Long-Term Clinical Efficacy of Cutting Balloon Angioplasty Followed by Bare Metal Stent Implantation for Treating Ostial Left Anterior Descending Artery Lesions

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ABSTRACT

Background: Drug-eluting stents (DES) are superior to bare metal stents (BMS) for treating ostial left anterior descending artery (LAD) lesions, but DES is not suitable for all patients in real life practice.

Hypothesis: We hypothesize that cutting balloon angioplasty (CBA) followed by BMS (CBA + BMS) for treating ostial LAD lesions is an alternative strategy.

Methods: In our study, 101 consecutive patients (51 with DES and 50 with CBA + BMS) with ostial LAD stenting were included for retrospective investigation between November 2003 and May 2005. The target vessel diameter was ≥ 3.0 mm.

Results: We compared the DES group with the CBA + BMS group, the rates of restenosis (10.3% versus 17.9%, $p = 0.386$), target lesion revascularization (TLR) (5.88% versus 10%, $p = 0.487$) and major adverse cardiac events (MACE) (7.84% versus 12%, $p = 0.525$) were similar at 6–8 months angiographic follow-up, but there were higher bleeding events in the DES group ($p = 0.033$). During a 2-year clinical follow-up, no myocardial infarction occurred in the 2 groups, the rates of TLR (7.84% versus 10%, $p = 0.741$) and MACE (9.8% versus 12%, $p = 0.723$) were also similar. The MACE-free survival rate was 90.2% versus 88% ($p = 0.723$).

Conclusions: The CBA + BMS combination has a good long-term clinical effect in the treatment of ostial LAD lesions; it might be an alternative strategy for patients with contraindication for DES implantation, or patients who cannot endure long-term dual antiplatelet medication, or in elderly patients.

Introduction

Ostial lesions of the coronary artery are a challenge for interventional cardiologists. Conventional balloon angioplasty is ineffective in treating ostial lesions because of high rates of immediate recoil and long-term restenosis. The higher concentration of elastic and muscle fibers around the ostium is the reason for the recoil after balloon inflations.¹ The restenotic rate occurs in approximately 15%–45% of patients after implantation of bare metal stents (BMS) for treating ostial left anterior descending artery (LAD) lesions.^{2,3} Randomized clinical trials have proved that the drug-eluting stent (DES) is superior to BMS in de novo lesions,^{4,5} but cardiologists are not yet confident of the long-term safety of DES.^{6,7} In addition, DES is not suitable for all patients, especially the elderly or patients with contraindication for DES implantation, or patients who cannot endure long-term dual antiplatelet medication. Cutting balloon angioplasty (CBA) followed by BMS (CBA + BMS) insertion in the treatment

of ostial LAD lesions is a feasible technique and has good clinical efficacy.^{2,8,9} We hypothesize that the CBA + BMS combination may be an alternative strategy for treating ostial LAD lesions. The purpose of this study was therefore to evaluate the long-term safety and efficacy of DES and CBA + BMS in patients with ostial LAD lesions.

Methods

Study Population

A total of 101 consecutive patients (51 with DES and 50 with CBA + BMS) with ostial LAD lesions were enrolled from November 2003 to May 2005. The angiographic inclusion criterion was the presence of a lesion with $\geq 70\%$ (vessel size ≥ 3.0 mm) diameter stenosis rising within 3 mm of the LAD orifice. The exclusion criteria were patients with known bleeding abnormalities, conditions that required life-long anticoagulation therapy, medical noncompliance, or an upcoming surgical procedure that might prompt

interruption of antiplatelet therapy. Informed consent was obtained from each patient approved by the institution's Human Research Committee.

Interventional Procedures

All patients were treated with aspirin and either ticlopidine or clopidogrel 3 days before the procedure. All procedures were performed via the femoral or radial approach, a bolus dose of unfractionated heparin (100 u/kg) was given after sheath insertion, and supplemented as needed to maintain an activated clotting time between 250 and 300 seconds throughout the procedure. The administration of glycoprotein IIb/IIIa inhibitors was left to the doctor's discretion. Aspirin was suggested indefinitely, and ticlopidine (500 mg per day) or clopidogrel (75 mg per day) was given for 1 mo for BMS, at least 3 mo for sirolimus-eluting stent, and 6 mo for paclitaxel-eluting stent after procedures.

