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Original article

The Japanese experience with sirolimus-eluting stent implantation in the infarct-related artery: Five years of observation from the J-PMS study

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ABSTRACT

Background: Long-term outcome and safety concerns regarding drug-eluting stents (DES) for acute myocardial infarction (AMI) treatment is still debated.
Methods and results: We analyzed data from 1937 patients with complete 5-year follow-up (94.5%) from a multicenter registry of sirolimus-eluting stents (J-PMS). The patients were divided into 2 groups: AMI ($n = 133$) and non-AMI ($n = 1804$) by clinical presentation of index procedure, and compared the outcomes. At 5-year follow-up, there were no significant differences in major adverse cardiac events (MACE), death, MI, or stent thrombosis between the groups. However, target vessel related events (TVF; revascularization, cardiac death, MI, thrombosis) were higher in the non-AMI group ($p = 0.03$). In the early phase (0–6 months), MACE and death/MI were higher in the AMI group (6.0% vs. 3.0%; $p = 0.02$ and 6.8% vs. 2.1%; $p < 0.001$). However, in the late phase (6–60 months), there was a difference in TVF between the 2 groups, with a steady increase in the non-AMI group ($p = 0.03$). Over 60% of patients with AMIs were started on dual antiplatelet therapy after stent implantation or on the same day. However, dual anti-platelet therapy duration was similar (867 ± 18 days in the AMI and 727 ± 57 days in the non-AMI group, $p = 0.5$). Frequency of bleeding was similar.
Conclusion: Five-year observation of AMI treatment using drug-eluting stent compared with non-AMI has no clinical disadvantage.

Introduction

Although most worldwide registry and meta-analysis data support the effectiveness of drug-eluting stent (DES) implantation for the treatment of acute myocardial infarction (AMI) [1–3], some conflicting results have been reported [4]. Pathological investigations claim that there are risks with DES for AMI during percutaneous coronary intervention (PCI) [5–7], but do not address the long-term safety of DES. In addition, the Japanese experience with AMI treatment using DES has not been well assessed [8]. Given this context, we investigated whether DES implantation for AMI should be discriminated from routine PCI using DES from 5 years of experience.

Methods

Patient selection

The Cypher™ Stent Japan Post-Marketing Surveillance Registry (J-PMS) is a post-marketing surveillance program mandated by the Japanese government as one of the conditions for regulatory approval. The study outline has been previously described [9,10]. Briefly, 2050 consecutive patients who underwent sirolimus-eluting stent (SES) implantation between September 2004 and September 2005 at 50 institutions representative of the clinical environment across Japan were enrolled. The indications for SES implantation were left to the discretion of each participating cardiologist. In this study, we analyzed 1937 patients with complete 5-year follow-up data (94.5% of the cohort). The patients analyzed were divided into 2 groups according to AMI status based on the clinical presentation during the index procedure. The AMI group ($n = 133$) included patients who received emergent acute infarct angioplasty ($n = 84$, 63.2%). The non-AMI group ($n = 1804$) included

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272 (15.1%) patients with on-label lesions. AMI was defined according to the criteria of each participating institution. The method used to measure the left ventricle ejection fraction (LVEF) depended on each institution. Any method of the following was available for records: echocardiography, left ventriculography, and radioisotope imaging.

In this study, we clarified the long-term clinical outcomes, including dual anti-platelet therapy (DAPT) duration after SES implantation, in the AMI and non-AMI groups. In addition, we included a specific analysis of long-term events associated with the infarct-related artery (IRA).

Data collection and outcomes

The post-marketing surveillance databases were developed by the Japanese branch of Johnson & Johnson (Warren, NJ, USA). Follow-up data were collected at 3, 8, and 12 months, and annually thereafter up to 5 years. An independent safety and efficacy evaluation committee adjudicated all reported and suspected events. The study was designed to focus on IRA failure, which corresponds to target vessel failure (TVF) in the non-AMI group. TVF was defined as cardiac death, recurrent MI, target vessel revascularization (TVR), and thrombosis associated with the IRA. Death was classified as all-cause or non-cardiac death. TVR was defined as a combination of target lesion revascularization (TLR) and revascularization remote from target lesion in the IRA territory (non-TL TVR). A major adverse cardiac event (MACE) was defined as a composite of all-cause death, MI, any TLR, and thrombosis. In this study, lesions meeting the Academic Research Consortium criteria for definite and probable stent thrombosis were considered stent thrombosis [11]. Bleeding definition was according to BARC (Bleeding Academic Research Consortium) definition: Type 2, 3, and 5 were included for this study [12].

Statistical analysis

Continuous variables are expressed as means ± standard deviation (SD) and categorical data are presented as frequencies. For comparisons between groups, the chi-square test, Fisher's exact test, or the Wilcoxon rank-sum test was used as appropriate. Time-to-event data are presented as Kaplan–Meier estimates, and values are expressed as means ± standard error of the mean (SEM). Survival analysis was performed using a log-rank test or Cox proportional hazards regression modeling with a step-wise selection process. Landmark analysis was performed to assess events occurring in different time periods. The landmark point was set at 6 months from the index procedure to avoid life-threatening conditions inherent to AMI. A p-value less than 0.05 was considered statistically significant. Statistical analyses were performed with SAS software, version 9.1.3 (SAS Institute, Cary, NC, USA).

