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Long-term Clinical and Angiographic Outcomes after Primary Stenting for ST Segment Elevation Myocardial Infarction Using a Paclitaxel-Eluting Stent : A Propensity Score-Matched Comparison with Bare-Metal Stents

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ABSTRACT

Objective : The long-term outcomes after primary stenting for patients with ST segment elevation myocardial infarction (STEMI) with paclitaxel-eluting stents (PESs : composed of TAXUS Express and TAXUS Liberte) in Japan where severe cardiac events are infrequent were compared with those for bare-metal stents (BMSs).

Methods : This retrospective, nonrandomized, single-center study was conducted in October 2013. STEMI patients treated with primary stenting using PESs (n=238) and BMSs (n=171) between September 2004 and December 2011 were enrolled. Baseline variables were adjusted using a propensity score-matched analysis.

Results : Among 194 baseline-adjusted patients who produced similar mean maximum balloon sizes (BMS, 3.51±0.46 mm ; PES, 3.51±0.41 mm ; p=0.993), the incidence of the clinical endpoint comprising cardiac death, nonfatal recurrent myocardial infarction, and definite stent thrombosis was not significantly different after PES placement (5.2% ; mean follow-up, 1,378±576 days) or after BMS placement (7.2% ; 1,120±576 days) (p=0.564). In 156 baseline-adjusted patients, the incidence of the angiographic endpoint (binary in-stent restenosis : % diameter stenosis >50% on secondary angiography) was significantly lower after PES placement (12.8% ; mean follow-up, 413±220 days) than after BMS placement (28.2%, 236±88 days) (p=0.019). PES was the only predictor of binary in-stent restenosis (odds ratio : 0.31, 95% confidence interval [CI] : 0.12-0.80, p=0.015).

Conclusion : The present study is the first to show the long-term equivalent clinical safety with superior angiographic outcomes of PES compared with BMS for primary stenting in Japanese daily clinical practice, although the balloon size was large. (Jikeikai Med J 2014 ; 61 : 77-86)

Key words : Paclitaxel-eluting stent, Primary stenting, Stent thrombosis, Cardiac mortality, Binary restenosis

INTRODUCTION

Drug-eluting stents (DESs) provide greater angiographic efficacy than bare-metal stents (BMSs) when used for primary stenting in patients with ST segment elevation myocardial infarction (STEMI). Their benefits include reduction in the incidence of binary in-stent restenosis, target lesion revascularization (TLR), and target vessel revascularization (TVR) without an increase in clinical safety concerns, such as very late stent thrombosis (VLST)[1]. The

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guidelines of the European Society of Cardiology (ESC) (2012) state that if a patient with STEMI has no contraindications to prolonged dual anti-platelet therapy (DAPT) and is likely to be compliant, a DES should be used for primary stenting instead of a BMS[2]. This issue has been reported for STEMI patients treated with sirolimus-eluting stents (SESs : Cypher Bx Velocity ; Cordis Corp., Miami, FL, USA) in Japan[3-6] and in Western countries[7,8]. The angiographic efficacy of the paclitaxel-eluting stent (PES : TAXUS Express and TAXUS Liberte ; Boston Sci., USA), another widely used first-generation DES, compared with that of the BMS for primary stenting in STEMI patients, is controversial according to the PASSION[9] and HORIZONS-AMI trials[10]. In addition, although SESs and PESs showed similar efficacies in electively treating stable stenosis[11], PESs had a disadvantageous angiographic impact compared to SESs in emergently treating unstable STEMI culprit lesions[12,13]. Furthermore, PESs potentially increased the incidences of re-infarction and VLST after placement in patients with STEMI[14]. The long-term outcomes of PESs in primary stenting for STEMI have not yet been compared with those of BMSs in Japan, and the guidelines of the Japanese Society of Cardiology (JSC) (2013) recommends that they be clarified[15].

