI versus NSTEMI or unstable angina pectoris) with respect to a significant association between the factors identified in multivariate Cox regression analyses and the primary study endpoint. Differences were assessed using the log-rank test. All analyses were two tailed, and all variables with a $p < 0.05$ were considered significant. All statistical analyses were performed using MedCalc statistical software version 18.10 (MedCalc Software bvba, Ostend, Belgium).

Results

Baseline and procedural characteristics at time of index PCI and ST event according to event occurrence at 1 year

The study endpoint occurred in 57 patients (23.5%) during the 1-year follow-up after the initial ST event (Fig. 1). Table 1 summarizes the baseline characteristics according to cumulative study endpoint occurrence at 1 year (57 patients with versus

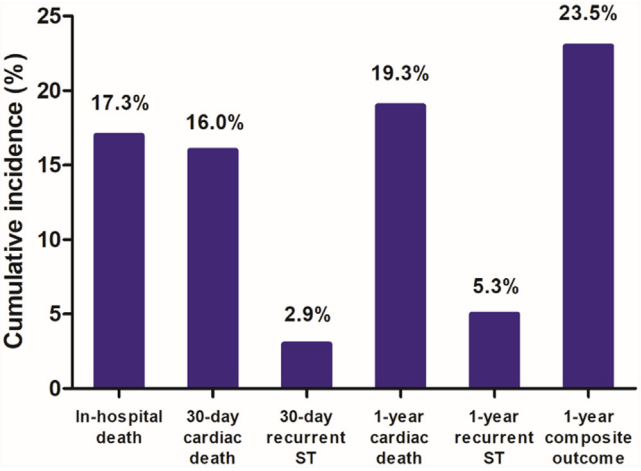

Fig. 1. Cumulative incidence of study endpoint. One-year composite outcome is a composite of cardiac death or recurrent ST.
ST, stent thrombosis.

186 patients without an event at 1 year). Patients with an event were older, more likely to be female, and less obese than patients without an event. The past medical history was comparable in the two groups. Antiplatelet agent use had been discontinued in 40 patients (16.5%), whereas 65.8% of patients were on dual antiplatelet therapy at the time of the initial ST. Among the laboratory findings, the hemoglobin level and glomerular filtration rate were lower in the event group. Patients without an event had lower levels of serum glucose, creatinine, HbA1c, N-terminal pro brain-type natriuretic peptide, and high-sensitivity C-reactive protein. Table 2 shows the procedural characteristics at the time of the index PCI according to event occurrence at 1 year. The diagnosis at the time of the index PCI and quantitative coronary analysis data were similar between the groups. Multivessel coronary artery disease was more often seen at the time of the index PCI in patients with than in those without an event (64.9% versus 48.9%, $p = 0.034$). The procedural characteristics and data on in-hospital care at the time of ST according to event occurrence at 1 year are shown in Table 3. At the time of ST, 63.8% of the study population presented with STEMI and 25.9% had NSTEMI, 45.3% had Academic Research Consortium-defined EST, 11.9% had LST, and 42.8% had VLST. STEMI and EST were more frequent in patients with an event. DES ST occurred in 86.4% (first-generation 44.4%, second-generation 42.0%) and BMS ST in 13.6%. ST management was similar in the two groups, with 89.3% of the patients receiving only balloon angioplasty. However, percutaneous mechanical circulatory support was administered more often in the event group. Among patients who had suffered an event, the left ventricular ejection fraction after ST was lower. Although a platelet function test was performed immediately after ST diagnosis in 85 patients, P2Y12 reactivity values were significantly higher in the event group. Status of antiplatelet after treatment of ST was also evaluated in 208 patients after exclusion of expired patients during PCI for ST. A total of 60 patients (28.8%) received prasugrel or ticagrelor, 8 patients (3.8%) received anticoagulation, and 62 patients (29.8%) received cilostazol in addition to dual antiplatelet therapy. All patients received dual antiplatelet therapy during at least 1 year after ST except for 3 patients who temporarily discontinued antiplatelet therapy due to major gastrointestinal bleeding.

