Clin. Cardiol. 29, 199–203 (2006)

Clinical Investigations

Safety and Efficacy with Drug-Eluting Stent in ST-Segment Elevation and Non-ST-Segment Elevation Myocardial Infarction

CHANG-BUM PARK, M.D., CHEOL WHAN LEE, M.D., BONG-KI LEE, M.D., YOUNG-HAK KIM, M.D., MYEONG-KI HONG, M.D., JAE-JOONG KIM, M.D., PH.D., SEONG-WOOK PARK, M.D., PH.D., SEUNG-JUNG PARK, M.D., PH.D.

Department of Medicine, Asan Medical Center, University of Ulsan, Seoul, Korea

Summary

Background: Drug-eluting stents (DES) have been shown to reduce the need for repeat revascularization compared with bare metal stents (BMS). However, there is little information regarding the safety and long-term efficacy of DES in patients with acute myocardial infarction (AMI).

Hypothesis: The aim of this study was to evaluate the safety and efficacy of DES in patients with AMI.

Methods: Data from 211 consecutive patients with AMI treated with DES were compared with those from 228 consecutive patients with AMI treated with BMS. All patients were treated within 7 days of symptom onset. The incidence of major adverse cardiovascular events ([MACE]: death, reinfarction, and target vessel revascularization) was evaluated at 30 days and 1 year.

Results: Baseline clinical and angiographic characteristics were similar for both stent groups. However, patients who received DES had longer lesion lengths (23.0 ± 12.7 vs. 18.8 ± 10.6 mm, respectively; $p < 0.001$) and smaller reference diameters (2.97 ± 0.52 vs. 3.19 ± 0.63 mm, respectively, $p < 0.001$). At 30 days, the incidence rates of MACE (DES vs. BMS: 2.2 vs. 1.9%, $p = 1.000$) and stent thrombosis (BMS vs. DES: 0.9 vs. 1.7%; $p = 0.434$) did not differ significantly between the groups. At 1 year, patients with DES had a lower rate of MACE (BMS vs. DES: 14.0 vs. 6.6%; $p = 0.011$) primarily due to a lower target vessel revascularization rate (BMS vs. DES: 9.6 vs. 4.8%; $p = 0.028$).

Conclusions: The DES appear to be superior to the BMS in reducing the risk of MACE in patients with AMI.

Key words: clinical outcome, myocardial infarction, stent

Introduction

Routine stent implantation has a better procedural success rate and clinical outcome than balloon angioplasty in patients presenting with acute myocardial infarction (AMI).[1–3] However, restenosis and repeat revascularization remain significant clinical problems, limiting the long-term success of percutaneous coronary intervention.[1, 2, 4]

Recently, drug-eluting stent (DES) implantation was shown to be effective in reducing restenosis compared with bare metal stent (BMS) implantation in elective patients,[5, 6] and DES implantation now comprises more than 80% of percutaneous coronary intervention in the United States.[7] Furthermore, worldwide DES use has grown rapidly in patients with AMI despite concerns about early thrombotic events and late restenosis.[8, 9] However, there is little information regarding the safety and efficacy of using DES in patients with AMI.

The present study is a retrospective analysis comparing clinical outcomes when using DES and BMS in consecutive patients with AMI.

Material and Methods

Patient Population

The study involved a total of 211 consecutive patients with AMI treated with DES within 7 days of symptom onset between March 2003 and July 2004 at the Asan Medical Center, Seoul, Korea. Data from this group were compared with those of a control group comprising 228 consecutive patients with AMI treated with conventional BMS within 7 days of symptom onset between April 2002 and February 2003. Patients with cardiogenic shock on admission or severe coronary artery disease requiring early bypass surgery were excluded.

This study was supported by grants from the CardioVascular Research Foundation and the Korea Health 21 R&D Project, Ministry of Health & Welfare, Korea (0412-CR02-0704-0001).

Address for reprints:

Seung-Jung Park, M.D., Ph.D.
Division of Cardiology
Asan Medical Center
University of Ulsan
388-1 Pungnap-dong, Songpa-gu
Seoul, 138-736, Korea
e-mail: sjpark@amc.seoul.kr

Received: October 15, 2005
Accepted with revision: December 7, 2005

Angioplasty Procedure

Of the DES group, 73.9% were implanted with Cypher stents (Johnson and Johnson Cordis, Miami Lakes, Fla., USA) and 26.1% were implanted with Taxus stents (Boston Scientific Corp., Natick, Mass., USA). In the BMS group, 23.2% were implanted with Jo stents (Jomed, Langendingen, Germany), 19% with BX sonic or BX velocity stents (Cordis, Johnson & Johnson, Warren, N.J., USA), 15.9% with Express stents (Boston Scientific Corp.) 13.4% with BE stents (Medtronic, Minneapolis, Minn., USA), and 28.5% with other stents.

