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Original article

# Post-discharge clinical and angiographic outcomes of patients presenting within 48 h of STEMI treated with paclitaxel- or sirolimus-eluting stents

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ABSTRACT

*Background and purpose:* The purpose of the present study was to examine the mid-term clinical and angiographic outcomes of patients with ST-segment elevation myocardial infarction (STEMI) who presented within 48 h and received paclitaxel-eluting stents (PES) or sirolimus-eluting stents (SES).

*Methods and results:* This study was a retrospective, non-randomized, single-center study. The post-discharge clinical outcomes of 357 consecutive patients who presented within 48 h of their first STEMI and received PES ($n = 163$) or SES ($n = 194$) between February 2007 and February 2009 were analyzed in May 2011. The incidence of post-discharge events (i.e. cardiac death and non-fatal recurrent MI) after PES placement (0.6%) did not significantly differ from that after SES placement (1.5%). Treatment with PES was not related to the risk of adverse events post-discharge (mean follow-up period for PES placement, $1170 \pm 243$ days; hazard ratio, 0.346; 95% CI, 0.036–3.371; $p = 0.361$). No definite stent thromboses developed after treatment with PES or SES. The incidence of binary in-stent restenosis (stenosis of more than 50% of the diameter at secondary angiography performed 10–18 months after the initial procedure) after PES placement (17.1%) was significantly higher than that after SES placement (4.8%; $p < 0.001$). PES placement was an independent predictor of binary in-stent restenosis (odds ratio, 3.892; 95% CI, 1.470–10.30; $p = 0.006$).

*Conclusions:* Retrospective examination of the post-discharge clinical course after placement of PES and SES showed favorable midterm clinical outcomes among Japanese STEMI patients treated within 48 h of onset. However, SES treatment resulted in superior angiographic outcomes compared to PES.



## 1. Introduction

Previous reports have confirmed the mid-term safety and efficacy of primary stenting using sirolimus-eluting stents (SES) in Japanese patients with ST-segment elevation myocardial infarction (STEMI) [1,2]. However, the safety and efficacy of paclitaxel-eluting stents (PES), drug-eluting stents (DES) approved for clinical use in Japan in May 2007, for STEMI patients are not well characterized in Japan. Therefore, it is important to compare the safety and efficacy of PES in the treatment of STEMI, including high-risk STEMI, to those of SES. This is particularly important for patients in Japan, where the incidence of cardiac events, such as stent thrombosis (ST) [3], is lower than that in western countries [1,4–6].

The benefits of late reperfusion (12–48 h after MI onset) have been established in clinical and experimental trials [7]. However, the safety and efficacy of DES use for the treatment of patients with STEMI patients presented within 48 h after MI onset have not been fully examined in Japan [8]. Further, the impact of late reperfusion by percutaneous coronary intervention (PCI) for STEMI patients, including asymptomatic patients and those with stable hemodynamic states, remains debatable [7–9].

Therefore, we retrospectively examined the mid-term post-discharge clinical and angiographic outcomes of 357 consecutive STEMI patients presenting within 48 h and treated with either PES or SES in a clinical setting. We compared the incidences of (A) post-discharge cardiac events, including cardiac death and nonfatal recurrent MI (re-MI), as the safety endpoints and (B) angiographic binary in-stent restenosis [more than 50% diameter stenosis (DS) in the follow-up angiogram (fu CAG)] as the efficacy endpoint.

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## 2. Methods

### 2.1. Population

The rationale of the almost unrestricted use of DESs, including their use in STEMI patients, has been previously reported [1,4,6]. From February 2007 to February 2009, the period prior to the approval of PES (TAXUS Liberte) for clinical use in Japan, 169 patients presenting within 48 h of their first STEMI and without prior coronary artery bypass grafts (CABG) were treated using PES; 198 were treated with SES, and 25 were treated with bare-metal stents. DESs were used in 93.6% of the cases. The incidence of in-hospital mortality after PES placement ($n = 6$, 3.6%) did not significantly differ from that after SES placement ($n = 4$, 2.0%) ($p = 0.37$). Of the 10 cases of in-hospital mortality, 6 deaths were due to cardiogenic shock and severe congestive heart failure (Killip class 3–4, defined below), 2 were caused by cardiac rupture, and 2 were caused by pneumonia. None of the cases matched the criteria for ST as defined by the Academic Research Consortium [3]. In May 2011, the clinical and angiographic outcomes in patients who were alive at discharge after treatment with PES ($n = 163$) were compared with those of patients who underwent treatment with SES ($n = 194$), as in our previous report [1]. Angiographic outcomes in the fu CAG until May 2011 were included. An additional fu CAG was planned approximately 10–18 months after stent placement and was performed in 75.5% (123/163) of PES patients and 75.8% (147/194) of SES patients (no significant difference). All patients were encouraged to undergo optimal medical therapy according to the guidelines for the management and prevention of secondary MI (Table 1), as outlined by the Japanese Circulation Society [10].

