Two-Year Follow-up of Sirolimus-Eluting Stents versus Paclitaxel-Eluting Stents in Acute Myocardial Infarction

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Int J Angiol 2012;21:53–58.

Abstract

It has been shown that drug-eluting stents (DESs) significantly reduce restenosis rate when compared with bare-metal stents in a broad range of patients with coronary artery disease. However, current data are limited about the efficacy of different DESs in treatment of ST segment elevation myocardial infarction (STEMI). The aim of this study was to compare the effectiveness and safety of sirolimus-eluting stents (SESs) with paclitaxel-eluting stents (PESs) in primary percutaneous coronary intervention. We retrospectively examined 127 STEMI patients who underwent primary percutaneous coronary intervention. PES group consisted of 79 patients and SES group consisted of 48 patients. Patients were analyzed for major adverse cardiac events (MACE) and stent thrombosis (ST). The mean follow-up period was 2 years. The mean age was 53 ± 11 years in the SES group and 59 ± 11 years in the PES group ($p = 0.03$). Baseline and procedural characteristics were similar in the two groups except stent lengths, which was longer in the SES group. Two-year MACE rates were 8.3% in the SES group and 16.4% in the PES group ($p = 0.28$). Rates for ST for SES and PES groups were as follows: early ST was 2.08 versus 2.53%; late ST was 2.08 versus 2.53%; and very late ST was 2.08 versus 2.53% ($p > 0.05$). There were no statistically significant differences in MACE and ST rates between the SES and PES groups in the 2-year follow-up period. High ST rates detected in our study need to be clarified with future prospective and randomized clinical trials.

Keywords
- sirolimus
- paclitaxel
- percutaneous coronary intervention
- myocardial infarction

The benefit of primary pecutaneous coronary intervention (PCI) using stents has been proved with numerous studies in ST segment elevation myocardial infarction (STEMI).[1,2] It has been shown that drug-eluting stents (DESs) significantly reduce restenosis and repeated interventions compared with bare metal stents in de novo noncomplex coronary lesions.[3–5] However, thrombotic state of STEMI raises some concerns over the incidence of stent thrombosis (ST) using DESs. Two recently published trials showed the safety and efficacy of paclitaxel-eluting stents (PESs) and sirolimus-eluting stents (SESs) in treatment of STEMI.[6,7] But clinical trials comparing different DESs in the treatment of STEMI are very limited. Here we report single-center real-world experience with 2 years of clinical outcomes in STEMI patients, comparing the results of PESs and SESs.

Methods

Patient Selection

This study was retrospective, single-center analysis of 127 consecutive STEMI patients who were treated with PESs (79 patients) and SESs (48 patients) between February 2004 and July 2007. All patients with STEMI including cardiogenic shock were included into the study. Use of SESs, PESs, and glycoprotein IIb/IIIa inhibitors was left to the operator's discretion. Stenting of the target lesion was performed using

DOI http://dx.doi.org/10.1055/s-0032-1302436.
ISSN 1061-1711.

standard interventional techniques, without routinely dilating stent after implantation. All patients received standard pharmacological therapy including unfractionated heparin, aspirin, and clopidogrel. Aspirin (80 to 300 mg/d) was maintained indefinitely and clopidogrel (75 mg/d) was prescribed for a minimum duration of 6 months.

Definitions and End Points

Patients were analyzed for ST and major adverse cardiac events (MACE) by using office follow-up charts and telephone interviews. Follow-up period began with in-hospital period and extended up to 2 years. MACE was defined as death, repeat myocardial infarction (MI) (STEMI and non-ST elevation myocardial infarction [NSTEMI]), target lesion revascularization, and target vessel revascularization. MI was defined as presence of at least two of the followings: ischemic symptoms, new electrocardiographic changes compatible with ischemia, and raised creatinine kinase-MB levels >3 times the upper limit of normal. Target lesion revascularization was defined as a repeat intervention (surgical or percutaneous) to treat luminal stenosis within the stent or proximal or distal 5-mm edge segments. Target vessel revascularization was defined as repeat surgical or percutaneous intervention driven by any lesion located in previously treated vessel. ST was defined as definite and probable according to the Academic Research Consortium.[8]

Statistical Analysis

Continuous variables were presented as mean $\pm$ 1 standard deviation. Yates chi-square or Fisher exact test was used to compare the groups on qualitative variables (comparison of two proportions). Unpaired Student *t* test or Mann-Whitney U-test was performed for group comparison with continuous, nonparametric, or parametric variables. All statistical analyses were performed using Instat (Instat V3.05 2000, GraphPad Software, San Diego, CA). For all analyses, a two-tailed $p < 0.05$ was considered statistically significant.