Stent implantation was performed using standard techniques. The postprocedural antithrombotic regimen consisted of a loading dose of clopidogrel (300 mg before intervention), lifelong aspirin (100 or 200 mg/day), and clopidogrel (75 mg/day) for at least 1 month in patients with BMS and for at least 6 months in patients with DES.

Definition and Follow-Up

A major adverse cardiovascular event (MACE) was defined as death, nonfatal reinfarction, and target vessel revascularization (TVR). Reinfarction was diagnosed by recurrent symptoms and/or electrocardiographic changes in association with re-elevation of creatine kinase (CK)-MB and troponin-I levels greater than twice the upper normal limit. Target vessel revascularization was defined as a repeat intervention (surgical or percutaneous) driven by any lesion located in the same epicardial vessel treated at the index procedure. Thrombotic stent occlusion was angiographically documented as a complete occlusion (Thrombolysis in Myocardial Infarction [TIMI] grade 0 or 1) or flow-limiting thrombi (TIMI flow grade 1 or 2) in a previously successfully treated artery.

All demographic, clinical, angiographic, and procedural characteristics were prospectively entered into the Asan Medical Center angiographic database. During follow-up, recordings of all repeat interventions and clinical information were collected by chart review or telephone interview.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and were compared using independent *t*-tests. Categorical variables between the two groups were compared using chi-square or Fisher's exact tests. The cumulative incidence of adverse events was estimated according to the Kaplan-Meier method and compared using log rank tests. Variables found to be significant by univariate analysis were entered into multivariate analysis to identify independent predictors of adverse events. A p value < 0.05 was considered to indicate a significant difference.

Results

Baseline and Procedural Characteristics

Baseline clinical and angiographic characteristics are summarized in Tables I and II. No patient in non-ST-segment ele-

TABLE I Baseline demographic and clinical characteristics of patients with acute myocardial infarction treated with bare metal or drug-eluting stents

	Bare metal stents (n = 228)	Drug-eluting stents (n = 211)	p Value
Age, years	58.9 ± 10.4	58.3 ± 12.5	0.379
Male (%)	181 (79.4)	173 (82.0)	0.138
STEMI (%)	143 (62.7)	133 (63.0)	0.864
NSTEMI (%)	85 (37.3)	78 (37.0)	0.864
Diabetes (%)	46 (20.2)	36 (17.1)	0.403
Hypertension (%)	95 (41.7)	80 (37.9)	0.422
Hypercholesterolemia (≥ 200 mg/dl) (%)	39 (17.1)	40 (19.0)	0.614
Current smoking (%)	89 (39.0)	80 (37.9)	0.81
Prior thrombolysis (%)	19 (7.5)	19 (6.0)	0.803
Prior myocardial infarction (%)	10 (4.4)	8 (3.8)	0.754
Prior PCI (%)	15 (6.6)	16 (7.6)	0.682
Prior CABG (%)	2 (0.9)	2 (0.9)	1
Primary PCI (%)	100 (43.9)	94 (44.5)	0.884
Time between symptom onset and PCI			
STEMI (h)	26.0 ± 34.1	28.7 ± 43.7	0.593
NSTEMI (days)	3.58 ± 1.78	3.41 ± 1.82	0.568
Statin (%)	82 (36.0)	130 (61.6)	< 0.001
Glycoprotein IIb/IIIa antagonist (%)	28 (12.3)	13 (6.2)	0.028
LVEF (%)	53.3 ± 10.2	52.4 ± 9.9	0.53

Abbreviations: STEMI = ST-segment elevation myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft, LVEF = left ventricular ejection fraction.