### 2.2. Procedures for stenting and antiplatelet therapy

The device used to restore coronary flow was selected based on the doctor's discretion. Therefore, this was a non-randomized study. Stents were implanted to cover the entire baseline lesion, and implantation was performed under the guidance of intravascular ultrasonography (IVUS-guide). When additional stent dilation was needed, high-pressure ballooning using a non-compliant balloon was performed. Because lesions after STEMI may develop due to slow or no reflow, a distal protection method using the PercuSurge GuardWire® (Medtronic, Santa Rosa, CA, USA) device in combination with a thrombosuction catheter was preferred.

Peri-procedural antiplatelet therapy was administered, as previously reported [1,4,6]. At the emergency care unit, before performing PCI, aspirin (162–200 mg) and ticlopidine (200 mg) were immediately administered orally. Although these prescriptions were not prospectively randomized, ticlopidine was prescribed for about 1 year in accordance with the recommended guidelines. Cilostazol (200–300 mg/day) or clopidogrel (75 mg/day) were administered at the doctor's discretion if ticlopidine administration showed adverse effects.

### 2.3. Follow-up angiography and quantitative coronary artery angiography

The time points at which fu CAG was performed are provided above. The quantitative coronary artery angiography (QCA) parameters were measured using the test circulatory system cardiovascular network system, as described previously [1,8]; their values were obtained at 3 points: before PCI (pre-procedural); immediately after successful PCI (post-procedural); and during the chronic phase (follow-up) (CAAS II system; Pie Medical, Maastricht, The Netherlands). The minimal lumen diameter (MLD), %DS, reference diameter, and lesion length were also measured. In cases showing occlusion thrombolysis in myocardial infarction (TIMI) grade 0–1 flow, pre-procedural MLD was considered as 0, and %DS was considered as 100. In addition, acute luminal gain (post-procedural MLD minus pre-procedural MLD) and late luminal loss (post-procedural MLD minus MLD during the chronic phase) were calculated. Binary in-stent restenosis (binary restenosis) was defined as %DS of <50% during the chronic phase. Target lesion revascularization (TLR) observed on the fu CAG was defined as elective or emergency repeated PCI or CABG, including in-stent restonosis, performed at the 5-mm proximal and distal stent margins [11]. The need for TLR was determined based on visual angiographic outcomes. The percentage of severe restenosis (%DS ≥ 70%) was estimated.

**Table 1**
Baseline characteristics of 357 patients who underwent primary stenting with PES or SES and were alive at discharge.