Results

The mean age was 53 ± 11 years in the SES group and 59 ± 11 years in the PES group ($p = 0.03$). There were no difference between the two groups in cardiovascular risk profile and cardiac history (►**Table 1**). Stent length was 26.2 ± 6.4 mm in the SES group and 21.7 ± 7.4 mm in the PES group and the

Table 1 Baseline Characteristics of the Study Groups

Characteristics	SES Group ($n = 48$)	PES Group ($n = 79$)	*p* Value
Age, year	53 ± 12	59 ± 12	0.034
Male sex	42 (87)	64 (81)	0.47
Family history	6 (13)	17(21)	0.29
Hyperlipidemia	32 (67)	56 (71)	0.76
Hypertension	25 (52)	51 (64)	0.22
Diabetes mellitus	12 (25)	21 (26)	0.84
Cigarette smoking	16 (33)	36 (45)	0.24
Cardiogenic shock	3 (6.2)	5 (6.3)	1.00
Cardiac history			
Previous MI	3 (6)	9 (11)	0.53
Previous PCI	3(6)	7(9)	0.74
Previous coronary artery bypass graft surgery	1 (2)	4 (5)	1.00
Coronary artery disease			
1 vessel	29 (61)	47 (59)	0.91
2 vessels	16(33)	19(24)	0.35
3 vessels	3 (6)	13 (17)	0.16
Target vessel			
Left anterior descending	28(58)	44 (56)	0.85
Right coronary artery	16 (34)	26 (33)	1.00
Circumflex artery	4 (8)	9 (11)	0.80
Symptom to angioplasty time-minute[a]	185 (110–360)	180 (60–360)	0.72

Note: Values are mean $\pm$ SD or *n* (%).
[a]Expressed as median (interquartile range).
SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2 Procedural Characteristics of the Study Groups

Characteristics	SES Group ($n = 48$)	PES Group ($n = 79$)	p Value
No. of stents implanted	1.2 ± 0.4	1.3 ± 0.5	0.27
Total length of stent (mm)	26.2 ± 6.4	21.7 ± 7.4	0.0004
Maximal size of stent (mm)	3.1 ± 0.3	3.1 ± 0.3	0.89
Maximal pressure (atm)	15.8 ± 3.9	15.7 ± 3.4	0.88
Tirofiban use – no.(%)	28 (58)	51 (49)	0.42
TIMI flow before PCI – no.(%)			
Grade 0–1	39 (81)	64 (81)	0.98
Grade 2–3	9 (19)	15 (19)	0.97
TIMI flow after PCI – no.(%)			
Grade 0–1	2 (4)	4 (5)	1.00
Grade 2–3	46 (96)	75 (95)	0.81
Peak CK level (U/L)	1990 ± 1750	2160 ± 1710	0.63
Peak CK-MB level (U/L)	218 ± 176	263 ± 217	0.29
Duration of clopidogrel treatment (mo)	9 ± 3.1	8.7 ± 3	0.64

Note: Values are mean ± SD or *n* (%).
SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary intervention; CK, creatinine kinase.

difference was statistically significant ($p = 0.0004$). Other procedural characteristics including thromboysis in myocardial infarction flow grades before and after PCI were not different in SES and PES groups (►**Table 2**). In-hospital death rates were 2.08% in the SES group and 2.53% in the PES group ($p = 1.00$). Two-year MACE rates were 8.3% in the SES group and 16.4% in the PES group ($p = 0.28$) (►**Table 3**). The individual components of MACE in patients with SES versus PES group were as follows: death, 6.25 versus 6.32% ($p = 1.00$); target lesion revascularization 2.08 versus 7.59% ($p = 0.25$); target vessel revascularization 0 versus 1.26% ($p = 1.00$); MI 6.25 versus 7.59% ($p = 1.00$); and ST 6.25 versus 7.59% ($p = 1.00$). Rates for early, late, and very late ST for SES and PES groups were as follows: early ST was 2.08 versus 2.53%; late ST was 2.08 versus 2.53%; and very late ST was 2.08 versus 2.53% ($p > 0.05$ for all comparisons).

Table 3 Clinical Outcomes at 2 Years in the Study Groups

Outcome	SES Group ($n = 48$)	PES Group ($n = 79$)	p Value
Death – no.(%)	3 (6.25)	5 (6.32)	1.00
TLR – no.(%)	1 (2.08)	6 (7.59)	0.25
TVR – no.(%)	1 (2.08)	7 (8.86)	0.25
MI – no.(%)	3 (6.25)	6 (7.59)	1.00
ST – no.(%)	3 (6.25)	6 (7.59)	1.00
Acute	0 (0)	1 (1.26)	1.00
Subacute	1 (2.08)	1 (1.26)	1.00
Late	1 (2.08)	2 (2.53)	1.00
Very late	1 (2.08)	2 (2.53)	1.00
Angiographically proven ST – no.(%)	1 (2.08)	4 (5.06)	0.64
MACE – no.(%)	4 (8.3)	13 (16.4)	0.28

SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; TLR, target lesion revascularization; TVR, target vessel revascularization; MI, myocardial infarction; ST, stent thrombosis; MACE, major adverse cardiac events.