Clinical outcomes and predictors of study endpoints

Fig. 1 shows the cumulative incidence of the study endpoint. The rates of in-hospital death, 1-year cardiac death, and 1-year

Table 1
Baseline characteristics of overall population according to event occurrence at 1-year.

	All population (n = 243)	With event (n = 57)	Without event (n = 186)	p-Value
Age, years	64.4 ± 12.4	69.4 ± 12.0	62.9 ± 12.2	0.001
Age ≥65 years	131 (53.9)	40 (70.2)	91 (48.9)	0.005
Male gender	169 (69.5)	31 (54.4)	138 (74.2)	0.004
Body mass index, kg/m^2	24.3 ± 3.9	23.4 ± 3.8	24.5 ± 4.0	0.052
Body mass index ≥25 kg/m^2	86 (35.4)	11 (19.3)	75 (40.3)	0.004
Atherosclerotic risk factors				
Hypertension	145 (59.7)	36 (63.2)	109 (58.6)	0.540
Diabetes mellitus	99 (40.7)	27 (47.4)	72 (38.7)	0.244
Dyslipidemia	22 (9.1)	6 (10.5)	16 (8.6)	0.658
Current or ex-smoking	108 (44.4)	20 (35.1)	88 (47.3)	0.104
Prior history of PCI before index procedure	35 (14.4)	9 (15.8)	26 (14.0)	0.733
Prior history of MI before index procedure	13 (5.3)	2 (3.5)	11 (5.9)	0.480
Prior history of cerebrovascular accident	9 (3.7)	1 (1.8)	8 (4.3)	0.373
Last LVEF before ST, %	56.5 ± 13.8	52.2 ± 14.8	57.8 ± 13.2	0.012
Time from index PCI to ST, days	77 (5, 1271)	11 (4, 923)	209 (6, 1285)	0.079
Status of antiplatelet at the time of ST				0.693
Dual antiplatelet	160 (65.8)	41 (71.9)	119 (64.0)	
Dual antiplatelet with anticoagulation	8 (3.3)	1 (1.8)	7 (3.8)	
Single antiplatelet	35 (14.4)	7 (12.3)	28 (15.1)	
Cessation of antiplatelet	40 (16.5)	8 (14.0)	32 (17.2)	
Laboratory findings at the time of ST				
Hemoglobin, g/dL	12.4 ± 2.1	11.5 ± 2.2	12.6 ± 2.0	0.001
Platelet count, ×10^3/μL	224 (193, 275)	223 (183, 275)	225 (196, 280)	0.394
Serum glucose, mg/dL	154 (113, 162)	160 (129, 202)	144 (109, 160)	0.001
Creatinine, mg/dL	0.9 (0.7, 1.1)	1.1 (0.9, 1.4)	0.9 (0.7, 1.1)	0.002
GFR, mL/min/1.73 m^2	74.7 ± 35.4	56.7 ± 34.4	80.2 ± 33.9	<0.001
Estimated GFR <60 mL/min/1.73 m^2	94 (38.7)	36 (63.2)	58 (31.2)	<0.001
Total cholesterol, mg/dL	156 ± 45	153 ± 40	157 ± 46	0.533
Triglyceride, mg/dL	121 ± 74	113 ± 51	123 ± 79	0.364
HDL-cholesterol, mg/dL	45 ± 20	44 ± 22	45 ± 19	0.687
LDL-cholesterol, mg/dL	95 ± 40	92 ± 35	95 ± 42	0.589
HbA1c, %	6.7 ± 1.6	7.3 ± 1.8	6.6 ± 1.5	0.031
N-terminal pro BNP, pg/mL	368 (93, 1982)	743 (245, 11040)	267 (88, 1493)	0.011
High-sensitivity CRP, mg/dL	0.3 (0.1, 1.3)	0.9 (0.2, 3.6)	0.3 (0.1, 1.0)	0.001

Values are n (%), mean ± SD, or median (25–75 percentile). BNP, brain-type natriuretic peptide; CRP, C-reactive protein; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; ST, stent thrombosis.