| | PES | SES | *p*-Value |
|---|---|---|---|
| *n* | 163 | 194 | |
| Age (years) | 64.1 ± 11.9 | 65.7 ± 11.2 | 0.190 |
| Male gender (%) | 82.8 | 79.4 | 0.410 |
| Diabetes (%) | 38.0 | 34.0 | 0.430 |
| Cardiac dysfunction (%) | 17.2 | 27.8 | 0.036 |
| Elapsed time ≤ 12 h (%) | 85.9 | 84.9 | 0.720 |
| Killip classification | 1.27 ± 0.76 | 1.34 ± 0.78 | 0.390 |
| First TIMI-grade 2–3 flow (%) | 35.0 | 35.1 | 0.990 |
| Rentrop grade 2–3 (%) | 19.0 | 17.5 | 0.720 |
| Single-vessel disease (%) | 40.5 | 52.1 | 0.029 |
| LAD (%) | 42.9 | 52.1 | 0.085 |
| RCA (%) | 47.2 | 33.0 | <0.01 |
| Calcification (%) | 6.1 | 3.6 | 0.260 |
| Bifurcation (%) | 42.9 | 36.6 | 0.220 |
| Thrombus (%) | 19.6 | 10.8 | 0.020 |
| Number of stents | 1.44 ± 0.65 | 1.30 ± 0.48 | 0.023 |
| Diameter of stent (mm) | 3.27 ± 0.43 | 3.32 ± 0.48 | 0.300 |
| Length of stent (mm) | 35.0 ± 16.4 | 32.2 ± 14.6 | 0.100 |
| Maximum pressure (atm) | 18.0 ± 2.9 | 19.1 ± 2.7 | <0.001 |
| IVUS use (atm) | 96.3 | 97.4 | 0.550 |
| Distal protection (%) | 71.2 | 74.2 | 0.520 |
| Thrombectomy (%) | 74.2 | 74.2 | 1.000 |
| Final TIMI-grade 2–3 flow (%) | 96.9 | 99.5 | 0.060 |
| Pre-procedure | | | |
| MLD (mm) | 0.337 ± 0.464 | 0.336 ± 0.506 | 0.980 |
| % Diameter stenosis | 87.9 ± 15.9 | 88.0 ± 17.8 | 0.960 |
| Post-procedure | | | |
| MLD (mm) | 2.58 ± 0.459 | 2.57 ± 0.457 | 0.840 |
| % Diameter stenosis | 13.6 ± 9.4 | 12.8 ± 9.4 | 0.420 |
| Reference diameter (mm) | 3.00 ± 0.569 | 2.97 ± 0.569 | 0.620 |
| Acute gain (mm) | 2.23 ± 0.635 | 2.23 ± 0.621 | 1.000 |
| Medication at discharge | | | |
| β-Blocker (%) | 80.4 | 78.9 | 0.730 |
| ACE-I/ARB (%) | 85.9 | 91.8 | 0.077 |
| Statin (%) | 87.7 | 87.6 | 0.980 |
| Total endpoint (*n*, %) | 1, 0.6 | 3, 1.5 | 0.400 |
| Cardiac death (*n*, %) | 1, 0.6 | 3, 1.5 | 0.400 |
| Non-fatal re-MI (*n*, %) | 0 | 0 | |
| Post-discharge observation duration (days) | 1170 ± 243 | 1148 ± 283 | 0.430 |

Variables related to patients, clinical condition, lesions, procedure, medication at discharge, and endpoint are shown. Definitions of abbreviations are provided in the text.

### 2.4. Endpoints

The safety endpoints of the clinical outcomes were (A) post-discharge events including death and excluding definite non-cardiac death and nonfatal re-MI. The efficacy endpoint of the angiographic outcome was (B) the incidence of binary restenosis (defined above).

### 2.5. Estimated variables

The variables used as baseline characteristics (patient data, clinical characteristics, lesion characteristics, and procedure at discharge) were defined as follows: age (age at stenting); male gender; diabetes (patients with diabetes mellitus); elapsed time within 12 h (if the interval between STEMI onset and hospital arrival was within 12 h); Killip classification; cardiac dysfunction (ejection fraction of left ventricle less than 40% as evaluated by ultrasonography or left ventriculogram); first TIMI grade 2–3 flow (TIMI-grade 2 or 3 flow at the first angiogram); Rentrop grade 2–3 (Rentrop grade 2 or 3 for collateral flow); single-vessel disease (only 1 diseased vessel of the native coronary artery); location of the culprit lesion in the left anterior descending artery (LAD) and right coronary artery (RCA); calcification (calcified lesions estimated using an angiogram and IVUS); bifurcation (bifurcative lesions requiring any treatment of the side branch); thrombus (thrombus-containing lesion); number of stents (number of implanted stents per lesion); diameter of stents (maximum diameter of the balloon used to dilate the stent); length of stent (length of the stented segment, calculated by adding the lengths of each stent regardless of overlap); maximum pressure (maximum pressure at the maximum diameter of the inflated balloon); IVUS use (availability of IVUS during PCI); distal protection (lesions treated with the PercuSurge GuardWire device or filter wire); thrombectomy (performing thrombectomy using any thrombosuction catheter); final TIMI grade 2–3 flow (post-procedural TIMI grade 2 or 3 flow); post-discharge observational period (duration in days monitored after discharge); medications at discharge: β-blocker (beta-adrenergic blockers); ACE-I/ARB (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers); statins (HMG-CoA reductase inhibitors). The lesion location, calcification, bifurcation, and thrombus variables were defined according to the American College of Cardiology/American Heart Association classification of lesions.