In the present study, we examined whether primary stenting using a PES for STEMI patients in a daily clinical environment was associated with better angiographic outcomes than a BMS, and if it was without long-term clinical safety concerns. Despite the current second-generation DES era, the long-term outcomes of PESs need to be clarified owing to the numerous daily outpatients. For this purpose, in this study, the long-term clinical and angiographic outcomes of PESs after primary stenting in 238 STEMI patients were compared with those of 171 BMS-treated STEMI patients by adjusting for baseline values using a propensity score matching analysis[16].

METHODS

Study design

This was a retrospective, nonrandomized, single-center study conducted at Saitama Cardiovascular Respiratory Center. The rationale was approved by the local ethics committee in March 2011. The retrospective examination was performed with the permission of the ethics committee, and the clinical follow-up was ascertained by hospital visit, phone, and letter in October 2013. The following were not prospectively randomized : stent selection (DES or BMS, after SES approval was obtained in August 2004) ; reperfusion methods used to achieve thrombolysis in myocardial infarction (TIMI) grade 3 flow, such as distal protection methods and thrombosuction using thrombectomy catheters to prevent the development of slow- or no-reflow phenomena ; the duration of thienopyridine agent administration ; assignment to follow-up angiography (fu-CAG) ; and drugs administered for secondary prevention[17]. All patients were informed of the intensive therapy of STEMI, including reperfusion, and consent was obtained from patients and/or their families in the Emergency Department.

Population

As previously reported, between September 2004 and December 2011, 980 STEMI patients, presenting within 12 h after onset, without prior coronary artery bypass grafts (CABGs), were treated with primary stenting at our institution[18]. Of these, 207 patients were treated using BMSs, whereas 773 received DESs. Thirty-six BMS-treated STEMI patients were excluded for the following definite clinical reasons : malignancy or need for examination of malignancy ($n=16$), anemia ($n=9$), preoperative state ($n=5$), gastrointestinal disease ($n=4$), and gastrointestinal bleeding ($n=2$). The details related to the number of STEMI patients treated by DESs and the tendency to use BMSs for large vessels were described previously[18]. In brief, 128 STEMI patients received TAXUS Express stents (Boston Scientific, Natick, MA, USA) and 110 received TAXUS Liberte stents (Boston Scientific, Natick, MA, USA). Thus, 409 STEMI patients were enrolled after primary stenting of native coronary culprit lesions with either PESs ($n=238$; between February 2007 and December 2011) or BMSs ($n=171$; between September 2004 and December 2011).

Antiplatelet therapy

Periprocedural antiplatelet therapy was administered as previously reported[3,4,12]. In the emergency care unit, aspirin (162-200 mg) and ticlopidine (200 mg) or clopidogrel (300 mg) were administered orally immediately before primary percutaneous coronary intervention (PCI). After the

procedure, ticlopidine (200 mg/day) or clopidogrel (75 mg/day) was prescribed for at least 2 weeks in the BMS group and for 12 weeks in the PES group according to the physician's discretion.

Endpoints

As the safety endpoint of the clinical outcomes, the primary endpoint was the cardiac event composite of death without definite noncardiac death (in-hospital mortality and post-discharge mortality), nonfatal recurrent myocardial infarction (nonfatal re-MI), and definite stent thrombosis (ST) as defined by the Academic Research Consortium (ARC)[19]. All-cause death was an additional clinical outcome of interest.

As the efficacy endpoint of the angiographic outcome, the secondary endpoint was the incidence of binary in-stent restenosis (defined below). A TLR observed on fu-CAG was defined as an elective emergency repeated PCI or CABG performed for in-stent restenosis, including both the 5 mm proximal and distal stent margins as well as definite ST. The need for TLR was determined based on visual angiographic outcomes, as in our previous reports[11].

Quantitative coronary artery angiography (QCA)

Fu-CAG was planned at approximately 6 to 12 months after BMS placement and 10 to 18 months after PES placement. The number of patients alive at discharge was 159 in the BMS group and 230 in the PES group (Table 3). Therefore, the percentages of patients undergoing fu-CAG in the BMS and PES groups were 73.0% (116 of 159) and 68.7% (158 of 230, $p=0.365$), respectively.