Table 2
Procedural characteristics at the time of index PCI of overall population and according to event occurrence at 1 year.

	All population (n = 243)	With event (n = 57)	Without event (n = 186)	p-Value
Diagnosis				0.602
Unstable angina pectoris	75 (30.9)	16 (28.1)	59 (31.7)	
STEMI	88 (36.2)	23 (40.4)	65 (34.9)	
NSTEMI	69 (28.4)	17 (29.8)	52 (28.0)	
Stable ischemic heart disease	11 (4.5)	1 (1.8)	10 (5.4)	
Mean stent diameter, mm	3.1 ± 0.3	3.0 ± 0.3	3.1 ± 0.3	0.236
Mean stent length, mm	24.1 ± 7.1	23.1 ± 6.0	24.4 ± 7.3	0.243
Total number of lesion	1.7 ± 0.7	1.9 ± 0.8	1.7 ± 0.7	0.080
Total number of stent	2.0 ± 1.1	2.2 ± 1.4	1.9 ± 1.0	0.101
Quantitative coronary analysis				
Pre-PCI RD, mm	3.1 ± 0.4	3.1 ± 0.5	3.1 ± 0.4	0.626
Pre-PCI DS, %	90.2 ± 11.7	88.6 ± 12.0	90.7 ± 11.6	0.245
Post-PCI DS, %	8.6 ± 11.5	9.9 ± 13.2	8.2 ± 10.9	0.362
Stent overlapping	66 (27.2)	21 (36.8)	45 (24.2)	0.060
IVUS-guided PCI	26 (10.7)	7 (12.3)	19 (10.2)	0.659
Chronic total occlusion	7 (2.9)	1 (1.8)	6 (3.2)	0.561
In-stent restenosis	20 (8.2)	7 (12.3)	13 (7.0)	0.203
Bifurcation lesion	117 (48.1)	25 (43.9)	92 (49.5)	0.459
Multivessel disease	128 (52.7)	37 (64.9)	91 (48.9)	0.034
ACC/AHA B2 or C lesion	196 (80.7)	48 (84.2)	148 (79.6)	0.438

Values are n (%), or mean ± SD. ACC, American College of Cardiology; AHA, American Heart Association; DS, diameter stenosis; IVUS, intravascular ultrasound; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RD, reference diameter; STEMI, ST-segment elevation myocardial infarction.

recurrent ST were 17.3%, 19.3%, and 5.3%, respectively. In multivariate Cox-regression analyses, the factors predictive of 1-year cardiac death or recurrent ST were EST [adjusted hazard ratio (HR): 2.23, 95% confidence interval (CI): 1.26–4.08, p = 0.006], BMS ST (HR: 2.42, 95% CI: 1.27–4.81, p = 0.045), serum level of glucose (HR: 1.03, 95% CI: 1.01–1.05, p = 0.048), and STEMI at initial ST (HR: 3.73, 95% CI: 1.82–7.65, $p < 0.001$). The use of prasugrel or ticagrelor after ST and preserved left ventricular ejection fraction

Table 3
Procedural characteristics and in-hospital care at the time of ST of overall population and according to event occurrence at 1 year.