### 2.6. Statistics

Baseline characteristics were expressed as mean ± standard deviation (SD). The PES and SES group variables (at both baseline and angiographic follow-up) were compared using unpaired *t*-tests for continuous values and $\chi^2$ tests or Fisher's exact tests for categorical values. The present study compared the safety and efficacy between SES and PES. Therefore, the following steps were performed in order to create a multivariate model: (a) clinical and angiographic variables were compared between endpoint-positive and endpoint-negative groups, and *p*-values for each comparison were calculated using $\chi^2$ test, Fisher's exact test, or *t* test (univariate analysis). (b) Multivariate analysis for predicting adverse safety and efficacy endpoints was performed; stent type (PES) was included as an independent variable, and other variables found to be significant in the univariate analysis were added. The Cox proportional hazard model was used by only including 1 variable (PES) in order to analyze the predictors of post-discharge events, because there were no significant differences between the patients with and without cardiac events in terms of baseline or lesion characteristics. Predictors of binary restenosis were analyzed using a logistic regression analysis by including 7 variables (first TIMI-grade 2–3 flow, calcification, PES, number of stents, length of stent, pre-procedural MLD, and pre-procedural %DS) (Table 4). In order to compare the properties of PES and SES, the predictors of binary in-stent restenosis were individually analyzed in the PES and SES groups, as described above. A *p*-value less than 0.05 was considered statistically significant. Stata for Windows version 8 (StataCorp, College Station, TX, USA) was used for statistical analysis.

## 3. Results

### 3.1. Baseline characteristics of patients who were alive at discharge

Table 1 shows the baseline characteristics of patients receiving primary stenting with PES ($n = 163$) and SES ($n = 194$). The percentages of cardiac dysfunction, single-vessel disease, RCA lesions, thrombus, number of stents, and maximum pressure significantly differed between the PES and SES groups. Baseline QCA, percentage of primary endpoints, and the post-discharge observational duration did not significantly differ between the groups.

### 3.2. Predictors of primary endpoint after discharge

When the baseline characteristics of patients who had cardiac events ($n = 4$) were compared with those without cardiac events after discharge ($n = 353$), there were no significant differences between the groups in terms of baseline or lesion characteristics (data not shown). Four patients died due to severe congestive heart failure without ST [3].

Using the Cox proportional hazard model, PES was not found to be related to post-discharge endpoints (hazard ratio, 0.346; 95% CI, 0.036–3.371; $p = 0.361$).

### 3.3. Baseline characteristics of patients and angiographic outcomes in fu CAG

Table 2 shows the baseline characteristics of patients in fu CAG and the results from the serial QCA after performing fu CAG. The percentage of single-vessel disease, mean number of stents, and maximum pressure were significantly different between the PES ($n = 123$) and SES ($n = 147$) groups. In addition, 3 variables from the follow-up QCA data significantly differed between the groups. There was significantly greater late luminal loss in the PES group than in the SES group. The incidences of binary restenosis, severe restenosis, and TLR were significantly higher in the PES group than in the SES group.

### 3.4. Baseline characteristics and angiographic outcomes of patients with and without binary restenosis

Table 3 shows the baseline characteristics of patients in fu CAG and the results from the serial QCA after performing fu CAG. The percentage of first TIMI-grade 2–3 flow, calcification, PES, mean number of stents, and mean length of stents were significantly different between those with binary restenosis ($n = 28$) and those without binary restenosis ($n = 242$). Two pre-procedural variables, 4 follow-up QCA variables, and late luminal loss differed significantly between the groups. The incidences of binary restenosis, severe restenosis, and TLR and the mean angiographic follow-up duration significantly differed between those with and without binary restenosis.