Discussion

In this study we compared the efficacy of SES and PES in real-world patients with acute STEMI undergoing primary PCI. There were no significant differences between the two stents regarding the incidence of 2-year MACE (8.3% in SES vs. 16.4% in PES; $p = 0.28$) and ST rates (6.25% in SES, 7.59% in PES; $p = 1.0$). Recent prospective trials which compared bare-metal stents with DESs in primary PCI showed superiority of DESs in terms of target vessel revascularization with similar rates of death, reinfarction, and ST.[7,9,10] TYPHOON and PASSION trials were large randomized clinical trials which investigate the safety and effectiveness of DESs in primary PCI.[7,8] The SES arm of TYPHOON and PES arm of PASSION study showed that 1-year MACE rates were 7.3 and 8.8% respectively.[7,8] There were also several published studies that compared SES with PES in elective patients. In SIRTAX trial 1012 stable and unstable patients are treated with SES and PES.[11] At the end of the study, investigators found fewer MACE after SES implantation, primarily by decreasing rates of clinical and angiographic restenosis.

Galløe et al compared SES with PES in broad range of patients including STEMI, NSTEMI, unstable angina pectoris, and stable angina.[12] In this randomized trial, there were no significant differences in clinical outcomes between patients receiving SES and PES. However, data from the comparison of the different DES type in primary PCI are very limited. The PROSIT trial randomized 308 patients with STEMI to SES and PES.[13] There were no differences regarding primary end points (death, reinfarction, ST, and target lesion revascularization) between two stents in 12-month follow-up (5.8% in SES vs. 11.7% in PES; $p > 0.05$). The results of that study were also consistent with our findings. T-SEARCH and RESEARCH registries compared SES and PES in different clinical situations including STEMI.[14] In the relatively small subgroup analysis the incidence of MACE was similar between SES and PES groups. ZEST-AMI trial compared the effectiveness of zotarilimus-eluting stent, SES, and PES in primary PCI patients.[15] This multicenter, prospective, and randomized trial included 328 STEMI patients. At 12 months, cumulative incidence rates of MACE between zotarilimus-eluting stent, SES, and PES groups were not different from each other.[15]

The rate of ST in our study (definite and probable according to Academic Research Consortium criteria) was 6.25% in the SES group and 7.59% in the PES group at 2 years. This rate was much higher than the previously reported rates of ST in large meta-analyses, which showed rates of cumulative ST to be 1.5% for SES and 1.8% for PES at 4 years.[16] It was also higher than 1.3% reported ST rate for the PES group in PROSIT trial.[13] In SES arm of TYPHOON trial ST rate at 1 year was 3.4% and in PES group in HORIZON-AMI trial ST rate at 1 year was 3.2%.[7,17] The difference between ST rates may be due to several reasons. First, the STEMI itself is an independent predictor of ST. In the report by Romano et al, ST rate at 2 years was 3.2% in real-world STEMI patients treated with DES which was higher than previous trial of DES that included only elective cases[18] (ST rate ranged from 0 to 1.1%). Second, the high rate of ST in our study may be related with patient characteristics, as 10% of our patients were in shock; in-hospital thrombotic rates and mortality was higher than previous randomized trials. Similarly, recent report of real-world patients showed 5.1% ST (definite and probable) at 6 months which was very high.[19] Third, the definition of ST may differ between trials. Some studies defined ST as angiographic documentation of thrombus in stented vessel. But this definition did not include Academic Research Consortium defined probable ST. Angiographic documentation of thrombus in the present study was 2.08% in the SES group and 5.06% in the PES group. Fourth, almost all currently available trials have provided relatively short-term data (<12 months) which did not reflect the incidence of very late ST (>1 year). In our trial very late ST rates were 2.08% in the SES group and 2.53% in the PES group, so high ST rates may be related with the 2-year follow-up period of our study. But at the end it is hard to draw clear conclusion regarding ST from such a small number of patients and bigger trials are needed to clarify this issue.

The most important limitations of our study were retrospective design, small sample size, and the lack of multivariable statistical analysis.

Conclusion

The present trial showed that in patients with STEMI who were undergoing primary PCI, SES and PES had similar outcomes in a 2-year follow-up period. The reason for high ST rates in our study need to be investigated with further prospective and randomized clinical trials.

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