	All population (n = 243)	With event (n = 57)	Without event (n = 186)	p-Value
Diagnosis at the time of ST				0.002
STEMI	155 (63.8)	47 (82.5)	108 (58.1)	
NSTEMI	63 (25.9)	9 (15.8)	54 (29.0)	
Unstable angina pectoris	25 (10.3)	1 (1.8)	24 (12.9)	
ARC definition of ST				0.045
Early ST	110 (45.3)	34 (59.6)	76 (40.9)	
Late ST	29 (11.9)	5 (8.8)	24 (12.9)	
Very late ST	104 (42.8)	18 (31.6)	86 (46.2)	
Stent type				0.159
Bare-metal stent	33 (13.6)	12 (21.1)	21 (11.3)	
1st-generation drug-eluting stent	108 (44.4)	22 (38.6)	86 (46.2)	
2nd-generation drug-eluting stent	102 (42.0)	23 (40.4)	79 (42.5)	
Target vessel				0.075
Left anterior descending	118 (49.6)	27 (47.4)	91 (50.3)	
Right coronary artery	74 (31.1)	13 (22.8)	61 (33.7)	
Left circumflex artery	38 (16.0)	13 (22.8)	25 (13.8)	
Others	8 (3.4)	4 (7.0)	4 (2.2)	
Location				0.102
Proximal	145 (59.7)	39 (68.4)	106 (57.0)	
Middle to distal	98 (40.3)	18 (31.6)	80 (43.0)	
Stent underexpansion	30 (12.3)	9 (15.8)	21 (11.3)	0.366
Pre-PCI TIMI flow 0	182 (74.9)	45 (78.9)	137 (73.7)	0.420
Management				0.590
Plain balloon angioplasty	217 (89.3)	52 (91.2)	165 (88.7)	
Stenting	26 (10.7)	5 (8.8)	21 (11.3)	
Thrombi aspiration	56 (23.0)	12 (21.1)	44 (23.7)	0.683
Intracoronary glycoprotein IIb/IIIa inhibitor	73 (30.0)	11 (19.3)	62 (33.3)	0.043
IABP or ECMO	20 (8.2)	14 (24.6)	6 (3.2)	<0.001
Platelet function test*				
Aspirin reactivity units	469 ± 75	488 ± 77	464 ± 74	0.258
P2Y12 reactivity units	278 ± 94	327 ± 76	265 ± 95	0.006
Status of antiplatelet after treatment of ST**				0.274
Dual antiplatelet with clopidogrel	78 (37.5)	12 (50.0)	66 (35.9)	
Dual antiplatelet with ticagrelor or prasugrel	60 (28.8)	5 (20.8)	55 (29.9)	
Dual antiplatelet with anticoagulation	8 (3.8)	2 (8.3)	6 (3.3)	
Triple antiplatelet with cilostazol	62 (29.8)	5 (20.8)	57 (31.0)	
LVEF after ST, %	51.3 ± 12.2	44.9 ± 13.4	53.3 ± 11.1	<0.001
LVEF ≤50% after ST	78 (32.1)	22 (38.6)	56 (30.1)	0.230

* Result was available in 85 patients among overall study population.
** Result was available in 208 patients after exclusion of expired patients during PCI for ST.
Values are n (%), or mean ± SD.
ARC, Academic Research Consortium; ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

Table 4
Predictors of composite outcome at 1-year.

	Hazard ratio	95% CI	p-Value
Age ≥65 years	1.16	0.59–2.30	0.669
Male gender	0.95	0.51–1.79	0.880
Body mass index ≥25 kg/m^2	0.58	0.29–1.16	0.126
LVEF before ST	1.01	0.99–1.03	0.460
Stent overlapping	1.55	0.88–2.72	0.132
Multivessel disease	1.09	0.60–2.02	0.767
Early ST (vs. late or very late ST)	2.23	1.26–4.08	0.006
Bare-metal stent ST	2.42	1.27–4.81	0.045
Post-PCI TIMI flow grade 3	0.57	0.29–1.12	0.103
STEMI at the time of ST	3.73	1.82–7.65	<0.001
Use of prasugrel or ticagrelor after ST	0.24	0.09–0.63	0.004
LVEF after ST	0.96	0.94–0.99	0.002
Hemoglobin	0.95	0.82–1.09	0.445
Serum glucose	1.03	1.01–1.05	0.048
Glomerular filtration rate <60 mL/min/1.72 m^2	1.92	0.97–3.78	0.060

CI, confidence interval; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction.