### 3.5. Predictors of binary restenosis after treatment with PES or SES for STEMI presenting within 48 h of onset

Table 4 shows the predictors of binary restenosis, which were identified using a logistic regression analysis. In the multivariate analysis, PES was the single predictor of binary restenosis in 270 STEMI patients after performing primary stenting with PES or SES. The length of the stent, calcification, pre-procedural %DS, number of stents, first TIMI-grade 2–3 flow, and pre-procedural MLD were not significant predictors of binary restenosis.

**Table 2**
Baseline characteristics and serial quantitative coronary angiography findings after follow-up secondary angiography in 270 patients who underwent primary stenting with PES or SES.

| | PES | SES | *p*-Value |
|---|---|---|---|
| *n* | 123 | 147 | |
| Age (years) | 62.9 ± 10.8 | 64.2 ± 10.2 | 0.310 |
| Male gender (%) | 87.0 | 81.0 | 0.180 |
| Diabetes (%) | 42.3 | 34.7 | 0.200 |
| Cardiac dysfunction (%) | 18.7 | 27.9 | 0.077 |
| Elapsed time ≤ 12 h (%) | 85.9 | 84.9 | 0.620 |
| Killip classification 3–4 (%) | 8.9 | 6.8 | 0.510 |
| First TIMI-grade 2–3 flow (%) | 35.0 | 29.9 | 0.378 |
| Rentrop grade 2–3 (%) | 19.5 | 21.1 | 0.748 |
| Single-vessel disease (%) | 43.1 | 57.1 | 0.021 |
| LAD (%) | 46.3 | 53.7 | 0.230 |
| RCA (%) | 43.9 | 32.7 | 0.058 |
| Calcification (%) | 5.7 | 2.0 | 0.110 |
| Bifurcation (%) | 43.9 | 36.1 | 0.190 |
| Thrombus (%) | 18.7 | 12.9 | 0.190 |
| Number of stents | 1.50 ± 0.65 | 1.32 ± 0.54 | 0.014 |
| Diameter of stent (mm) | 3.27 ± 0.41 | 3.33 ± 0.48 | 0.270 |
| Length of stent (mm) | 36.3 ± 17.3 | 32.8 ± 15.0 | 0.080 |
| Maximum pressure (atm) | 18.2 ± 2.9 | 19.2 ± 2.5 | <0.01 |
| IVUS use (atm) | 95.9 | 98.0 | 0.329 |
| Distal protection (%) | 71.5 | 77.6 | 0.260 |
| Thrombectomy (%) | 76.4 | 78.2 | 0.730 |
| Final TIMI-grade 2–3 flow (%) | 97.6 | 99.3 | 0.220 |
| Pre-procedure | | | |
| MLD (mm) | 0.334 ± 0.471 | 0.283 ± 0.471 | 0.380 |
| % Diameter stenosis | 88.4 ± 15.6 | 90.2 ± 15.8 | 0.350 |
| Post-procedure | | | |
| MLD (mm) | 2.58 ± 0.457 | 2.58 ± 0.446 | 1.000 |
| % Diameter stenosis | 14.5 ± 9.7 | 12.7 ± 9.1 | 0.120 |
| Reference diameter (mm) | 3.03 ± 0.553 | 2.97 ± 0.553 | 0.370 |
| Follow-up | | | |
| MLD (mm) | 2.19 ± 0.820 | 2.48 ± 0.652 | <0.01 |
| % Diameter stenosis | 29.2 ± 21.7 | 22.0 ± 15.2 | <0.01 |
| Reference diameter (mm) | 3.07 ± 0.563 | 3.17 ± 0.554 | 0.140 |
| Lesion length (mm) | 6.13 ± 4.02 | 5.10 ± 3.59 | 0.028 |
| Acute gain (mm) | 2.24 ± 0.616 | 2.29 ± 0.595 | 0.499 |
| Late luminal loss (mm) | 0.382 ± 0.789 | 0.094 ± 0.513 | <0.001 |
| Medication at discharge | | | |
| β-Blocker (%) | 82.9 | 85.7 | 0.530 |
| ACE-I/ARB (%) | 91.9 | 93.2 | 0.680 |
| Statin (%) | 93.5 | 92.5 | 0.750 |
| Binary restenosis (%) | 17.1 | 4.8 | <0.001 |
| Follow-up %DS ≥ 70 (%) | 7.3 | 2.0 | 0.036 |
| TLR (%) | 18.7 | 6.8 | <0.01 |
| Angiographic follow-up duration (days) | 432± 221 | 430± 211 | 0.940 |

Variables related to patients, clinical condition, lesions, and procedure, and the angiographic outcomes are shown. Definitions of abbreviations are provided in the text.

