Journal of Cardiology (2008) **51**, 189—195

ELSEVIER

JOURNAL of CARDIOLOGY
Official Journal of the Japanese College of Cardiology
www.elsevier.com/locate/jjcc

ORIGINAL ARTICLE

The efficacy of bare metal stent implantation for patients with acute myocardial infarction in the drug-eluting stent era

Hajime Fujimoto (MD)*, Susumu Tao (MD), Jun Masuda (MD), Haruo Mitani (MD), Sachiko Ito (MD), Yo Fujimoto (MD), Akiko Maehara (MD), Sugao Ishiwata (MD), Tetsu Yamaguchi (MD), Minoru Ohno (MD)

Department of Cardiovascular Center Medicine, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo 105-8470, Japan

Received 7 February 2008; accepted 21 March 2008
Available online 21 April 2008

KEYWORDS
1425 Myocardial infarction;
Treatment;
1640 Stent;
1605 Restenosis

Summary
Background: Although several trials have demonstrated the safety of drug-eluting stent (DES) implantation for acute myocardial infarction (AMI) patients, care must be exercised when DES are implanted in AMI cases because of the risk of in-stent thrombosis or adverse side effects of antiplatelet agents. On the other hand, recently, there has been much improvement in bare metal stents (BMSs), and thus, the efficacy of BMS implantation should be reevaluated.
Methods: We investigated the primary and long-term outcome of BMS implantation for AMI patients in the DES era (July 2004 to December 2006; $n = 97$ [Group 1]) and compared the results with those in the pre-DES era (January 2002 to June 2004; $n = 81$ [Group 2]), retrospectively.
Results: The most frequently used BMS in Group 1 was the Driver stent (63.9%) and in Group 2 the Duraflex stent (44.4%). Stent length and diameter were not significantly different between Group 1 and Group 2. The rates of in-stent restenosis, and target lesion revascularization were lower in Group 1 than in Group 2. Restenosis frequently occurred in small vessel lesions and in lesions that had required more than 10 atm fully to dilate the pre-dilatation balloon at the primary PCI.
Conclusions: Currently available BMSs are much more effective than old-type BMSs. However, DES implantation may be considered for small vessel diseases and lesions that need high pressure to dilate.

* Corresponding author. Tel.: +81 3 3588 1111x7185; fax: +81 3 3582 7068.
E-mail address: hafujimoto-circ@umin.ac.jp (H. Fujimoto).

0914-5087/$ — see front matter
doi:10.1016/j.jjcc.2008.03.001

Background

Many studies have shown that primary percutaneous coronary intervention (PCI) is an effective treatment for acute myocardial infarction (AMI) patients [1—5]. Especially, primary stent implantation for AMI patients improves the reperfusion rate and decreases cardiovascular events and restenosis rates following percutaneous coronary intervention [6—8]. The restenosis rates of old-type bare metal stents (BMSs) such as Palmatz-Schatz, Wiktor, and Gianturco-Rubin were reported 17—25%, respectively [9,10]. Today, drug-eluting stents (DESs) are widely used. DESs have reduced the rates of in-stent restenosis (ISR) and target lesion revascularization (TLR) compared with BMSs [11,12], Recently, two randomized studies of the safety and efficacy of DES implantation for AMI patients were published [13,14]. In one study, sirolimus-eluting stents were more efficacious than BMSs in reducing the rates of restenosis and target-vessel revascularization. In the other study, taxolimus-eluting stents were not superior to BMSs for reduction of target lesion revascularization and major cardiac events. However, while the two studies showed similarities in the results obtained with DESs (TLR rates were 5.6% and 5.3%, respectively), the results obtained for BMSs were different (TLR rates were 13.4% and 7.8%, respectively), thereby affecting the conclusions of each study. Thus it may be of value to reevaluate the efficacy of recent BMS implantation for AMI patients. Several studies have suggested that the mechanism of ISR after BMS implantation for AMI patients is different from that of patients with stable angina pectoris (AP) [13,14]. Therefore DES may not be as beneficial for AMI patients as for stable AP patients. In addition, care should be exercised for DES implantation in AMI patients because of the risk of acute, subacute, and late thrombosis after DES implantation or adverse side effects of antiplatelet agents.