The size of the cutting balloon (CB) was selected in accordance with an estimated ratio 1 : 1 for diameter of CB/reference vessel; the length of CB was selected according to the length of the target stenosis; the inflation pressure was increased gradually to reach 6–12 atmospheres. Stent implantation was performed using a direct stenting technique, or after predilation (pressure < 12 atmospheres) with a balloon in the DES group.

Quantitative Coronary Analysis

Quantitative coronary angiography (QCA) was made using a validated, edge detection system (MED CON QCA software). The result was reviewed and analyzed by 2 independent experienced interventional cardiologists. The lesion type was evaluated according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines. The reference vessel diameter was measured using the normal segment proximal to the lesion. A successful implantation of angiographic stent was defined as a final residual stenosis < 30% with thrombosis in myocardial infarction flow grade 3. Procedural success was considered as the achievement of angiographic success without in-hospital major adverse cardiac events (MACE). Angiographic restenosis was defined as diameter stenosis > 50% within a previously stented segment (5 mm proximal and distal to stent) using follow-up angiogram. In-stent late luminal loss was defined as the difference in minimal luminal diameter (MLD) between immediate and angiographic follow-up after the procedure. Bleeding events included a major bleeding event (gastrointestinal bleeding, cerebral hemorrhage) and a minor bleeding event (gingival bleeding, subcutaneous bleeding, and nasal bleeding). The target lesion revascularization (TLR) was defined as clinically driven coronary artery bypass grafting or repeat percutaneous transluminal coronary angioplasty (PTCA) because of restenosis or closure of the target lesion.

Study Endpoints and Follow-up

The primary study endpoint was the 2-year MACE rate, a composite of death, recurrent myocardial infarction, and target lesion or vessel revascularization. Secondary endpoints were the rates of binary stenosis, TLR, and bleeding events at 6–8 months angiographic follow-up.

Angiographic follow-up was suggested for all patients at 6–8 months, or sooner if noninvasive evaluation or clinical presentation suggested the presence of ischemia after the procedure. Clinical follow-up was by telephone contact or an office visit.

Statistical Analysis

Continuous variables are described as mean $\pm$ standard deviation, and comparison between groups was made with Student's *t* test, and nonparametric Mann-Whitney U test categorical variables are reported as percentage or proportions and compared with Fisher's exact test and chi-square test. The Kaplan-Meier method was employed for analyses of MACE-free rate. All reported *p*-values were 2-sided, and *p* < 0.05 was considered statistically significant. All statistical analyses were performed with SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL).

Results

Baseline Clinical and Angiographic Characteristics

The clinical information of the 101 studied patients is presented in Table 1. There were no significant differences in baseline clinical characteristics including age, sex, prior myocardial infarction, current smoker and coronary risk profiles between the 2 groups.

Basic angiographic characteristics are shown in Tables 2 and 3. There were no statistical differences in lesion type, left ventricular ejective fraction, reference vessel diameter, MLD, lesion length, stent diameter, stent length, postintervention MLD, and acute gain between the 2 groups.

Major Adverse Cardiac Events in Hospitalization

In the DES group, the rate of MACE in-hospital following DES implantation was 1.96%, which attributed to acute myocardial infarction caused by subacute thrombosis after the procedure (confirmed by coronary artery angiography). No MACE occurred in the CBA + BMS group.