### 3.6. Individual predictors of binary restenosis after treatment with PES or SES for STEMI presenting within 48 h of onset

In a univariate analysis, in the PES group, the percentage of diabetes (61.9%), first TIMI-grade 2–3 flow (14.3%), the mean number of stents (2.05 ± 0.865), the mean length of stents (50.7 ± 20.3 mm), pre-procedural MLD (0.098 ± 0.257 mm), and pre-procedural %DS (96.4 ± 9.8) in the binary restenosis ($n = 21$) group were significantly different from those without binary restenosis (38.2%, 39.2%, 1.39 ± 0.616, 33.3 ± 15.2 mm, 0.382 ± 0.491 mm, and 86.7 ± 16.1) ($n = 102$) ($p < 0.05$, <0.05, <0.001, <0.001, <0.001, and <0.001, respectively).

In the SES group, the percentage of calcification (14.3%), the mean number of stents (1.86 ± 0.69), the mean length of stents (51.3 ± 21.9 mm), and IVUS use (71.4%) in the binary restenosis ($n = 7$) group were significantly different from those (1.4%, 1.29 ± 0.52, 31.9 ± 14.0 mm, and 99.3%) without binary restenosis ($n = 140$) ($p < 0.05$, <0.05, <0.05, and <0.001, respectively).

**Table 3**
Baseline characteristics and serial quantitative coronary angiography findings after follow-up secondary angiography of patients with or without binary restenosis after underwent primary stenting with PES or SES.

| | Binary restenosis | No binary restenosis | *p*-Value |
|---|---|---|---|
| *n* | 28 | 242 | |
| Age (years) | 63.4 ± 9.52 | 63.6 ± 10.6 | 0.917 |
| Male gender (%) | 85.7 | 83.5 | 0.761 |
| Diabetes (%) | 53.6 | 36.4 | 0.076 |
| Cardiac dysfunction (%) | 32.1 | 22.7 | 0.267 |
| Elapsed time ≤ 12 h (%) | 75.0 | 86.0 | 0.126 |
| Killip classification 3–4 (%) | 7.1 | 7.9 | 0.895 |
| First TIMI-grade 2–3 flow (%) | 14.3 | 34.3 | 0.032 |
| Rentrop grade 2–3 (%) | 25.0 | 19.8 | 0.521 |
| Single-vessel disease (%) | 39.3 | 52.1 | 0.200 |
| LAD (%) | 53.6 | 50.0 | 0.720 |
| RCA (%) | 32.1 | 38.4 | 0.516 |
| Calcification (%) | 10.7 | 2.9 | 0.038 |
| Bifurcation (%) | 42.9 | 39.3 | 0.712 |
| Thrombus (%) | 25.0 | 14.5 | 0.145 |
| PES (%) | 75.0 | 42.1 | <0.001 |
| Number of stents | 2.00 ± 0.816 | 1.34 ± 0.561 | <0.001 |
| Diameter of stent (mm) | 3.19 ± 0.488 | 3.31 ± 0.444 | 0.214 |
| Length of stent (mm) | 50.8 ± 20.3 | 32.5 ± 14.5 | <0.001 |
| Maximum pressure (atm) | 18.2 ± 2.79 | 18.8 ± 2.76 | 0.281 |
| IVUS use (atm) | 92.9 | 97.5 | 0.168 |
| Distal protection (%) | 85.7 | 73.6 | 0.160 |
| Thrombectomy (%) | 78.6 | 77.3 | 0.876 |
| Final TIMI-grade 2–3 flow (%) | 96.4 | 98.8 | 0.334 |
| Pre-procedure | | | |
| MLD (mm) | 0.100 ± 0.257 | 0.330 ± 0.484 | <0.001 |
| % Diameter stenosis | 96.3 ± 9.80 | 88.5 ± 16.0 | <0.001 |
| Post-procedure | | | |
| MLD (mm) | 2.55 ± 0.442 | 2.56 ± 0.452 | 0.910 |
| % Diameter stenosis | 15.0 ± 9.54 | 13.4 ± 9.38 | 0.394 |
| Reference diameter (mm) | 3.02 ± 0.501 | 3.00 ± 0.559 | 0.843 |
| Follow-up | | | |
| MLD (mm) | 0.879 ± 0.523 | 2.52 ± 0.557 | <0.001 |
| % Diameter stenosis | 70.4 ± 16.7 | 20.1 ± 9.89 | <0.001 |
| Reference diameter (mm) | 2.90 ± 0.438 | 3.15 ± 0.567 | <0.01 |
| Lesion length (mm) | 8.30 ± 3.47 | 5.30 ± 3.75 | <0.001 |
| Acute gain (mm) | 2.45 ± 0.525 | 2.25 ± 0.610 | 0.061 |
| Late luminal loss (mm) | 1.67 ± 0.579 | 0.058 ± 0.434 | <0.001 |
| Medication at discharge | | | |
| β-Blocker (%) | 96.4 | 83.1 | 0.065 |
| ACE-I/ARB (%) | 89.3 | 93.0 | 0.480 |
| Statin (%) | 96.4 | 92.6 | 0.449 |
| Binary restenosis (%) | 100.0 | 0.0 | <0.001 |
| Follow-up %DS ≥ 70 (%) | 42.9 | 0 | <0.001 |
| TLR (%) | 89.3 | 3.3 | <0.001 |
| Angiographic follow-up duration (days) | 328± 126 | 443± 221 | <0.001 |

