

# Long-term outcomes of simple crossover stenting from the left main to the left anterior descending coronary artery

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**Background/Aims:** Although complex bifurcation stenting in patients with non-left main (LM) bifurcation lesions has not yielded better clinical outcomes than simpler procedures, the utility of complex bifurcation stenting to treat LM bifurcation lesions has not yet been adequately explored.

**Methods:** In the present study, patients who underwent LM-to-left anterior descending (LAD) coronary artery simple crossover stenting to treat significant de novo distal LM or ostial LAD disease, in the absence of angiographically significant ostial left circumflex (LCX) coronary artery disease, were consecutively enrolled. The frequencies of 3-year major adverse cardiovascular events (MACEs; cardiac death, myocardial infarction, and target lesion revascularization), were analyzed.

**Results:** Of 105 eligible consecutive patients, only 12 (11.4%) required additional procedures to treat ostial LCX disease after main vessel stenting. The mean percentage diameter of ostial LCX stenosis increased from  $22.5\% \pm 15.2\%$  to  $32.3\% \pm 16.3\%$  ( $p < 0.001$ ) after LM-to-LAD simple crossover stenting. The 3-year incidence of MACEs was 9.7% (cardiac death 2.2%; myocardial infarction 2.2%; target lesion revascularization 8.6%), and that of stent thrombosis 1.1%. Of seven cases (7.5%) requiring restenosis, pure ostial LCX-related repeat revascularization was required by only two.

**Conclusions:** Simple crossover LM-to-LAD stenting without opening of a strut on the LCX ostium was associated with acceptable long-term clinical outcomes.

**Keywords:** Percutaneous coronary intervention; Coronary stenosis; Stents; Outcome

## INTRODUCTION

Percutaneous coronary intervention (PCI) using drug-eluting stents (DESs) is commonly used to treat bifurcation coronary artery disease [1-3]. Use of two stents (a complex strategy) was not associated with better clinical outcomes than one-stent strategies when

non-left main (LM) bifurcation PCI was performed [4-6]. Therefore, provisional strategy is generally used to treat non-LM bifurcation. Also, the routine use of final kissing balloon dilation in patients with non-LM bifurcation lesions, treated via main vessel stenting, did not yield clinical outcomes better than those afforded in the absence of such dilation [5,7]. However, few data

on treatment of LM bifurcation lesions are available. One pilot study showed convincingly that fraction flow reserve (FFR)-guided PCI in the left circumflex (LCX) coronary artery, performed after LM-to-left anterior descending (LAD) coronary artery simple crossover stenting, reduced the need for additional procedures [8]. Therefore, the aim of the present study was to evaluate the long-term safety and efficacy of LM-to-LAD simple crossover stenting, without opening of a strut on the LCX ostium.

## METHODS

### Study population

Patients with *de novo* distal LM or ostial LAD disease, but without significant ostial LCX disease (visually estimated stenosis < 50% of the arterial diameter), and with Medina classification scores of 1,1,0/1,0,0/0,1,0, were consecutively enrolled from April 2004 to June 2009 when they attended the Keimyung University Dongsan Medical Center. We excluded patients requiring additional bifurcation procedures (performed at the discretion of attending physicians) because of significant ostial LCX jailing evident after predilation of the main vessel or simple crossover stenting. A patient was not eligible if she/he had undergone primary or emergent PCI intervention to treat acute coronary syndrome; had undergone previous coronary artery bypass graft surgery; exhibited severe left ventricular dysfunction (left ventricular ejection fraction < 35%); had a major life-threatening illness; or exhibited contraindications to aspirin or clopidogrel.

### Procedure and outcomes

PCI was performed using standard interventional techniques. Antiplatelet and antithrombotic agents were prescribed in line with current PCI guidelines [9]. Implanted stents were commercially available DESs in all cases (sirolimus-eluting stents in 56 cases [60%]; everolimus-eluting stents in 14 [15%]; paclitaxel-eluting stents in 12 [13%]; and zotarolimus-eluting stents in 11 [12%]). All coronary angiograms were analyzed using standard definitions and measurements, following American Heart Association guidelines [10]. A guiding catheter was used for calibration and in performance

of edge-detection quantitative coronary angiography (Quantcor QCA, Pie Medical, Maastricht, the Netherlands). An experienced operator performed QCA on three segments (the proximal main vessel, the distal main vessel, and the side branch). Variables measured included the reference diameter, the minimal lumen diameter, and the extent of stenosis (% vessel diameter).

The primary outcome was a composite of major adverse cardiac events (MACEs), defined as cardiac death, myocardial infarction, and any target lesion revascularization (TLR), by 3 years after the index procedure. Death was defined as all-cause mortality. Myocardial infarction was defined as a 3-fold or greater elevation of the creatine kinase-MB level, or new Q-waves evident in two or more contiguous electrocardiographic leads. Each TLR included target vessel PCI and bypass surgery of the lesion of interest, thus LM-to-LAD or ostial LCX, when symptoms and/or signs of ischemia were evident. Clinical follow-up was performed by physicians via medical chart review or telephone interview. Angiographic follow-up data were gathered at the discretion of attending physicians (thus not routinely).