In this study, we investigated the primary and long-term outcome of BMS implantation for AMI patients in the DES era by comparing the results with those in the pre-DES era, retrospectively.

Methods

Subjects

From July 2004 to December 2006, 99 patients underwent PCI in our hospital. BMSs were implanted in 97 of the 99 patients. Primary, and long-term outcomes of these 97 patients (Group 1) were compared with the results of 81 sequential AMI patients who underwent primary PCI (BMS implantation) from January 2002 to June 2004 (Group 2).

Primary end point

The primary end point was a composite of major adverse cardiac and cerebrovascular events (death from cardiac causes, myocardial infarction, and ischemia-driven TLR) within the first 12 months of follow-up. TLR was defined as revascularization for a stenosis within the stented region or within 5 mm of the distal or proximal edges of the stent.

Successful stenting was defined as a final stenosis of less than 50% of the vessel diameter after implantation of the study stent. Treatment success was defined as a final stenosis of less than 50% of the vessel diameter after any percutaneous intervention.

Quantitative coronary angiography

Coronary angiograms were digitally recorded at baseline, post procedure, and at follow-up with an automated edge-detection system (CAAS II, Pie Medical Imaging). The single projection in which a stenosis appeared to be most severe was used. A contrast-filled nontapered catheter tip was used for calibration and reference diameter was determined by interpolation. Quantitative measurements included the diameter of the reference vessel, the minimal luminal diameter, and the extent of diametric stenosis defined as [(reference vessel diameter − minimal lumen diameter)/reference vessel diameter] × 100. We defined ISR as stenosis of at least 50% of the minimal luminal diameter in the stented area and within the margins 5 mm proximal and distal to each stent edge.

Statistical analysis

Quantitative data are presented as mean ± standard deviation (S.D.) and the categorical data as frequencies (percentages). Continuous variables were compared using the unpaired *t*-test. Binary variables were compared by means of the Fisher exact test. Statistical significance was defined as p value of less than 0.05. All statistical analyses were performed using JMP 5 software (SAS Institute, Cary, NC, USA).

Table 1 Baseline patient characteristics

	Group 2: pre-DES era January 2002—June 2004 ($n=81$)	Group 1: DES era July 2004—December 2006 ($n=97$)	p
Age (year)	66.7 ± 9.9	66.8 ± 9.2	0.78
Male, *n* (%)	71 (87.7)	79 (81.4)	0.26
Hypertension, *n* (%)	45 (55.6)	57 (58.8)	0.67
Hyperlipidemia, *n* (%)	51 (63.0)	58 (59.8)	0.67
Diabetes mellitus, *n* (%)	38 (46.9)	41 (42.3)	0.54
Smoking, *n* (%)	51 (63.0)	67 (69.1)	0.39
Hyperuricemia, *n* (%)	11 (13.6)	14 (10.3)	0.87
Hemodialysis, *n* (%)	5 (6.2)	7 (7.2)	0.78
ACE-I or ARB, *n* (%)[a]	55 (67.9)	79 (81.4)	0.037
Statin, *n* (%)[a]	38 (46.9)	69 (71.1)	0.0009

[a] The percentage of the patients who had been taking or started to take statin or rennin—angiotensin system inhibitors such as angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB).

Results

Baseline and procedural characteristics

Baseline characteristics of the enrolled patients are shown in Table 1. The percentage of the patients who had been taking or started to take statin or rennin—angiotensin system inhibitors such as angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) was statistically significantly higher in Group 1 than in Group 2. Other baseline patient characteristics were not significantly different between Group 1 and Group 2.