The QCA parameters were measured using the TCS cardiovascular network systems (CAAS-2 and -5 systems, Netherlands), as described previously[11]. Values were obtained at three points : before PCI (preprocedural), immediately after successful PCI (postprocedural), and in the chronic phase (follow-up). The minimal lumen diameter (MLD), % diameter stenosis (%DS), reference diameter (RD), and lesion length were measured. In addition, acute gain (postprocedural MLD minus preprocedural MLD) and late luminal loss (postprocedural MLD minus follow-up MLD) were calculated. Binary in-stent restenosis (binary restenosis) was defined as a %DS of >50% at fu-CAG. In occluded lesions, %DS was defined as 100 and the MLD was defined as 0.

Statistical Analyses

Baseline characteristic variables are expressed as the mean±standard deviation (SD). Variables and endpoints in the BMS group were compared with those in the PES group using unpaired t-tests for continuous values and χ^2 or Fisher's tests for categorical values. Since the present study was a retrospective historical comparison, a propensity score matching analysis was performed to adjust the baseline values between the two groups[16]. The caliper widths for the adjustment in Tables 2 and 4 were 0.01 and 0.01, respectively. After baseline adjustment, cumulative clinical endpoint-free ratios in the BMS and PES groups were analyzed by constructing Kaplan-Meier curves and were compared using the log-rank test. In addition, a Cox proportional hazard model was used to assess predictors of the primary endpoint. Logistic regression analysis was used to assess predictors of the secondary endpoint after the baseline adjustment. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using the Stata for Windows Version 13 software (StataCorp, College Station, TX, USA).

Results

Baseline characteristics and incidences of the clinical outcomes

Table 1 shows the baseline characteristics of patients in the BMS group ($n=171$) and the PES group ($n=238$). Baseline variables that differed significantly between groups included the percentages of single vessel disease, cardiac dysfunction, Killip class 3-4, left anterior descending (LAD), and left circumflex artery (LCx), as well as the mean serum creatinine (Cr) level at presentation, number of stents, stent diameter, stent length, maximum pressure, post-procedural MLD, post-procedural RD, and acute gain.

The incidences of the primary endpoint, all-cause death, nonfatal re-MI, and total definite stent thrombosis, as well as the mean clinical observational duration differed significantly between the groups.

Adjusted baseline characteristics and incidences of the primary endpoint

Table 2 shows the adjusted baseline characteristics of patients in the BMS and PES groups ($n=97$ in each arm). The incidence of the primary endpoint was not significantly

Table 1. Patients' baseline characteristics and incidences of the clinical endpoint

(*n*)	BMS 171	PES 238	*p*-value
Age (yr)	65.9±13.3	66.0±12.2	0.938
Male sex (%)	80.0	81.5	0.723
Serum Ht at presentation	41.8±6.3	42.1±4.6	0.596
Serum LDH at presentation	294±183	306±186	0.516
Serum Cr at presentation	1.08±1.22	0.89±0.35	0.048
Diabetes (%)	42.7	39.1	0.463
Single vessel disease (%)	59.1	44.1	0.003
Cardiac dysfunction (%)	31.6	19.3	0.004
Killip classification 3–4 (%)	23.4	10.9	0.001
LAD (%)	55.0	39.5	0.002
LCx (%)	6.4	17.2	0.001
RCA (%)	36.3	42.4	0.208
First TIMI grade flow 0–1 (%)	69.6	62.2	0.121
Rentrop grade 0–1 (%)	81.3	83.6	0.540
Severe calcification (%)	7.0	5.5	0.517
Massive thrombus (%)	15.2	15.5	0.925
IVUS guide (%)	96.5	98.3	0.238
Number of stents	1.16±0.47	1.37±0.60	<0.001
Diameter of stent (mm)	3.70±0.60	3.31±0.42	<0.001
Length of stent (mm)	27.8±13.1	36.5±17.8	<0.001
Maximum pressure (atm)	17.4±3.35	18.2±2.67	0.010
Final TIMI grade flow 2–3 (%)	94.2	96.6	0.227
Serum peak CK-MB	385±306	345±348	0.218
Pre-procedural MLD (mm)	0.29±0.49	0.31±0.43	0.668
Pre-procedural %DS	90.4±15.1	88.6±15.0	0.233
Post-procedural MLD (mm)	2.80±0.59	2.53±0.48	<0.001
Post-procedural %DS	10.8±8.9	12.7±11.1	0.055
Post-procedural RD (mm)	3.16±0.60	2.92±0.55	<0.001
Acute gain (mm)	2.48±0.78	2.19±0.67	<0.001
Clinical observational duration (day)	1,038±558	1,431±575	<0.001
Primary endpoint (%)	10.5	3.4	0.003
In-hospital mortality (%)	7.0	3.4	0.091
All-cause death (%)	8.8	4.6	0.090
Cardiac death (%)	4.7	2.5	0.237
Nonfatal reccurent myocardial infarction (%)	1.8	0.0	0.040
Definite stent thrombosis (%)	1.8	0.0	0.040
Early definite stent thrombosis (%)	0.6	0.0	0.238
Late definite stent thrombosis (%)	1.2	0.0	0.094
Very late definite stent thrombosis (%)	0.0	0.0	1.000

