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Letter to the Editor

Safety and effectiveness of sirolimus-eluting stent implantation for in-stent restenosis of the unprotected left main coronary artery ☆

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Abstract

The present study examined the alternative treatment of sirolimus-eluting stent (SES) implantation for in-stent restenosis (ISR) of the unprotected left main coronary artery (LMCA). Twelve patients underwent SES deployment for bare-metal ISR in the LMCA. ISR were 24±11 mm in length and located at the ostial ($n=1$) and distal ($n=11$) portion of LMCA. Bifurcation lesions were treated with one of three techniques: the stent crossing the left circumflex artery ($n=7$), kissing stenting ($n=2$) or the Crush technique ($n=2$). All procedures were performed using intravascular ultrasound guidance. Periprocedural CK-MB elevation ≥3 times normal occurred in 2 patients. There were no cases of significant narrowing in the left circumflex artery after the procedure. At the one-year follow-up, one patient died and there were no incidents of myocardial infarction or target lesion revascularization. The present study suggests that SES implantation may be a feasible therapeutic option for treating ISR in unprotected LMCA.

Keywords: Left main coronary artery; In-stent restenosis; Sirolimus-eluting stent

While bypass surgery is generally the treatment of choice for in-stent restenosis (ISR) of the unprotected left main coronary artery (LMCA), some patients have been successfully treated using repeat intervention [1–8]. The present report describes sirolimus-eluting stent (SES) (Cypher, Cordis, Johnson and Johnson Corp, Miami, Florida) implantation for ISR at the unprotected LMCA in a very small cohort of patients.

1. Methods

Among the 140 patients who underwent elective bare metal stenting for de novo unprotected LMCA stenosis, ISR developed in 37 patients. Twelve of these 37 ISR were treated by SES implantation. The inclusion criteria were ISR (diameter stenosis >50%) in an unprotected LMCA, history of angina or documented myocardial ischemia, normal left ventricular function, ISR after single bare-metal stenting, and informed written consent. ISR after complex procedures such as kissing-, Y-, or T-stenting, totally occluded ISR, or a left ventricular ejection fraction ≤40% were excluded. Additionally, patients with contraindications for antiplatelets or sirolimus were also excluded.

The procedures for ISR at the LMCA were similar to those for de novo LMCA stenosis [6,9–11]. During the procedure, all patients received unfractionated heparin to maintain an activated clotting time of ≥250 s. All patients received aspirin indefinitely and a loading dose of 300 mg clopidogrel followed by 75 mg daily for 6 months. In addition, 200 mg cilostazol was also administered as a loading dose, followed by 100 mg twice daily for 1 month [12].

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The incidences of death, non-fatal Q wave myocardial infarction and repeat revascularization were evaluated during the follow-up. Repeat angiography was routinely performed at 6 months or earlier if clinically indicated. Angiographic results were analyzed with an on-line quantitative angiographic analysis system (CASS, Pie Medical, Netherlands). The angiographic restenosis was defined as a diameter stenosis ≥50% in the stented segment or the LCx at the follow-up. An untreated diminutive LCx with a ≥50% diameter stenosis post-procedure and at the follow-up was not considered restenosed.

2. Results

The mean age was 57±14 years old, with 10 (83%) male, 5 smokers, 3 hypertensives, and 2 diabetics. Seven patients presented with stable angina. Other than 1 focal narrowing of the ostium, 11 had diffuse ISR (9 diffuse intrastent, 2 proliferative) according to Mehran's classification [13]. The 11 ISR involving bifurcation were treated by stenting across the LCx (n=7), kissing stenting (n=2), or the Crush technique (n=2). The mean lesion length and the stented segment length were 24±11 mm and 28±12 mm, respectively. The mean number of SES per lesion was 1.6±0.5. Final kissing balloon dilation was performed in 7 cases: routinely attempted in all cases of kissing stenting (n=2) and Crush technique (n=2); selectively performed in 3 cases with significant compromise of the LCx after stenting across it. It was not needed in the others due to diminutive LCx or no development of significant LCx narrowing. More than half of the patients (58.3%) underwent IVUS-guided extreme overdilation with a balloon larger than the nominal stent size after SES deployment. Neither the intra-aortic balloon pump nor glycoprotein IIb/IIIa inhibitors were used. There was no in-hospital death, stent thrombosis, Q-wave myocardial infarction or urgent bypass surgery. Periprocedural CK-MB elevation ≥3 times normal occurred in two patients with ISR in the distal bifurcation, and these were treated with the Crush technique.

During the follow-up (11.9±8.2 months), there was one death. He was a 74-year-old with ISR in the bifurcation, in whom 2 SES had been deployed from the LMCA ostium to the mid portion of the left anterior descending artery across the LCx. Eighteen months later, he underwent an endoscopic polypectomy and discontinued taking aspirin at his discretion. He subsequently died in his sleep. Of the others, there were no incidents of myocardial infarction or target lesion revascularization. Follow-up angiography was performed in 9 patients (Table 1). The remaining patients refused to undergo angiography and had no symptom of angina. There were one recurrent restenosis at the LCx ostium, which had been treated using the Crush technique. The patient with re-ISR was discharged without further intervention, and has remained asymptomatic.