Variables related to patients, clinical condition, lesions, and procedure, and the angiographic outcomes are shown. Definitions of abbreviations are provided in the text.

**Table 4**
Predictors of binary restenosis.

| | Odds ratio | 95% CI | | *p*-Value |
|---|---|---|---|---|
| | | Lower limb | Upper limb | |
| PES | 3.892 | 1.470 | 10.30 | <0.01 |
| Length of stent | 1.048 | 0.991 | 1.108 | 0.102 |
| Calcification | 2.301 | 0.479 | 11.05 | 0.298 |
| Pre-procedure % diameter stenosis | 1.049 | 0.877 | 1.255 | 0.600 |
| Number of stents | 1.225 | 0.289 | 5.185 | 0.783 |
| First TIMI-grade 2–3 flow | 1.165 | 0.141 | 9.607 | 0.888 |
| Pre-procedure MLD | 0.751 | 0.002 | 360.1 | 0.928 |

Predictors of binary restenosis analyzed using logistic regression analysis are shown. PES was an independent predictor of binary restenosis. Definitions of abbreviations are provided in the text.

**Table 5**
Predictors of binary restenosis after treatment with (A) PES and (B) SES.

| | Odds ratio | 95% CI | | *p*-Value |
|---|---|---|---|---|
| | | Lower limb | Upper limb | |
| (A) PES | | | | |
| Diabetes | 2.384 | 0.795 | 7.15 | 0.121 |
| Length of stent | 1.030 | 0.965 | 1.100 | 0.377 |
| Pre-procedure % diameter stenosis | 1.090 | 0.838 | 1.419 | 0.521 |
| Number of stents | 1.651 | 0.313 | 8.715 | 0.555 |
| First TIMI-grade 2–3 flow | 1.804 | 0.073 | 44.60 | 0.719 |
| Acute gain | 1.107 | 0.309 | 3.966 | 0.876 |
| Pre-procedure MLD | 1.217 | 0.000 | 11167 | 0.966 |
| (B) SES | | | | |
| Calcification | 28.54 | 1.609 | 505.9 | 0.022 |
| IVUS use | 0.048 | 0.003 | 0.901 | 0.042 |
| Length of stent | 1.143 | 0.977 | 1.337 | 0.094 |
| Number of stents | 0.082 | 0.001 | 6.437 | 0.261 |

Predictors of binary restenosis analyzed using logistic regression analysis are shown respectively in (A) PES and (B) SES groups. In the PES groups, there were no significant predictors of binary restenosis. In the SES groups, 2 variables were predictors of binary restenosis. Definitions of abbreviations are provided in the text.