The baseline characteristics and incidences of the clinical endpoint in the BMS (n=171) and PES groups (n=238) were compared. The variables used as baseline characteristics, particularly the patient, angiographic, and procedural characteristics, and QCA were as follows: age at primary stenting; male sexresults of the blood sample analyses obtained at presentation as follows: serum hematocrit (Ht) count, and levels of creatinine (Cr), creatine kinase isoenzyme (CK-MB); diabetes mellitus status; single vessel disease; cardiac dysfunction (left ventricle ejection fraction of less than 40 as evaluated on ultrasonography, left ventriculography, or scintigraphy); Killip classification grade 3 or 4; culprit lesion located in the left anterior descending artery (LAD), left circumflex artery (LCx), right coronary artery (RCA); TIMI flow grade 0 or 1 on the first angiogram; Rentrop grade 0 or 1 for the collateral flow; severe calcification (estimated using an angiogram and IVUS); massive thrombus (the previous 3 variables were defined according to the ACC/AHA classification of lesions); IVUS guide (IVUS availability during PCI); final TIMI flow grade 2 or 3 (postprocedural); number of stent (number of implanted stents per lesion); diameter of stent (the maximum diameter of the balloon used to dilate the stent); length of stent (stent length calculated by adding the length of each stent, regardless of overlap); maximum pressure (maximum pressure at the maximum inflation diameter of the balloon); peak serum myocardial CK-MB (serum peak CK-MB) measured every 3 hours after primary stenting, and clinical observational duration (the clinical observational duration from presentation until the observation period). The others variables are described in the text.

Table 2. Adjusted baseline characteristics and incidences of the clinical endpoint