Table 1
Quantitative angiographic analysis results

Follow-up angiography, n (%)	9 (75.0%)
Left main artery	
Proximal reference diameter, mm	3.88±0.59
Minimal luminal diameter, mm	
Before procedure	1.31±0.41
After procedure	3.47±0.63
At follow-up	3.35±0.67
Acute gain, mm	2.15±0.39
Late loss, mm	0.23±0.40
Restenosis	0 (0%)
Left anterior descending artery	
Distal reference diameter, mm	2.84±0.56
Minimal luminal diameter, mm	
Before procedure	0.92±0.42
After procedure	2.99±0.34
At follow-up	2.85±0.47
Acute gain, mm	2.08±0.57
Late loss, mm	0.15±0.25
Restenosis	0 (0%)
Left circumflex artery	
Distal reference diameter, mm	2.83±0.57
Minimal luminal diameter, mm	
Before procedure	1.82±0.92
After procedure	2.93±0.74
At follow-up	2.32±0.84
Acute gain, mm	0.92±0.73
Late loss, mm	0.60±0.70
Restenosis	1 (11.1%)
Overall restenosis	1 (11.1%)

All measurements were performed in the stented segment.

3. Discussion

The present study demonstrated SES implantation was technically feasible in highly selected patients with ISR in the unprotected LMCA and normal left ventricular function. Despite concerns about the complexity associated with performing interventions in restenotic lesions, this study showed 100% of device success. It also found that long term outcomes were somewhat favorable, and there were no episodes of repeat revascularization for one-year post-intervention. These results were comparable to earlier randomized trials on the use of SES for ISR, which were excluded LMCA ISR [14,15]. Furthermore, these were not inferior to those for de novo LMCA lesions [10,16]. Although this study was not sufficiently powered to show that SES use could be extended to the treatment of ISR in the unprotected LMCA, it might provide valuable information on its potential as an alternative therapeutic option in selected patients.

The late loss for the LCx was approximately 0.60 mm in this study. Considering small population, one episode of restenosis at the LCx may influence overestimation of the late loss. In present study, a relatively high incidence of periprocedural myocardial infarction may represent the presence of multiple stents and the worst lesion characteristics, with subsequent complex procedures.

One patient died 18 months after intervention. This patient had a combination of circumstances contributed to a

thrombotic event, including aspirin discontinuation, complex lesion characteristics, and a long stented length requiring 2 SES. Late stent thrombosis might be suggested as one of a probable cause of death. It deserves special emphasis on the necessity of continued antiplatelet therapy in SES implantation.

The present study had some limitations. First, it was a single-center, non-randomized observational study in highly selected patients with extremely limited number. Second, the follow-up duration was relatively short. Thus, while the present data might be a little bit promising, these results should not necessarily apply to all patients with ISR after percutaneous treatment of unprotected LMCA.

References

[1] Silvestri M, Barragan P, Sainsous J, et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. J Am Coll Cardiol 2000;35:1543–50.
[2] Park SJ, Hong MK, Lee CW, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. J Am Coll Cardiol 2001;38:1054–60.
[3] Black A, Cortina R, Bossi I, Choussat R, Fajadet J, Marco J. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. J Am Coll Cardiol 2001;37:832–8.
[4] Tan WA, Tamai H, Park SJ, et al. Long-term clinical outcomes after unprotected left main trunk percutaneous revascularization in 279 patients. Circulation 2001;104:1609–14.
[5] Takagi T, Stankovic G, Finci L, et al. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. Circulation 2002;106:698–702.
[6] Park SJ, Lee CW, Kim YH, et al. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. Am J Cardiol 2002;90:374–8.
[7] Park SJ, Park SW, Hong MK, et al. Long-term (three-year) outcomes after stenting of unprotected left main coronary artery stenosis in patients with normal left ventricular function. Am J Cardiol 2003;91:12–6.
[8] Hu FB, Tamai H, Kosuga K, et al. Intravascular ultrasound-guided directional coronary atherectomy for unprotected left main coronary stenosis with distal bifurcation involvement. Am J Cardiol 2003;92:936–40.
[9] Park SJ, Park SW, Hong MK, et al. Stenting of unprotected left main coronary artery stenosis: immediate and late outcomes. J Am Coll Cardiol 1998;31:37–42.
[10] Park SJ, Kim YH, Lee BK, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. J Am Coll Cardiol 2005;45:351–6.
[11] Colombo A, Stankovic G, Orlic D, et al. Modified T-stenting technique with crushing for bifurcation lesions: immediate results and 30-day outcome. Catheter Cardiovasc Interv 2003;60:145–51.
[12] Lee SW, Park SW, Hong MK, et al. Triple versus dual antiplatelet therapy after coronary stenting impact on stent thrombosis. J Am Coll Cardiol 2005;46:1833–7.
[13] Mehran R, Dangas G, Abizaid AS, et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcomes. Circulation 1999;100:1872–8.
[14] Kastrati A, Mehilli J, von Beckerath N, et al. Sirolimus-eluting stent or paclitaxel-eluting stent vs balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. JAMA 2005;293:165–71.
[15] Neumann FJ, Desmet W, Grube E, et al. Effectiveness and safety of sirolimus-eluting stents in the treatment of restenosis after coronary stent placement. Circulation 2005;111:2107–11.
[16] Arampatzis CA, Lemos PA, Hoye A, et al. Elective Sirolimus-eluting stent implantation for left main coronary artery disease: six month angiographic follow-up and 1-year clinical outcome. Catheter Cardiovasc Interv 2004;62:292–6.