Lesion characteristics and procedural characteristics are shown in Table 2. Lesion characteristics were not significantly different between Group 1 and Group 2. The most frequently used BMS in Group 1 was the Driver stent (63.9%) and in Group 2 it was Duraflex (44.4%) (Fig. 1). Stent length and diameter were not significantly different between in Group 1 and in Group 2.

Clinical outcome

Clinical outcomes are shown in Table 3. The ratio of major adverse cerebral and cardiac events except TLR rate was not significantly different between Group 1 and Group 2. TLR rate was significantly lower in Group 1 than in Group 2 (5.1% in Group 1 vs. 16.0% in Group 2, $p=0.016$).

Angiographic analysis

Among the 178 enrolled patients, 123 patients (68 in Group 1 and 55 in Group 2) underwent follow-up CAG. Quantitative coronary angiography (QCA) findings of the 123 patients are shown in Table 4. Although reference diameter, minimal lumen diameter (MLD), and percent diametric stenosis before and after PCI were not significantly different between Group 1 and Group 2, MLD, percent diametric stenosis, late loss and binary restenosis rate in- and distal-portion of the stents were significantly lower in Group 1 than in Group 2.

Characteristics of restenotic lesions

Among the 68 patients who underwent follow-up CAG in Group 1, in-stent restenosis occurred in 5 cases. Stent diameter was smaller in the restenosis group than non-restenosis group (Table 5). For the 4 of the 5 restenosis lesions, high pressure (more than 10 atm) was needed to fully dilate the predilatation balloon at the primary PCI. That is, it was suspected that AMI occurred by the formation of thrombus in the chronic severe stenotic lesions. The rest of the restenosis lesion was small vessel lesion with a diameter of 2.13 mm of vessel diameter.

Discussion

The major finding of this study was that implantation of currently available BMSs in AMI patient provides better outcome than old-type BMSs and the results are comparable to those of DESs. This improvement in outcome of the currently available BMSs may be due to several reasons. First, improvements in the material and structural design of the BMS may have contributed to the better results. In our study, the Driver stent was most frequently used in the DES era. There are several reports suggesting that the long-term outcome of the Driver stent is better than the outcome achieved with the old-type BMS [15,16], because of the better structure and material of the Driver stent. Next, the wide use of renin—angiotensin system inhibitors and statins in recent years may be related to the bet-

Table 2 Lesion and procedure characteristics

	Group 2: pre-DES era January 2002—June 2004 ($n=81$)	Group 1: DES era July 2004—December 2006 ($n=97$)	p
LAD, n (%)	28 (34.6)	33 (34.0)	0.94
LCX, n (%)	15 (18.5)	17 (17.5)	0.86
RCA, n (%)	36 (44.4)	45 (46.4)	0.80
LMT, n (%)	2 (2.5)	2 (2.1)	0.86
Stent length (mm)	20.3 ± 3.3	21.0 ± 5.8	0.65
Stent diameter (mm)	3.02 ± 0.41	3.12 ± 0.43	0.58
Number of stents	1.02 ± 0.16	1.03 ± 0.17	0.80

LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMT, left main trunk.