Table 5 shows the predictors of binary restenosis after treatment with (A) PES and (B) SES, which were identified using a logistic regression analysis. In the multivariate analysis in (A), there was no significant predictor of binary restenosis. In (B), both calcification and IVUS use were significant predictors of binary restenosis after treatment with SES.

## 4. Discussion

This study found favorable post-discharge clinical outcomes among Japanese patients with STEMI treated with either PES or SES within 48 h of onset. Specifically, with a mean follow-up period of more than 1100 days, the cardiac outcomes were similar to the values without definite ST [3] (Table 1). Thus, this study confirmed the mid-term safety of SES for STEMI patients in a clinical setting in Japan [1,2] and provided the first demonstration for that of PES. In contrast to the patients selected for previous prospective randomized studies [12–14], the present study included high-risk patients with complex lesion-related cardiac events, ST events, and binary restenosis, such as those with Killip 3–4 classifications [15], bifurcation [16], calcification [17], thrombus lesions [18], and longer stents [19] (Table 1). In addition, our study included patients who did not use glycoprotein IIb/IIIa inhibitors [20], up to 40% diabetic patients [21], and a relatively high percentage of cardiac dysfunction [22], factors that are representative of the daily practice environment in Japan. Thus, we demonstrated the mid-term safety of primary stenting using first-generation DESs (SES and PES) for STEMI patients presenting within 12 h of onset in Japan [1,2] and the feasibility of late reperfusion for STEMI patients treated 12–48 h of onset in a daily practice environment. Further long-term observation should be continued to clarify the safety and efficacy of primary stenting using DES for STEMI patients in Japan [8].

The present study found that PES had inferior angiographic outcomes compared to SES in STEMI patients (Tables 2 and 4). The magnitude of late luminal loss in the PES group was approximately 4 times greater than that in the SES group, although the periprocedural QCA data did not significantly differ (Table 2). In addition, the risk for binary restenosis was approximately 4 times higher in those treated with PES (Table 4). This is consistent with a report showing that SES had superior angiographic outcomes than PES in STEMI patients [23]. Additional reports have shown statistical equivalency in terms of binary restenosis and clinical target lesion revascularization between PES and SES for the treatment of de novo stable lesions [24,25]. This intergroup discrepancy in the angiographic efficacy for de novo stable lesions and causal lesions of STEMI may be a result of differences in the stents' properties. First, sirolimus has a potent anti-restenotic effect for biologically active lesions, such as the causal lesion of STEMI. Second, SES uses a closed-cell based platform, allowing better diffusion of the drug into the remodeling vessel compared to the open-cell based platform of PES [24,26]. Although our multivariate analysis did not identify significant predictors of binary in-stent restenosis using PES, PES was disadvantageous for low pre-procedural TIMI-flow, high pre-procedural %DS, and low MLD at primary reperfusion therapy [Table 5(A)]. The present study indicates that SES is preferred for primary stenting of STEMI patients compared to PES, except for lesions with severe calcification and in cases where IVUS cannot be used [Table 5(B)]. Thus, the disadvantages of first-generation DESs (SES and PES) for primary PCI of STEMI patients need to be examined in the second-generation DESs.

The present study had several limitations. First, this was a retrospective, non-randomized, and single-center analysis. A few variables, such as LAD and RCA lesions, left ventricular dysfunction, thrombus, and number of stents, significantly differed between the PES group and the SES group (Table 1). However, none of these variables was related to safety or efficacy endpoints (Table 4). Second, although this cohort included late-reperfused STEMI patients, who comprised approximately 15% of the group (Table 1), the safety of late reperfusion should be confirmed in a larger cohort. Third, the duration of dual antiplatelet therapy was based on the doctor's judgment according to a recent report [27]. The number of patients that discontinued medical therapy, including dual antiplatelet therapy, was not fully examined. However, there was no increase in the number of post-discharge events or definite ST events (Table 1). Fourth, other consistent predictors for cardiac events in STEMI patients, such as renal dysfunction and anemia, were not fully assessed.

## 5. Conclusions

The mid-term (mean interval, 1100–1200 days) safety of PES for Japanese STEMI patients that presented within 48 h of onset in a clinical practice setting was favorable, with a survival rate statistically equivalent to that of SES. However, PES was consistently inferior to SES in the angiographic outcomes of STEMI cases.

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