Angiographic Follow-up at 6–8 Months

Angiographic analysis results are shown in Tables 3 and 4. The rate of coronary angiographic follow-up was similar in the 2 groups. Late loss (LL, 0.26 ± 0.20 versus 1.36 ± 0.24 , *p* < 0.001) was less in the DES group than in the CBA + BMS group. The rates of in-stent restenosis, TLR, and MACE showed no significant difference. There were more bleeding events (15.7% versus 2%, *p* = 0.033) in the DES group (including 2 cases with gastrointestinal bleeding, 1

Table 1. Comparison of Clinical Data Between 2 Groups

Parameters, n (%)	DES n = 51	CBA + BMS n = 50	<i>p</i> -Value
Patient characteristics			
Men	46 (90.2%)	41 (82%)	0.233
Age (y)	56 ± 12.4	54.6 ± 10.5	0.740
Unstable angina pectoris	43 (84.3%)	34 (68%)	0.054
Diabetes mellitus	10 (19.6%)	9 (18%)	0.836
Hypertension	22 (43%)	26 (52%)	0.373
Hypercholesterol	11 (22%)	17 (34%)	0.163
Previous myocardial infarction	18 (35)	14 (28%)	0.431
Current smoker	30 (58.8%)	29 (58%)	0.933
Previous percutaneous coronary intervention	8 (15.6%)	3 (6%)	0.118
Prior coronary artery bypass graft	2 (3.9%)	4 (8%)	0.386
Unstable angina pectoris was defined according to the Braunwald classification. Abbreviations: DES, drug-eluting stent; BMS, bare metal stent.			

case with cerebral hemorrhage and 5 cases with minor bleeding), among which there was no significant difference between the 2 groups ($p = 0.495$), while the trend of minor bleeding events was in favor of the CBA + BMS group but was not statistically significant ($p = 0.269$).

Clinical Follow-up at 2 Years

The 2-year clinical follow-up outcomes are shown in Table 4. There was no difference in the rates of follow-up, TLR, MACE, and death between the 2 groups. Cardiac death occurred in 2 patients: 1 in the DES group died of late thrombosis, the other in the CBA + BMS group died of heart failure. The MACE-free survival rate was a little higher in the DES group (90.2% versus 88%, $p = 0.723$) (Figure 1).

Discussion

The main findings of this study are as follows: (1) the CBA + BMS combination has good long-term efficacy and safety in the treatment of ostial LAD stenosis; (2) a higher percentage of all-cause bleeding happened in the DES group compared with CBA + BMS group during 6–8 months follow-up; (3) the CBA + BMS combination may be an alternative strategy for treating ostial LAD lesions in elderly patients or patients with contraindication for DES implantation or patients who cannot endure long-term dual antiplatelet treatment in the DES era.

Table 2. Angiographic Data Between 2 Groups

Parameters, n(%)	DES n = 51	CBA + BMS n = 50	<i>p</i> -Value
Coronary lesion characteristics			
Calcification	2 (4)	6 (12)	0.133
Eccentric	43 (84.3)	37 (74)	0.202
Lesion type (ACC/AHA)			
B	31 (60.8)	35 (70)	0.331
C	20 (39.2)	13 (26)	0.157
Lesion characteristics			
De novo	48 (94.1)	49 (98)	1.000
Left ventricular ejective fraction (%)	64 ± 22	62 ± 18	0.372
Multiple coronary disease	30 (58.8)	20 (40)	0.490
Abbreviations: DES, drug-eluting stent; BMS, bare metal stent; ACC/AHA, American College of Cardiology/American Heart Association.			

Coronary intervention of ostial LAD lesions remains a challenging task to interventional cardiologists because operating ostial lesions was a high-risk procedure and had a high restenotic rate compared with other site lesions of coronary arteries.^{2,3} It is well known that the lack of efficacy of PTCA in ostial lesions results in suboptimal resident stenosis, and this leads to a higher restenosis rate as documented in the published data.¹ Directional atherectomy may have advantages for treating ostial lesions; however, it may not provide a significant impact on the restenosis because it cannot completely eliminate acute recoil and arterial remodeling.^{10,11} Coronary stenting is effective in minimizing recoil and reducing restenosis, but in-stent restenosis for ostial lesions still remains a problem.¹²

The CB is a unique angioplasty device used in percutaneous coronary interventions. The advantage of CB is its ability to reduce vessel stretch and injury by scoring the vessel longitudinally rather than causing an uncontrolled disruption of the atherosclerotic plaque. The increased plaque reduction and smaller vessel expansion may represent a reduction in vessel wall injury and thus potentially contribute to a favorable healing process.¹² The CB also dilates the target vessel with less force to decrease the risk of a neoproliferative response and in-stent restenosis, which had been confirmed in a clinical setting.¹³ Coronary stenting is effective in minimizing recoil and reducing restenosis. Therefore, a combination of the 2 treatment modalities may be a reasonable approach with synergistic effects. The CBA + BMS combination was widely used in our hospital before