after ST were associated with a reduced incidence of the study endpoint (Table 4). Kaplan–Meier estimates for the composite study endpoint according to stent type (BMS versus DES ST), ST type (EST versus LST or VLST), and diagnosis at the initial ST event (STEMI versus NSTEMI or unstable angina pectoris) are shown in Fig. 2. The predictors of cardiac death and recurrent ST at 1 year were similarly determined (Table 5). Independent predictors of cardiac death were EST, BMS ST, STEMI at ST, and serum levels of

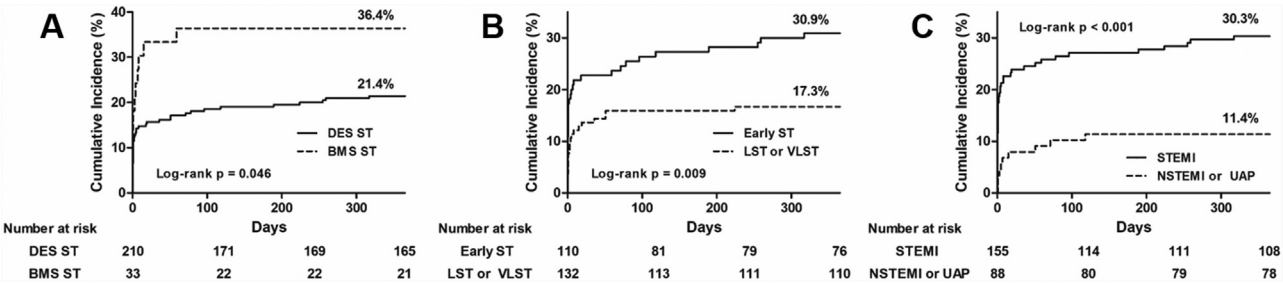

Fig. 2. Kaplan–Meier estimates for the composite of cardiac death of recurrent ST. Cumulative incidence of study endpoint according to (A) stent type (BMS versus DES ST), (B) types of ST (early ST versus LST or VLST), and (C) diagnosis at initial ST event (STEMI versus NSTEMI or UAP).
BMS, bare-metal stent; DES, drug-eluting stent; LST, late stent thrombosis; NSTEMI, non-ST-segment elevation myocardial infarction; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction; UAP, unstable angina pectoris; VLST, very late stent thrombosis.

Table 5
Predictors of cardiac death and recurrent ST at 1-year.

	Hazard ratio	95% CI	*p*-Value
Cardiac death			
Age ≥65 years	1.98	0.87–4.49	0.102
Male gender	0.74	0.38–1.45	0.385
Stent overlapping	1.63	0.89–3.00	0.117
Multivessel disease	1.12	0.57–2.19	0.739
Early ST (vs. late or very late ST)	1.99	1.06–3.74	0.032
Bare-metal stent ST	2.67	1.21–5.19	0.035
Post-PCI TIMI flow grade 3	0.58	0.29–1.14	0.115
STEMI at the time of ST	4.89	2.13–11.24	<0.001
Use of prasugrel or ticagrelor after ST	0.12	0.03–0.49	0.003
LVEF after ST	0.97	0.95–0.99	0.022
Serum glucose	1.04	1.01–1.06	0.008
Glomerular filtration rate <60 mL/min/1.72 m^2	1.95	0.93–4.06	0.077
Recurrent ST			
Dyslipidemia	3.43	0.92–12.79	0.066
Late or very late ST (vs. early ST)	3.69	1.01–13.49	0.048
Use of prasugrel or ticagrelor after ST	0.84	0.23–3.06	0.790
LVEF after ST	0.96	0.92–0.99	0.029

CI, confidence interval; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction.

glucose; predictors of recurrent ST were LST or VLST (versus EST). The use of prasugrel or ticagrelor after ST was the only preventive factor for cardiac death, not a recurrent ST. Preserved left ventricular ejection fraction after ST was not only associated with a reduced incidence of cardiac death, but also reduced incidence of recurrent ST.

Discussion

Our main findings are that the composite endpoint occurred in 23.5% of the study population; the cumulative rates of 1-year cardiac death and recurrent ST were 19.3% and 5.3%, respectively; predictors of a 1-year composite endpoint were EST, BMS ST, serum levels of glucose, and STEMI at initial ST; and predictors of 1-year recurrent ST were LST and VLST vs. EST.