TABLE II Qualitative and quantitative angiographic and procedural characteristics of the study population

	Bare metal stents (n = 228)	Drug-eluting stents (n = 211)	p Value
Multivessel disease (%)	125 (54.8)	125 (59.2)	0.35
Treated artery			
Left anterior descending (%)	127 (55.7)	103 (48.8)	0.149
Left circumflex (%)	16 (7.0)	39 (18.5)	< 0.001
Right coronary artery (%)	79 (34.6)	60 (28.4)	0.162
Others [a] (%)	6 (2.6)	9 (4.3)	0.346
Complex lesion (B2 & C) (%)	138 (60.5)	137 (64.9)	0.375
Procedural characteristics			
Lesion length, mm	18.8 ± 10.6	23.0 ± 12.7	< 0.001
Reference vessel diameter, mm	3.19 ± 0.63	2.97 ± 0.52	< 0.001
Pre-minimal luminal diameter, mm	0.75 ± 0.61	0.72 ± 0.60	0.528
Post-minimal luminal diameter, mm	3.0 ± 0.6	2.8 ± 0.5	< 0.001
Preprocedural TIMI flow			0.363
0 (%)	90 (39.5)	81 (38.4)	
I (%)	14 (6.1)	12 (5.7)	
II (%)	26 (11.4)	33 (15.6)	
III (%)	97 (42.9)	85 (40.3)	
Postprocedural TIMI III flow	213 (93.4)	201 (95.3)	0.658

[a] Others: left main disease, saphenous vein graft.
Abbreviation: TIMI = Thrombolysis In Myocardial Infarction.

vation myocardial infarction (NSTEMI) was treated within 12 h after symptom onset. Of ST-segment elevation myocardial infarction (STEMI), 85 patients in the BMS group (37.3%) and 83 patients in the DES group (39.3%) were treated within 12 h from symptom onset. Elective post-MI percutaneous coronary intervention (PCI) was performed in all patients with NSTEMI and in 43 patients (30.1%) with BMS and 38 patients (28.6%) with DES. Neither rescue nor patients with late recurrent MI were observed. There was no difference between the DES and BMS groups in terms of risk factors, prior MI, prior intervention, prior bypass surgery, prior thrombolysis, and proportion of STEMI. However, patients with DES had longer lesion lengths (23.0 ± 12.7 vs. 18.8 ± 10.6 mm, $p < 0.001$), smaller reference diameters (2.97 ± 0.52 vs. 3.19 ± 0.63 mm, $p < 0.001$), and smaller postprocedural minimal lesion diameters (MLD) (2.8 ± 0.5 vs. 3.0 ± 0.6 mm, $p < 0.001$) compared with patients with BMS.

Clinical Outcomes

Clinical outcomes at 30 days and 1 year are presented in Table III. There was no significant difference between patients with DES and BMS in terms of the incidence of cardiac death, reinfarction, or TVR. Two patients with DES (0.9%) and two

TABLE III Clinical outcomes at 30 days and 1 year

	Bare metal stents (n = 228)	Drug-eluting stents (n = 211)	p Value
30-day MACE (%)	5 (2.2)	4 (1.9)	1
Death (%)	1	0	1
MI (%)	4 (1.8)	4 (1.9)	1
TVR (%)	0	0	
Stent thrombosis (%)	2 (0.9)	4 (1.9)	0.434
One-year MACE (%)	32 (14.0)	14 (6.6)	0.011
Death (%)	3 (1.3)	0 (0)	0.249
MI (%)	7 (3.1)	5 (2.4)	0.653
TVR (%)	22 (9.6)	9 (4.2)	0.028
Late stent thrombosis (%)	2 (0.9)	0 (0)	0.5

Abbreviations: MACE = major adverse cardiac events, MI = myocardial infarction, TVR = target vessel revascularization.

patients with BMS (1.9%) experienced stent thrombosis within 30 days (p = 0.434). In addition, the incidence of MACE was also similar between the two groups at 30 days. In contrast, 1-year follow-up showed the incidence of MACE was significantly lower in patients with DES than in patients with BMS (6.6 vs. 14.0%, respectively, p = 0.011), mainly due to the lower TVR rate (4.3 vs. 9.9%, respectively, p = 0.028). Late stent thrombosis with subsequent reinfarction developed in two patients with BMS, but not in patients with DES. Major adverse cardiovascular event-free survival at 12 months was 93.4% in the DES and 86.0% in the BMS group (p = 0.028, by log rank test) (Fig. 1). Multivariate analysis showed use of DES was a significant independent predictor of death, reinfarction, or repeat revascularization at 1 year (hazard ratio: 0.509, 95% confidence interval 0.299–0.867, p = 0.013).