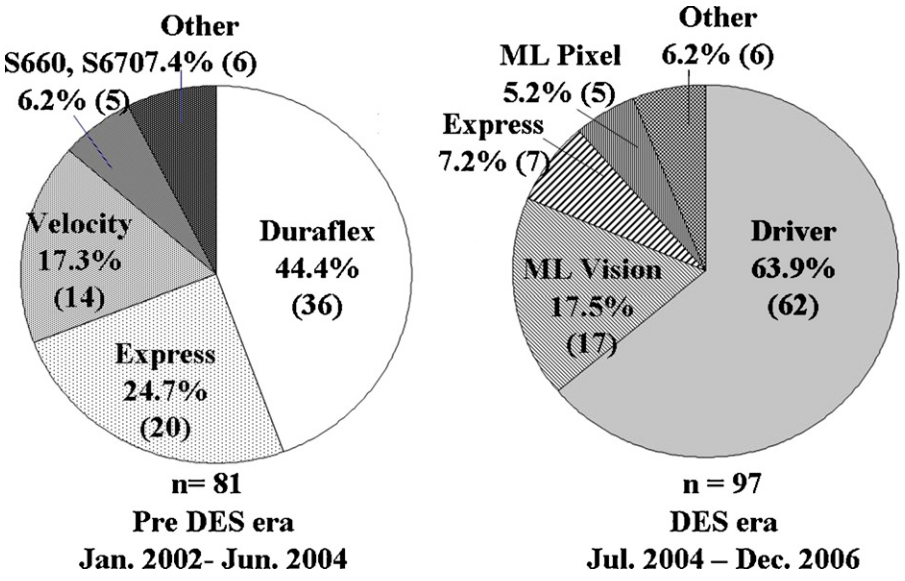

Figure 1 Types of bare metal stents.

ter results of recent AMI treatment. Several small sized studies suggest that ACE-Is and ARBs have anti-inflammatory effects, and may reduce the rate of ISR [17,18]. Recently, statins have been more widely used than before, based on the guideline that recommends rigid control of the plasma LDL cholesterol level to reduce major adverse cardiac events [19]. Statins also have anti-inflammatory effects, which may suppress neointima formation [20,21]. Although there is no solid evidence that ACE-Is, ARBs, and statins reduce the rate of ISR, the anti-inflammatory effects of these drugs might affect the rate of ISR and TLR after PCI for AMI patients.

In our study, the long-term outcome of currently available BMS implantation in AMI patients

Table 3 Clinical outcome

	Group 2: pre-DES era January 2002—June 2004 ($n=81$)	Group 1: DES era July 2004—December 2006 ($n=97$)	p
Acute or late thrombosis, n (%)	1 (1.2)	1 (1.0)	0.90
Cardiac death, n (%)	3 (3.6)	2 (2.1)	0.51
Myocardial infarction, n (%)	1 (1.2)	0 (0.0)	0.90
Cerebrovascular events, n (%)	0 (0.0)	0 (0.0)	—
TLR, n (%)	13 (16.0)	5 (5.1)	0.016
In-hospital death, n (%)	2 (2.5)	2 (2.1)	0.86
Follow-up length (months)	11.7 ± 2.1	12.0 ± 1.7	

TLR, target lesion revascularization.

Table 4 Serial QCA data

	Group 2: pre-DES era January 2002—June 2004 ($n = 55$)	Group 1: DES era July 2004—December 2006 ($n = 68$)	p
Reference diameter (mm)			
Preintervention	2.78 ± 0.30	2.79 ± 0.32	0.82
MLD (mm)			
Preintervention	0.36 ± 0.22	0.38 ± 0.25	0.55
Postintervention			
Proximal	2.59 ± 0.19	2.60 ± 0.20	0.74
In-stent	2.55 ± 0.18	2.59 ± 0.21	0.75
Distal	2.58 ± 0.22	2.59 ± 0.24	0.85
Follow-up			
Proximal	2.50 ± 0.19	2.43 ± 0.30	0.17
In-stent	1.77 ± 0.66	2.00 ± 0.43	0.027
Distal	2.29 ± 0.42	2.39 ± 0.27	0.11
Diametric stenosis (%)			
Preintervention	86.9 ± 7.7	86.4 ± 8.7	0.60
Postintervention			
Proximal	6.2 ± 2.3	5.8 ± 2.6	0.34
In-stent	7.6 ± 2.2	7.2 ± 2.5	0.35
Distal	8.0 ± 2.3	7.5 ± 2.6	0.41
Follow-up			
Proximal	9.6 ± 3.8	11.9 ± 9.2	0.085
In-stent	36.9 ± 23.6	29.2 ± 14.8	0.028
Distal	18.1 ± 15.1	13.3 ± 7.7	0.026
Late loss (mm)			
Proximal	0.10 ± 0.13	0.17 ± 0.29	0.077
In-stent	0.79 ± 0.66	0.58 ± 0.42	0.034
Distal	0.29 ± 0.41	0.16 ± 0.26	0.045
Binary restenosis (%)			
Proximal	0.0	0.0	—
In-stent	20.0	7.4	0.038
Distal	5.5	1.5	0.22
In-segment	20.0	7.4	0.038
Follow-up length (months)	7.27 ± 1.51	7.38 ± 1.50	0.58