Several studies have assessed clinical outcomes after ST. The cumulative mortality 1 year after definite DES ST has been reported to be 10–20% [10–13]. The long-term mortality beyond 1 year after definite DES ST is relatively high, even in patients administered a potent P2Y12 inhibitor [8]. In a previous study that evaluated BMS patients, the 6-month incidence of recurrent ST was 12% [14]. According to data from a large registry, including patients who received a DES, the 1-year incidence of recurrent ST after stent implantation is 4.6% [15]. Our results on cardiac mortality and the incidence of recurrent ST at 1 year are similar to those of other studies, but cardiac mortality was much higher in BMS- than in DES-treated patients. A study that compared ST with respect to DES versus BMS reported a similarly poor outcome despite different clinical outcomes in these two groups [16]. The baseline and angiographic profiles of our 210 patients with DES ST and 33 patients with BMS ST did not significantly differ, except for a larger proportion of elderly patients in the BMS ST group (data not shown). Among the reported advantages of BMS versus DES are their better mechanical properties, including a low profile as well as better trackability and crossability [17]. Many clinical circumstances and angiographic profiles not registered in the current study might have impacted BMS selection.

In our study, ST was associated with the sudden cessation of antiplatelet agent use in 16.5% of the study population. These patients accounted for 8.2% of those with EST, 13.8% of those with LST, and 26.0% of those with VLST. Although the premature discontinuation of dual antiplatelet therapy is the single most important predictor of ST occurrence [18], EST is also closely related to lesion characteristics and inadequate postprocedural lumen dimensions [19]. Consequently, the higher rate of antiplatelet discontinuation in the VLST group suggests that ST occurrence was mainly due to antiplatelet discontinuation rather than to procedural factors. However, we could not fully evaluate the timing or cause of antiplatelet discontinuation. The occurrence of adverse cardiac events after antiplatelet therapy cessation depends on various clinical circumstances [20] that should be investigated in further studies. The EST patients in our study had

the worst clinical outcomes in terms of higher composite outcomes and cardiac death at 1 year, in agreement with the results of other studies [21]. The predictors of recurrent ST have yet to be definitively determined. In one small study, large post-procedural vessel diameter and larger residual thrombus burden were identified as predictors of recurrent ST [22], whereas our study identified LST or VLST. Although advanced neo-atherosclerosis with neo-intimal rupture and thrombosis is the most common mechanism underlying definite VLST [23], detailed information on the lesion characteristics of our patients was not available and the number of recurrent ST events was too small. In the current study, about 30% of patients received triple antiplatelet therapy including cilostazol after treatment of ST. Because the current study analyzed patients during long-term period, the strategy of antiplatelet use after ST was somewhat different from current management which recommends the use of potent P2Y12 inhibitors after ST. The use of potent P2Y12 inhibitors, prasugrel or ticagrelor, was associated with reduced study endpoint mainly driven by reduced cardiac mortality at 1 year. However, prasugrel or ticagrelor could not reduce the incidence of recurrent ST, and the cause of it was that recurrent ST as study endpoint was only definite ST, and too small number of recurrent ST. This issue is very important to optimally manage fatal ST, and should be investigated in further studies.

Our study had several limitations. Although patients with ST who were seen at a large tertiary center during a period of 14 years were included, the study population was relatively small and only 33 patients had been treated with a BMS. Thus, the unacceptably high mortality in this group remains unexplained. In addition, we could not fully evaluate the lesion characteristics of our patients, and the reasons for the discontinuation of antiplatelet therapy, which is related to the cause and mechanism of ST, were unknown.

In conclusion, recurrent ST or cardiac death in the year after an initial ST event occurred in ~25% of patients treated for definite ST. BMS ST, serum levels of glucose, STEMI, and early ST after the initial ST were associated with adverse cardiac events. LST or VLST were identified as a predictor of recurrent ST at 1 year.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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