(*n*)	BMS 97	PES 97	*p*-value
Age (yr)	65.7±12.9	64.6±13.6	0.723
Male sex (%)	79.4	78.4	0.862
Serum Ht at presentation	42.4±5.2	41.8±4.8	0.237
Serum LDH at presentation	294±143	302±178	0.658
Serum Cr at presentation	0.88±0.25	0.93±0.38	0.762
Diabetes (%)	40.2	38.1	0.746
Single vessel disease (%)	54.6	55.7	0.889
Cardiac dysfunction (%)	25.8	35.1	0.170
Killip classification 3-4 (%)	14.4	19.6	0.369
LAD (%)	52.6	51.5	0.889
LCx (%)	8.2	6.2	0.527
RCA (%)	37.1	42.3	0.456
First TIMI grade flow 0-1 (%)	71.1	68.0	0.612
Rentrop grade 0-1 (%)	78.4	72.2	0.330
Severe calcification (%)	4.1	6.2	0.527
Massive thrombus (%)	10.3	13.4	0.491
IVUS guide (%)	95.9	100.0	0.157
Number of stents	1.21±0.52	1.23±0.47	0.532
Diameter of stent (mm)	3.51±0.46	3.51±0.41	0.993
Length of stent (mm)	29.5±13.7	31.8±14.3	0.336
Final TIMI grade flow 2-3 (%)	97.9	97.9	1.000
Serum peak CK-MB	406±313	392±450	0.354
Pre-procedural MLD (mm)	0.29±0.48	0.29±0.42	0.678
Pre-procedural %DS	90.2±15.4	88.9±15.7	0.558
Post-procedural MLD (mm)	2.67±0.52	2.65±0.46	0.790
Post-procedural %DS	10.9±8.8	11.4±11.0	0.890
Post-procedural RD (mm)	3.03±0.52	3.02±0.58	0.845
Acute gain (mm)	2.38±0.72	2.36±0.69	0.535
Clinical observational duration (day)	1,120±576	1,378±576	< 0.001
Primary endpoint (%)	7.2	5.2	0.564
In-hospital mortality (%)	5.2	5.2	1.000
All-cause death (%)	6.2	6.2	1.000
Cardiac death (%)	3.1	2.1	0.655
Nonfatal reccurent myocardial infarction (%)	1.0	0.0	0.317
Definite stent thrombosis (%)	1.0	0.0	0.317
Early definite stent thrombosis (%)	0.0	0.0	1.000
Late definite stent thrombosis (%)	1.0	0.0	0.317
Very late definite stent thrombosis (%)	0.0	0.0	1.000

The adjusted baseline characteristics and incidences of the clinical endpoint in the BMS and PES groups (n=97 each) were compared. The variables are described in the text and Table 1.

different between the groups. The mean clinical observational duration (not adjusted) differed significantly between the groups.

Predictors of primary endpoint after baseline adjustment

Cumulative primary endpoint-free ratios in the BMS and PES groups were not significantly different (n=97 in each arm, p=0.53) (Fig. 1).

In the Cox proportional hazard analysis, Killip class 3-4 (hazard ratio [HR] : 80.8, 95% confidential interval [95% CI], 1.49-4379, p=0.031), post-procedural %DS (HR : 2.91, 95% CI, 1.06-8.01, p=0.039), severe calcification (HR : 56.7, 95% CI, 1.16-2779, p=0.042), and serum peak-creatinine kinase (CK)-myoglobin (MB) level (HR : 1.00, 95% CI, 1.00-1.01, p=0.042) were predictors of the primary endpoint. PES was not significantly related to the primary endpoint (HR : 1.13 ; 95% CI, 0.08-16.2, p=0.929).

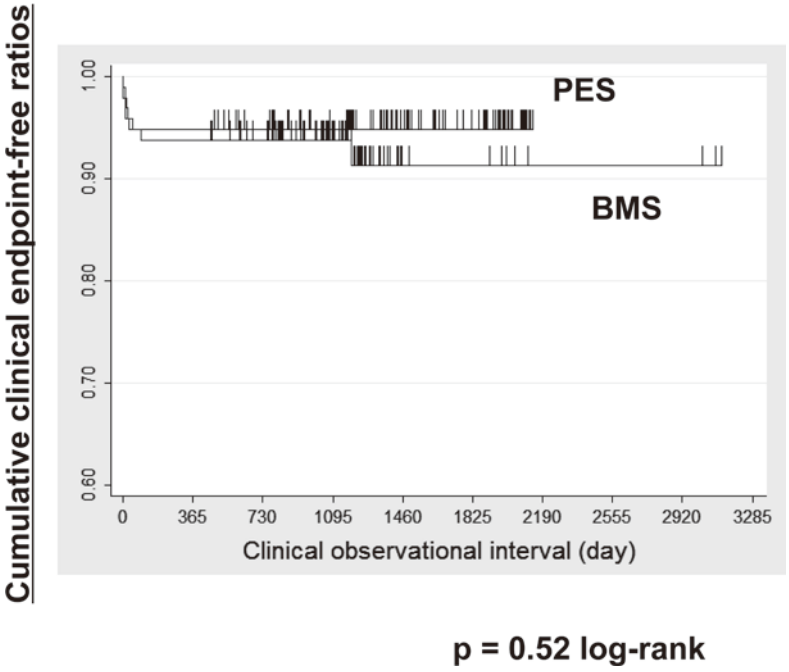

Fig. 1. Cumulative primary endpoint-free ratios
The log-rank test reveals that the cumulative primary endpoint-free ratio in the PES group compared to that in the BMS group is not significantly different.