Table 5 Comparison of resnosis group and non-restenosis group in Group 1

	In-segment restenosis (−) ($n = 63$)	In-segment restenosis (+) ($n = 5$)	p
Diabetes mellitus (%)	41.3	40.0	0.96
Stent diameter (mm)	3.19 ± 0.41	2.80 ± 0.45	0.047
Stent length (mm)	20.8 ± 4.4	24.4 ± 4.10	0.083
Lesions that needed more than 10 atm to fully dilate the pre-dilatation balloon	30.2	80.0	0.023

was much better than that in stable angina patients. Several studies have suggested that the mechanism of in-stent restenosis after BMS implantation for AMI patients is different from that for stable angina pectoris patients [20,21]. The pathophysiology of unstable plaques is different from that of the stable atherosclerotic lesions [22]. The process of neointimal formation in the stent may also be different between ACS lesions and stable atherosclerotic lesions. DES using anti-cancer drugs or immunosuppressant drugs might not be as beneficial for the treatment of AMI patients as for stable angina patients.

Although several trials support the safety of DES implantation for AMI patients [11,12], there are unsolved problems in DES implantation for AMI patients. The risk of acute, subacute, and late thrombosis after DES implantation is still controversial. At least, patients must continue taking antiplatelet agents for much longer after DES implantation than after BMS implantation, because of the delay of neointima formation after DES implantation. It is often unclear whether AMI patients can take antiplatelet agents without side effects or hemorrhagic complications. Patients must continue to take antiplatelets after DES implantation much longer than after BMS implantation. Therefore, we must be careful to implant DES in the patients for whom the safety of antiplatelet therapy is unclear.

In our study, ISR lesions had two characteristics. First, ISR often occurred after implantation of BMS with a small diameter because of the small vessel size. It had been well known that small vessel disease is a high risk factor of restenosis after stent implantation. As with small vessel lesions in which stents with a diameter of more than 2.5 mm cannot be implanted, it may be better to implant DES to reduce the rate of ISR. Second, many restenosis lesions had needed high-pressure dilatation at the primary PCI. Sometimes ACS occurs by thrombus formation in a chronic stenotic lesion. Such lesions may have bimodal characteristics of ACS and stable atherosclerosis. As with such 'acute on chronic' lesions, DES may be more effective to suppress ISR than BMS.

Study limitation

This study was a retrospective study with a small number of patients. A randomized study with a larger patient population will be necessary to confirm the results.

Conclusions

The primary and long-term outcomes of recent BMS implantations in AMI patients is better than those of previous BMS implantations and may be as good as those obtained with Cypher stents, unless the vessel diameter is small or the lesion accompanies severe chronic stenosis. Even in the DES era, BMS is suitable as the first choice for treatment of AMI patients.