Table 3. Quantitative Angiography and Technical Data

Parameters (mm)	DES n = 51	CB+BMS n = 50	p-Value
Preintervention			
Reference diameter	3.41 ± 0.29	3.53 ± 0.42	0.154
MLD	0.39 ± 0.28	0.41 ± 0.24	0.937
Diameter stenosis, %	89 ± 4.56	88 ± 6.66	0.861
Lesion length	13.01 ± 2.26	12.48 ± 2.01	0.209
Post CB dilation	—	3.29 ± 0.32	—
Acute gain	—	2.86 ± 0.27	—
Technical data			
Maximal balloon size	3.2 ± 0.29	3.3 ± 0.31	0.077
Stent length	13.9 ± 1.93	13.0 ± 2.77	0.056
Stent diameter	3.40 ± 0.26	3.53 ± 0.37	0.077
Postintervention			
Reference diameter	3.56 ± 0.33	3.57 ± 0.40	0.052
MLD	3.53 ± 0.22	3.54 ± 0.37	0.113
Acute gain	3.01 ± 0.36	3.13 ± 0.48	0.415
Follow-up at 6–8 months			
Reference diameter	3.54 ± 0.34	3.42 ± 0.25	<0.001
MLD	3.27 ± 0.22	2.23 ± 0.28	<0.001
Late loss	0.26 ± 0.20	1.36 ± 0.24	<0.001

Abbreviations: DES, drug-eluting stent; BMS, bare metal stent; CB, cutting balloon; MLD, minimal luminal diameter.

the DES era and the immediate follow-up outcomes were satisfying.⁸

From the present study, we found that a higher percentage of the all-cause bleeding happened in the DES group, among which the major bleeding events showed no significant difference between the 2 groups. The reason for a higher percentage of bleeding in the DES group may be related to the long-term dual antiplatelet medication. The major reason for lower bleeding events for the CBA + BMS group might be associated with short-time dual antiplatelet medications. The results suggested that the CBA + BMS combination might provide an alternative selection for the patients who need to interrupt antiplatelet medication treatment, or patients who cannot endure long-term dual antiplatelet medication, or in elderly patients.

With the wide use of DES in practice, a DES implanted in the ostial LAD lesions had been reported.⁴ The baseline characteristics of the study were similar to our study, but there were differences in the percentage of eccentric

Table 4. Comparison of Short- and Long-Term Clinical Outcomes Between 2 Groups

Parameters, n, (%)	DES n = 51	CBA + BMS n = 50	p-Value
Follow-up at 6–8 mo			
Myocardial Infarction	0	0	—
Coronary artery angiogram	56.8 (29/51)	56 (28/50)	0.930
Death	1.96 (1/51)	0	1.000
Major adverse cardiac events	7.84 (4/51)	12 (6/50)	0.525
Restenosis rate	10.3 (3/29)	17.9 (5/28)	0.386
Target lesion revascularization	5.88 (3/51)	10% (5/50)	0.487
Late stent thrombosis	1.96 (1/51)	0	1.000
All-cause bleeding	15.7 (8/51)	2 (1/50)	0.033
2-y clinical follow-up			
Clinical follow-up rate	96.1(49/51)	98 (49/50)	0.984
Angina pectoris	19.6 (10/51)	20 (10/50)	0.961
Myocardial infarction rate	0	0	—
Death	1.96 (1/51)	2 (1/50)	1.000
Major adverse cardiac events	9.8 (5/51)	12 (6/50)	0.723
Target lesion revascularization	7.84 (4/51)	10 (5/50)	0.741
Very late stent thrombosis	1.96 (1/51)	0	1.000

Abbreviations: DES, drug-eluting stent; BMS, bare metal stent.