Baseline characteristics and incidences of the secondary endpoint in patients who underwent fu-CAG

Table 3 shows the baseline characteristics of patients who underwent fu-CAG in the BMS group ($n=116$) and the PES group ($n=158$). All three post-procedural parameters, both follow-up parameters, acute gain and late luminal loss, and the angiographic follow-up duration all differed significantly between the BMS and PES groups. The proportion of patients who experienced the secondary endpoint was significantly lower in the BMS group than in the PES group.

Adjusted baseline characteristics and incidence of the secondary endpoint

Table 4 shows the adjusted baseline characteristics and the incidence of the secondary endpoint in the BMS and SES groups ($n=78$ in each arm). The mean follow-up MLD, %DS, and late luminal loss differed significantly between the BMS and PES groups.

The incidences of the secondary endpoint and TLR were significantly higher in the BMS group than in the PES group.

Predictors of binary restenosis after baseline adjustment

In the 156-patient angiographic cohort, PES (odds ratio : 0.311, 95% CI, 0.12-0.80 ; $p=0.015$) was a significant predictor of the secondary endpoint according to the logistic regression analysis.

DISCUSSION

This was the first study conducted in Japan that compared primary stenting using PESs with BMSs for STEMI patients. The results demonstrate : 1) the long-term, clinical, statistically equivalent safety of PESs, and 2) the benefit provided by DESs in lowering the risk of binary restenosis (angiographic efficacy). As background, although this issue was consistently confirmed in patients receiving SESs[3-8], the first-approved DES in Japan, the safety and efficacy of PESs, the second-approved DES in Japan, for primary stenting in STEMI patients have not been demonstrated in Japan hitherto. The guidelines of the JSC (2013) state that due to a lack of original reports in Japan, long-term outcomes after primary stenting using DESs for patients with STEMI should be compared with those after primary stenting using BMSs[15]. In addition, the PASSION

Table 3. Baseline characteristics and the angiographic outcomes

(*n*)	BMS 116	PES 158	*p*-value
Pre-procedural MLD (mm)	0.31±0.51	0.30±0.45	0.906
Pre-procedural %DS	90.1±15.4	89.3±15.1	0.668
Post-procedural MLD (mm)	2.81±0.56	2.57±0.47	<0.001
Post-procedural %DS	10.4±8.7	12.9±10.4	0.013
Post-procedural RD (mm)	3.16±0.60	2.98±0.54	0.011
Follow-up MLD (mm)	1.83±0.85	2.17±0.74	<0.001
Follow-up %DS	36.0±24.0	26.8±20.4	<0.001
Acute gain (mm)	2.48±0.74	2.27±0.61	0.008
Late luminal loss (mm)	1.04±1.13	0.55±0.97	<0.001
Angiographic follow-up duration (days)	266±211	458±292	<0.001
Binary restenosis (%)	23.3	12.7	0.021
Target lesion revascularization (%)	24.1	15.2	0.062

The baseline characteristics and angiographic outcomes in the patients who underwent fu-CAG with BMS (n=116) or PES (n=158) were compared. In order to simplify the Table, only QCA data and the outcomes were shown. The variables are described in the text and Table 1.