References

[1] Ribeiro EE, Silva LA, Carneiro R, D'Oliver LG, Gasquez A, Amino JG, et al. Randomized trial of direct coronary angioplasty versus intravenous streptokinase in acute myocardial infarction. J Am Coll Cardiol 1993;22:376—80.
[2] Zijlstra F, De Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680—4.
[3] Primary Angioplasty in Myocardial Infarction Study Group. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1993;328:673—9.
[4] Mayo Coronary Care Unit and Catheterization Laboratory Groups. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. N Engl J Med 1993;328:685—91.
[5] Zijlstra F, Beukema WP, van't Hof AWJ, Liem A, Reiffers S, Hoorntje JCA, et al. Randomized comparison of primary coronary angioplasty with thrombolytic therapy in low risk patients with acute myocardial infarction. J Am Coll Cardiol 1997;29:908—12.
[6] Ribichini F, Steffenino G, Dellavalle A, Ferrero V, Vado A, Feola M, et al. Comparison of thrombolytic therapy and primary coronary angioplasty with liberal stenting for inferior myocardial infarction with precordial ST-segment depression: immediate and long-term results of a randomized study. J Am Coll Cardiol 1998;32:1687—94.
[7] Stent versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction Study Investigators. Coronary stenting plus platelet glycoprotein IIb/IIIa blockade compared with tissue plasminogen activator in acute myocardial infarction. N Engl J Med 2000;343:385—91.
[8] Stone GW, Brodie BR, Griffin JJ, Costantini C, Morice MC, St Goar FG, et al. Clinical and angiographic follow-up after primary stenting in acute myocardial infarction: the Primary Angioplasty in Myocardial Infarction (PAMI) stent pilot trial. Circulation 1999;99:1548—54.
[9] Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003;349:1315—23.
[10] Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002;346:1773—80.
[11] Spaulding C, Henry P, Teiger E, Beatt K, Bramucci E, Carrié D, et al., TYPHOON Investigators. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. N Engl J Med 2006;355:1093—104.

[12] Laarman GJ, Suttorp MJ, Dirksen MT, van Heerebeek L, Kiemeneji F, Slagboom T, et al. Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. J Engl J Med 2006;355: 1105—13.
[13] Sketch Jr MH, Ball M, Rutherford B, Popma JJ, Russell C, Kereiakes DJ, Driver Investigators. Evaluation of the Medtronic (Driver) cobalt—chromium alloy coronary stent system. Am J Cardiol 2005;95:8—12.
[14] Legrand V, Kelbaek H, Hauptmann KE, Glogar D, Rutsch W, Grollier G, et al., CLASS Investigators. Clinical and angiographic analysis with a cobalt alloy coronary stent (driver) in stable and unstable angina pectoris. Am J Cardiol 2006;97:349—52.
[15] Ujiie Y, Hirosaka A, Mitsugi M, Ohwada T, Igarashi M, Kijima M, et al. Effects of angiotensin-converting enzyme inhibitors or an angiotensin receptor blocker in combination with aspirin and cilostazol on in-stent restenosis. Int Heart J 2006;47:173—84.
[16] Nishikawa H, Miura S, Shimomura H, Tsujita K, Okamura K, Zhang B, et al. Combined treatment with statin and angiotensin-receptor blocker after stenting as a useful strategy for prevention of coronary restenosis. J Cardiol 2005;45:107—13.
[17] Souza-Costa DC, Sandrim VC, Lopes LF, Gerlach RF, Rego EM, Tanus-Santos JE. Anti-inflammatory effects of atorvastatin: modulation by the T-786C polymorphism in the endothelial nitric oxide synthase gene. Atherosclerosis 2007;193:438—44.
[18] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection. Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106: 3143—3421.
[19] Kleemann R, Princen HM, Emeis JJ, Jukema JW, Fontijn RD, Horrevoets AJ, et al. Rosuvastatin reduces atherosclerosis development beyond and independent of its plasma cholesterol-lowering effect in APOE*3-Leiden transgenic mice: evidence for antiinflammatory effects of rosuvastatin. Circulation 2003;108:1368—74.
[20] Schaefer A, Klein G, Fischer D, Meyer GP, Drexler H, Hausmann D. Mechanism of coronary artery restenosis after stenting for acute myocardial infarction. Am J Cardiol 2004;94:1037—40.
[21] Tanaka A, Kawabayashi T, Nishihori Y, Oe H, Namba M, Nishida Y, et al. In-stent restenosis and lesion morphology in patients with acute myocardial infarction. Am J Cardiol 2003;92:1208—11.
[22] Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes. N Engl J Med 1992;326:242—50.