Results

Patient and lesion characteristics

Patient characteristics of the 2 groups are shown in Table 1. A higher proportion of patients in the AMI group had LVEF < 30% ($p = 0.019$) and multi-vessel disease ($p = 0.02$), but there was a higher proportion of patients with a history of MI or previous revascularization in the non-AMI group ($p < 0.001$). Hypertension ($p = 0.04$) and dyslipidemia ($p = 0.008$) were more frequently seen in the non-AMI group, but there was a higher percentage of current smokers in the AMI group ($p < 0.001$).

Lesion characteristics are presented in Table 2.The number of de novo lesions and occluded vessels was higher in the AMI group ($p < 0.001$), but there were no significant differences in parameters

Table 1
Patient characteristics.

	AMI ($n = 133$)	Non-AMI ($n = 1804$)	P-Value
Mean age, years	66.9 ± 11.7 (133)	67.2 ± 9.7 (1804)	0.86
Age ≥ 75 years	40 (30.1)	431 (23.9)	0.12
Male sex	106 (79.7)	1358 (75.3)	0.30
LVEF < 30%	9 (8.1)	52 (3.4)	0.02
BMI, kg/m^2	24.2 ± 3.8 (132)	24.0 ± 3.2 (1799)	0.97
Previous MI	25 (18.8)	720 (39.9)	<0.001
Previous PCI	28 (21.1)	1065 (59.0)	<0.001
Previous CABG	1 (0.8)	158 (8.8)	<0.001
Diabetes	47 (35.3)	795 (44.1)	0.06
Insulin treated diabetes	9 (6.8)	189 (10.5)	0.23
Dialysis	3 (2.3)	97 (5.4)	0.15
Hypertension	82 (61.7)	1273 (70.6)	0.04
Dyslipidemia	61 (45.9)	1043 (57.8)	0.01
Peripheral vascular disease	6 (4.5)	119 (6.6)	0.46
Cerebrovascular disease	10 (7.5)	138 (7.6)	0.95
Family history of CAD	12 (9.0)	119 (6.6)	0.28
Current smoker	49 (36.8)	316 (17.5)	<0.001
Multi-vessel disease	68 (51.1)	729 (40.4)	0.02

AMI, acute myocardial infarction; LVEF, left ventricular ejection fraction; BMI, body mass index; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CAD, coronary artery disease. Values are means ± SD (n) or n (%).

Table 2
Lesion characteristics.

	AMI ($n = 133$)	Non-AMI ($n = 1804$)	P-Value
Number of lesions	147	2168	
Target vessel			0.41
RCA	40 (27.2)	666 (30.7)	0.41
LAD	73 (49.7)	943 (43.5)	0.15
LCX	27 (18.4)	476 (22.0)	0.35
LMT	7 (4.8)	83 (3.8)	0.51
ACC/AHA type B2/C	123 (86.6)	1743 (80.6)	0.08
De novo	144 (98.0)	1681 (77.5)	<0.001
In-stent restenosis	2 (1.4)	340 (15.7)	<0.001
Concentric	66 (46.8)	959 (45.5)	0.80
Mod./sev. calcification	21 (14.3)	375 (17.3)	0.43
Bifurcation	57 (38.8)	715 (33.0)	0.15
Ostial location	22 (15.0)	377 (17.4)	0.50
Total occlusion	47 (32.0)	207 (9.5)	<0.001
QCA data			
Lesion length, mm	17.4 ± 10.4	17.4 ± 10.2	0.85
Ref. diameter, mm	2.53 ± 0.58	2.57 ± 0.60	0.94
MLD			
Pre, mm	0.49 ± 0.49	0.77 ± 0.48	<0.001
Post, mm	2.29 ± 0.68	2.25 ± 0.66	0.42
% DS			
Pre, %	80.7 ± 18.3	70.6 ± 16.6	<0.001
Post, %	19.2 ± 13.2	19.0 ± 13.8	0.86
Procedural data			
Direct stenting	37 (25.2)	472 (21.8)	0.35
Rotablator usage	0 (0.0)	91 (4.2)	0.004
IVUS usage	107 (72.8)	1582 (73.0)	0.96
Maximum pressure, atm	16.0 ± 4.0 (197)	16.0 ± 3.5 (2899)	0.67
Stent diameter, mm	3.05 ± 0.36 (197)	2.99 ± 0.36 (2900)	0.03
Total stent length, mm	29.5 ± 14.1 (147)	28.7 ± 14.9 (2168)	0.25
Number of stents per patient	1.48 ± 0.74 (133)	1.60 ± 0.82 (1804)	0.10
Number of stents per lesion	1.34 ± 0.59 (147)	1.34 ± 0.60 (2168)	0.97
Post-dilatation	75 (51.0)	1002 (46.2)	0.27

AMI, acute myocardial infarction; RCA, right coronary artery; LAD, left anterior descending; LCX, left circumflex; LMT, left main trunk; ACC/AHA, American College of Cardiology/American Heart Association; Mod./Sev., moderate or severe; QCA, quantitative coronary angiography; MLD, minimal luminal diameter; % DS, percent diameter stenosis; IVUS, intravascular ultrasound. Values are means ± SD n (%).