Table 4. Adjusted baseline characteristics and incidences of the primary endpoint (binary restenosis)

(*n*)	BMS 78	PES 78	*p*-value
Age (yr)	62.5±11.5	63.7±13.4	0.520
Male gender (%)	84.6	91.0	0.225
Serum Cr at presentation	0.84±0.23	0.88±0.36	0.546
Diabetes (%)	41.0	38.5	0.732
LAD (%)	60.3	62.8	0.694
LCx (%)	6.4	6.4	1.000
RCA (%)	33.3	30.8	0.715
First TIMI grade flow 0-1 (%)	73.1	66.7	0.336
Rentrop grade 0-1 (%)	75.6	78.2	0.695
Severe calcification (%)	2.6	1.3	0.564
Massive thrombus (%)	15.4	14.1	0.808
IVUS guide (%)	94.9	97.4	1.000
Number of stents	1.24±0.56	1.24±0.46	0.643
Diameter of stent (mm)	3.58±0.45	3.57±0.40	0.753
Length of stent (mm)	30.8±15.4	31.9±11.3	0.166
Final TIMI grade flow 2-3 (%)	97.4	100.0	0.157
Serum peak CK-MB	389±292	356±286	0.542
Pre-procedural MLD (mm)	0.24±0.42	0.20±0.34	0.870
Pre-procedural %DS	90.9±15.4	92.9±11.6	0.758
Post-procedural MLD (mm)	2.69±0.54	2.76±0.40	0.537
Post-procedural %DS	10.4±8.6	9.4±8.6	0.447
Post-procedural RD (mm)	3.03±0.52	3.07±0.55	0.860
Follow-up MLD (mm)	1.67±0.73	2.34±0.80	<0.001
Follow-up %DS	38.2±22.9	26.1±19.8	0.003
Acute gain (mm)	2.45±0.70	2.55±0.56	0.430
Late luminal loss (mm)	1.08±1.09	0.62±1.04	0.003
Angiographic follow-up duration (days)	236±88	413±220	<0.001
Binary restenosis (%)	28.2	12.8	0.019
Target lesion revascularization (%)	29.5	14.1	0.014

The adjusted baseline characteristics and incidences of the primary endpoint in the BMS and PES groups (n=78 each) were compared. The variables are described in the text and Table 1.

trials did not find an advantage of PESs over BMSs in STEMI patients in terms of TLR at 1[9] and 5[20] years. In contrast, in the TYPHOON studies[8,21], SESs showed superior angiographic outcomes compared to BMSs. Higher risks of binary in-stent restenosis and TLR have been reported after PES placement in STEMI patients compared with those after SES placement[12,13]. Finally, in a meta-analysis from Western countries, the incidences of re-infarction and stent thrombosis at >1 year of primary stenting with PESs were significantly increased compared with those after BMSs[14]. Therefore, although PESs are not currently available, their long-term clinical safety and angiographic efficacy for primary stenting in STEMI had to be evaluated in comparison with BMSs in Japan, where the incidence of severe cardiac events, including stent thrombosis, is lower than that in the West[4,22,23]. To the best of our knowledge, the present study was the first to show the long-term statistically equivalent safety without definite stent thrombosis and the significantly better angiographic efficacy of PESs in primary stenting for STEMI patients compared to BMSs placed largely under the guidance of intravascular ultrasound (IVUS) in the present DES era.