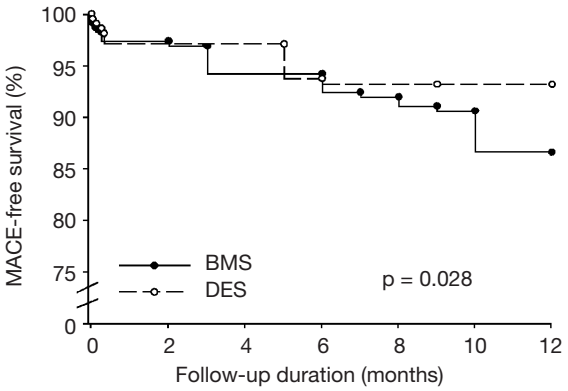

FIG. 1 Survival free of cardiac death, reinfarction, or target vessel revascularization in drug-eluting stent (DES) and bare metal stent (BMS) groups. MACE = major adverse cardiac events.

Discussion

The present study showed that DES was safe in the treatment of AMI and had similar rates of procedural success, in-hospital adverse events, and stent thrombosis compared with BMS. Furthermore, DES significantly reduced the incidence of major adverse events at 1 year despite the fact that patients with DES had more unfavorable baseline characteristics such as longer lesion length, shorter reference diameter, and smaller postprocedural minimal lesion diameter compared with patients with BMS. These results suggest that DES is superior to BMS in the treatment of AMI.

The thrombogenic coronary condition in patients with AMI[8] coupled with a theoretical tendency for hypercoagulability[9] and delayed re-endothelialization[10, 11] with DES, can potentially increase the risk of thrombotic complications and adversely affect outcomes after DES implantation during the acute phase of MI. However, regardless of these contradictory laboratory findings, we found there was no difference in stent thrombosis rates between patients with DES and BMS at 30 days and 1 year, nor in rates of MI or mortality. These findings are consistent with previous reports indicating that DES may be safe in the setting of AMI.[12–15]

Use of DES in patients with AMI resulted in reduced rates of MACE at 1 year (BMS vs. DES: 14.0 vs. 6.6; p = 0.011), mainly due to a lower TVR rate (BMS vs. DES: 9.6 vs. 4.3%; p = 0.028), similar to patients with stable ischemic syndrome.[16] Moreover, the TVR rate in patients with DES was almost unchanged from 8 months (3.8%) to 1 year (4.2%), whereas the TVR rate continued to increase during this period in patients with BMS (from 4.8 to 9.6%, respectively). The Rapamycin Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) study using sirolimus-eluting stents for AMI[12] and the subgroup analysis of the TAXUS-IV study of acute coronary syndrome[13] showed that DES implantation reduced the incidence of adverse events at 6 months to 1 year mainly due to a better TVR rate between 8 months to 1 year; this did not change for DES, as was the case in the present study. Thus, our results confirm that DES are effective in preventing repeat revascularization in the subset of unstable atherosclerotic lesions responsible for acute occlusions and suggest that further advantages of DES over BMS for AMI might be observed as follow-up durations increase.

In the present study, four patients with DES experienced MI, which occurred primarily within 30 days. In contrast, four with BMS experienced MI between 30 days and 1 year. The mortality rates were 1.3 and 0% for patients with BMS and DES, respectively. These mortality rates are considerably lower than those reported in other studies[12, 17, 18] which may reflect the inclusion of patients with NSTEMI and the exclusion of patients with cardiogenic shock on admission in the present study population. Other studies including patients with NSTEMI and STEMI showed similar low rates of mortality.[14]

Limitations

There were several potential limitations to this study. First, it was a retrospective, nonrandomized, single-center registry study of DES implantation in AMI. Second, the choice of DES was left to the physician, leading to possible selection bias. Third, our findings were derived from a select population of patients with AMI, and it may not be possible to generalize our results to all patients with AMI. Despite these limitations, we believe this study demonstrates the safety and efficacy of DES in routine clinical practice for the treatment of AMI.

Conclusion

Drug-eluting stents for the treatment of acute myocardial infarction are safe and more effective in reducing the risk of major adverse events when compared with bare metal stents. However, further large-scale randomized trials will be needed to verify these promising initial results.

References

1. Stone GW, Grines CL, Cox DA, Garcia E, Tcheng JE, Griffin JJ, Guagliumi G, Stuckey T, Turco M, Carroll JD, Rutherford BD, Lansky AJ: Compari-