lesions (59.3%), lesion length (9.32 ± 4.8 for BMS group and 9.43 ± 4.2 for DES group), diameter stenosis (66 ± 17 for BMS group and 66 ± 18 for DES group), and angiographic follow-up rate (78.5%); DES had advantages over BMS in late lumen loss (0.32 ± 0.8 mm versus 1.23 ± 0.9 mm, $p < 0.0001$), restenosis rate (5.7% versus 31.3%, $p = 0.01$), and MACE rate (9.3% versus 32.6%, $p = 0.015$) at 9-month follow-up after procedures.³ In our study, there were no significant differences in rates of in-stent restenosis, TLR, and MACE between the 2 groups at 6–8-month angiographic follow-up. These results extended to 2-year clinical follow-up. There are some possible explanations for the different results: (1) there were more complex lesions in our study, which may be attributed to higher restenosis rates in the DES group compared to prior study³; (2) the use of CB could result in less vessel wall trauma, which may account for lower rate of restenosis; (3) the size of the target vessel

Figure 1. Cumulative MACE-free survival rate at 2-years clinical follow-up.

(diameter ≥ 3.0 mm) may contribute to large acute gain, lumen diameter and lumen area; (4) the lower angiographic follow-up rate and small sample in our study may limit the statistical power. We speculate that the CBA + BMS combination might have a better effect for revascularizing ostial LAD with larger vessel size, but further study may be needed to ascertain these issues.

Conclusions

In the present small sample study, the CBA + BMS combination had satisfactory clinical results in the treatment of ostial LAD lesions. It may be an alternative strategy for treating ostial LAD lesions in patients with contraindication for DES implantation, or patients who cannot endure dual long-term antiplatelet medication, or in elderly patients.

Limitation

The major limitations of this study were its retrospective design, the sample of both arms was smaller and the

angiographic follow-up rate was relative lower, which may weaken the power of the conclusion. These results should not necessarily apply to all patients with ostial LAD lesions.

References

1. Brown R, Kochar B, Maniet ER, et al. Effects of coronary angioplasty using progressive dilation on ostial stenosis of the left anterior descending artery. *Am J Cardiol.* 1993;71:245–247.
2. Park SJ, Lee CW, Hong MK, Kim JJ, Park SW. Stent placement for ostial left anterior descending coronary artery stenosis acute and long-term (2-year) results. *Catheter Cardiovasc Interv.* 2000;49:267–271.
3. Tsagalou E, Stankovic G, Iakovou I, et al. Early outcome of treatment of ostial de novo left anterior descending coronary artery lesions with drug-eluting stents. *Am J Cardiol.* 2006;97(2):187–191.
4. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med.* 2003;349(14):1315–1323.
5. Stone GW, Ellis SG, Cox DA, et al; TAXUS-IV Investigators. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med.* 2004;350(3):221–231.
6. Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. *J Am Coll Cardiol.* 2006;48(12):2584–2591.
7. Mauri L, Hsieh WH, Massaro JM, et al. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med.* 2007;356(10):1020–1029.
8. Chen JL, Gao RL, Yang YJ, et al. Evaluation on the safety and efficacy of cutting balloon (Chinese). *Chin J Cardiol.* 2002;(30):263–264.
9. Ajani AE, Kim HS, Castagna M, et al. Clinical utility of the cutting balloon. *J Invasive Cardiol.* 2001;13:554–557.
10. Simonton CA, Leon MB, Baim DS, et al. 'Optimal' directional coronary atherectomy: final results of the Optimal Atherectomy Restenosis Study (OARS). *Circulation.* 1998;97(4):332–339.
11. Zampieri P, Colombo A, Almagor Y, Maiello L, Finci L. Results of coronary stenting of ostial lesions. *Am J Cardiol.* 1994;73(12):901–903.
12. Muramatsu T, Tsukahara R, Ho M, et al. Efficacy of cutting balloon angioplasty for lesions at the ostium of the coronary arteries. *J Invasive Cardiol.* 1999;11(4):201–206.
13. Inoue T, Sakai Y, Hoshi K, et al. Lower expression of neutrophil adhesion molecule indicates less vessel wall injury and might explain lower restenosis rate after cutting balloon angioplasty. *Circulation.* 1998;97:2511–2518.