DESs have shown consistent clinical non-inferior safety with angiographic efficacy in the primary stenting of STEMI patients compared to BMSs[1]. However, in this DES era, BMSs have been used for primary stenting during emergency procedures in the following three STEMI groups : 1) Patients for whom there was a concern regarding the duration of thienopyridine (DAPT) treatment owing to a definite and/or suspicious clinical diagnosis (excluded in the present study)[2] ; 2) Similar to the previous category, patients with potential provisional problems necessitating DAPT cessation during intense clinical treatment ; and 3) Patients with lower risks for binary restenosis and TLR, such as those with large vessels (large reference diameter and large-sized balloon inflation under the guidance of IVUS)[24,25]. The present baseline characteristics in the BMS group reflected these concepts : the large mean stent diameter (3.70 mm) (2,3), the close to 1 (1.16) mean number of stents used in the culprit lesion[26] (2, 3), the higher proportions of patients with single vessel disease (approximately 60%) (2), and the higher proportions of patients with cardiac dysfunction (approximately 30%) and Killip classification 3-4 (approximately 1/4) (2) (Table 1). Thus, in these patients undergoing primary stenting in the present DES era, the baseline variables in the BMS group were significantly different than those in the PES group (Table 1). Therefore, a propensity score-matched analysis was used to adjust the baseline values to estimate the effects of the treatments where potential bias may exist[16]. Both the unadjusted (Table 1) and adjusted (Table 2) baseline values in the present study better reflected the clinical setting by including patients at higher risk for cardiac events and binary restenosis than those enrolled in previous prospective randomized studies[7-10,20], such as those with higher incidences of diabetes (38% vs. 31%)[20], cardiac dysfunction (35%), and Killip classification 3-4 (19.6%), and those with higher mean peak CK-MB levels (392 IU/dL) and stent length (31.8 mm vs. 19 mm)[20] (Table 2). Despite the multiple baseline disadvantages, the cardiac mortality rate following primary stenting (5.2% in 97 baseline-adjusted STEMI patients over approximately 4 years) (Table 2) was not higher than that previously reported by randomized studies (6.9% in 155 STEMI patients treated using SESs during 5 years in the SEAMI trial[7], 7.6% in 355 STEMI patients treated by SESs during 4 years in the TYPHOON study[8], >15.0% in 310 STEMI patients treated by PESs during 5 years in the PASSION trial)[20]. In contrast with the former meta-analysis[14], definite stent thrombosis was not observed in the present small PES group (Tables 1 and 2). The incidences of severe cardiac events in the PES group were not significantly different from those in the BMS group (Table 2), and PES was not associated with the primary endpoint. Therefore, the clinical outcomes of the present STEMI cohort undergoing primary stenting using PESs in a clinical setting were considered acceptable. In addition, the present study demonstrated the long-term safety of primary stenting using PESs in Japan, where most stents were placed under the guidance of IVUS. Further long-term outcomes should be examined because the timing of VLST was different after DES and BMS implantation[27].

The present study is also the first to confirm, by adjusting baseline values, the better angiographic outcomes of PESs in primary stenting compared to those after BMS placement in Japan (Tables 3, 4). DESs could be beneficial over BMSs for reducing the incidences of binary in-stent restenosis and TLR, particularly in complex lesions such as those in STEMI patients[28,29]. The mean late luminal loss observed after PES placement in STEMI patients (0.62 mm) (Table 4) was higher than the 0.40 to 0.50 range re-

ported in a previous study on PES use for patients receiving all-comer elective treatment[11]. This reflects the complexity of the present STEMI culprit lesions. Therefore, in this study, the angiographic outcomes differed between the STEMI patients treated with PESs and BMSs in a daily clinical setting, although the adjusted mean postprocedural reference diameter (approximately 3.0–3.1 mm) and the mean balloon size (approximately 3.6 mm) resulted in lower risks of binary restenosis and TLR with BMS[24,25] (Table 4). Therefore, although the present study examined whether BMSs for large vessels might offset the advantage of PESs for primary stenting[24,25], PESs showed superior angiographic outcomes compared to BMSs, which was consistent with the results of the HORIZONS-AMI study[10]. The impact of the short stent length of BMSs for primary stenting in STEMI patients is worthy of examination[26] to further clarify the benefit of BMSs for primary stenting.

The present retrospective, nonrandomized, single-center analysis had several limitations. First, there remained confounders and bias, although the representative baselines related to the treated stents were adjusted using a propensity score matching analysis, as shown in Tables 2 and 4. Second, a much larger trial, such as the HORIZONS-AMI study[10], is needed to demonstrate statistical significance, particularly regarding the frequency of definite stent thrombosis. Third, the selection of stents, such as BMSs, PESs, or other DESs, and the selection of treatment with PCI or CABG were not prospectively randomized. The duration of DAPT as well as other predictors of long-term clinical outcomes were not fully examined.

Conclusion

The present single-center retrospective study showed that, compared with BMSs placed largely under IVUS guidance, PESs were associated with long-term safety without definite stent thrombosis and with angiographic efficacy in primary stenting for STEMI patients in Japanese daily clinical practice.

Authors have no conflict of interest.

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