son of angioplasty with stenting, with or without abciximab, acute myocardial infarction. *N Engl J Med* 2002;346:957–966
2. Grines CL, Cox DA, Stone GW, Garcia E, Mattos LA, Giambartollmei A, Brodie BR, Madonna O, Eijgelshoven M, Lansky AJ, O'Neill WW, Morice MC: Stent primary angioplasty in myocardial infarction study group. Coronary angioplasty with or without stent implantation for acute myocardial infarction. *N Engl J Med* 1999;341:1949–1956
3. Keeley EC, Boura JA, Grines CL: Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review of 23 randomized trials. *Lancet* 2003;361:13–20
4. Odell A, Dudnason T, Andersson T, Jidbratt H, Grip L: One-year outcome after percutaneous coronary intervention for stable and unstable angina pectoris with or without application of general usage of stents in unselected European patient groups. *Am J Cardiol* 2002;90:112–118
5. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE, for the SIRIUS Investigators: Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315–1323
6. Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, Turco M, Caputo R, Bergin P, Greenberg J, Popma JJ, Russell ME, for the TAXUS-IV Investigators: Polymer-based, paclitaxel-eluting stents in patients with coronary artery disease. *N Engl J Med* 2004;350:221–231
7. Mark DS, Ratko TA, Matuszewski KA, Oinonen MJ, Cummings JP. Clinical and financial impact of drug eluting stents: The US academic experience. *J Am Coll Cardiol* 2005;45(suppl A):73A
8. Antman EM, Braunwald E: ST-elevation myocardial infarction: Pathology, pathophysiology, and clinical features. In *Braunwald's Heart Disease*, 7th ed. (Eds. Zipes DP, Libby P, Bonow RO, Braunwald E.), pp. 1141–1165. Philadelphia: WB Saunders, 2005
9. Barbinska A, Markell MS, Salifu MO, Akord M, Ehrlich YH, Kornecki E: Enhancement of human platelet aggregation and secretion induced by rapamycin. *Nephrol Dial Transplant* 1998;13:3153–3159
10. Jeanmart H, Malo O, Carrier M, Nickner C, Desjardins N, Perrault LP: Comparative study of cyclosporine and tacrolimus vs. newer immunosuppressants mycophenolate mofetil and rapamycin on coronary endothelial function. *J Heart Lung Transplant* 2002;21:990–998
11. Virmani R, Farb A, Kolodgie FD: Histopathologic alterations after endovascular radiation and antiproliferative stents: Similarities and differences. *Herz* 2002;27:1–6
12. Lemos PA, Saia F, Hoye A, McFadden E, Sianos G, Smits PC, van der Giessen WJ, Feyter P, Domburg RT, Serruys PW: Short-and long-term clinical benefit of sirolimus-eluting stents compared to conventional bare metal stents for patients with acute myocardial infarction. *J Am Coll Cardiol* 2004;43:704–708
13. Moses JW, Mehran R, Nikolsky E, Lasala JM, Corey W, Albin G, Hirsch C, Leon MB, Russel ME, Ellis ST, Stone GW: Outcomes with the paclitaxel-eluting stent in patient with acute coronary syndromes: Analysis from the TAXUS-IV trial. *J Am Coll Cardiol* 2005;45:1165–1171
14. Weber F, Schneider H, Schwarz C, Holzhausen C, Petzsch M, Nienaber CA: Sirolimus-eluting stents for percutaneous coronary intervention in acute myocardial infarction. *Z Kardiol* 2004;93:938–943
15. Cheneau E, Rha SW, Kuchulakanti PK, Stabile E, Kinnaird T, Torguson R, Pichard AD, Satler LF, Kent KM, Waksman R: Impact of sirolimus-eluting stents on outcomes of patients treated for acute myocardial infarction by primary angioplasty. *Cathet Cardiovasc Intervent* 2005;65:469–472
16. Sousa JE, Costa MA, Sousa AG, Abizaid AC, Seixas AC, Abizaid AS, Feres F, Mattos LA, Falotico R, Jaeger J, Popma JJ, Serruys PW: Two-year angiographic and intravascular ultrasound follow-up after implantation of sirolimus-eluting stents in human coronary arteries. *Circulation* 2003;107: 381–383
17. Valgimigli M, Percoco G, Malagutti P, Campo G, Ferrari F, Barbieri D, Cicchitelli G, McFadden EP, Merlini F, Ansani L, Guardigli G, Bettini A, Parrinello G, Boersma E, Ferrari R, and the STRATEGY Investigators: Tirofiban and sirolimus-eluting stent vs. abciximab and bare-metal stent for acute myocardial infarction. *J Am Med Assoc* 2005;293:2109–2117
18. Saia F, Lemos PA, Lee CH, Arampatzis CA, Hoye A, Degertekin M, Tanabe K, Sianos G, Smits PC, McFadden E, Hofma SH, Giessen WJ, Feyter PJ, Domburg RT, Serruys PW: Sirolimus-eluting stenting implantation in ST-elevation acute myocardial infarction. *Circulation* 2003;108:1927–1929