### Statistical analysis

Data are expressed as mean  $\pm$  SD for continuous variables and as percentages for discrete variables. Differences between continuous variables were compared using Student *t* test or by analysis of variance. Categorical variables were compared using chi-square tests, non-parametric chi-square tests, or Fisher exact test, as appropriate. Cumulative incidences of MACEs were estimated using the Kaplan-Meier method. All calculated *p* values were two-sided, and a difference was considered statistically significant at  $p < 0.05$ . All statistical analyses were performed using the SPSS version 20 (IBM Co., Armonk, NY, USA).

## RESULTS

Of the 105 consecutive patients with *de novo* distal LM or ostial LAD disease, but without significant ostial LCX disease, 12 (11.4%) underwent additional procedures in the LCX ostium after main vessel stenting. Therefore, final follow-up analysis was performed on only 93 patients. Patient baseline clinical characteristics,

**Table 1. Baseline characteristics of all patients (n = 93)**

Characteristic	Value
Age, yr	62.0 ± 9.5
Male gender	69 (74.2)
History	
Diabetes	26 (28.0)
Hypertension	44 (47.3)
Current smoker	39 (41.9)
Hypercholesterolemia	33 (35.5)
Previous PCI	9 (9.7)
Left ventricular ejection fraction, %	58.6 ± 10.9
ACS presentation	39 (41.9)
Extent of disease	
Left main artery	51 (54.2)
Left anterior descending coronary artery	70 (75.2)
Left circumflex coronary artery	11 (11.8)
Right coronary artery	22 (23.7)
Medina classification of the left main artery	
1, 1, 1	25 (26.9)
1, 0, 0	26 (28.0)
0, 1, 0	42 (45.2)

Values are presented as mean ± SD or number (%).

PCI, percutaneous coronary intervention; ACS, acute coronary syndrome.

angiographic characteristics, and quantitative coronary angiographic results, are summarized in Tables 1 and 2. Mean patient age was 62.0 ± 9.5 years (males, 75.5%), and 28.0% had diabetes. The mean left ventricular ejection fraction was 58.6% ± 10.6%. On baseline angiography, the distal reference vessel diameter of the LCX was 3.1 ± 0.5 mm. The mean stenosis of the ostial LCX (percentage of vessel diameter) increased after LM-to-LAD crossover stenting, from 22.5% ± 15.2% to 32.3% ± 16.3% ( $p < 0.001$ ).

Three-year follow-up clinical data were obtained for all patients. Angiographic follow-up data were available for 73 (78.5%). During the follow-up period, the 3-year MACE rate was 9.7% (cardiac death 2.2%, myocardial infarction 2.2%, and TLR 8.6%) (Fig. 1). One case (1.1%) of stent thrombosis was noted. Of seven restenotic cases, pure ostial LCX-associated repeat revascularization was required by only two. The relevant locations are shown in a schematic bifurcation diagram (Fig. 2). Event-free

**Table 2. Procedural results (n = 93)**

Variable	Value
Preprocedure	
LM-to-LAD	
Reference vessel diameter, proximal, mm	3.7 ± 0.4
Reference vessel diameter, distal, mm	3.2 ± 0.5
Minimal lumen diameter, mm	0.6 ± 0.3
Stenosis, % diameter	82.2 ± 9.6
LM-to-LCX	
Reference vessel diameter, distal, mm	3.1 ± 0.5
Minimal lumen diameter, mm	2.4 ± 0.7
Stenosis, % diameter	22.5 ± 15.2
Lesion length, mm	20.7 ± 5.8
LM procedure	
Stent length, mm	22.6 ± 5.3
Stent diameter, mm	3.5 ± 0.3
Procedures for other lesions	
LAD	34 (36.6)
LCX	19 (20.4)
RCA	11 (11.8)
No. of stents placed, except in LM	
Single	24 (25.8)
Multiple	21 (22.6)
Postprocedure	
LM-to-LAD	
Minimal lumen diameter, mm	3.2 ± 0.4
Stenosis, % diameter	10.2 ± 4.0
LM-to-LCX	
Minimal lumen diameter, mm	2.1 ± 0.7
Stenosis, % diameter	32.3 ± 16.3

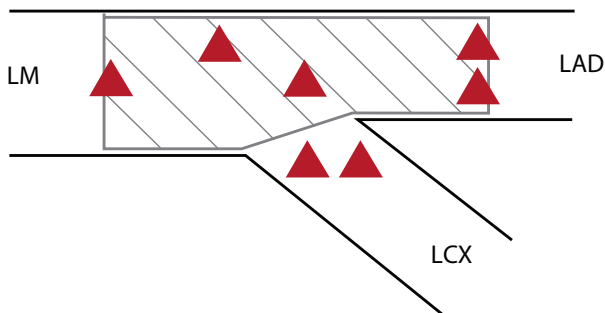
Values are presented as mean ± SD or number (%).

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

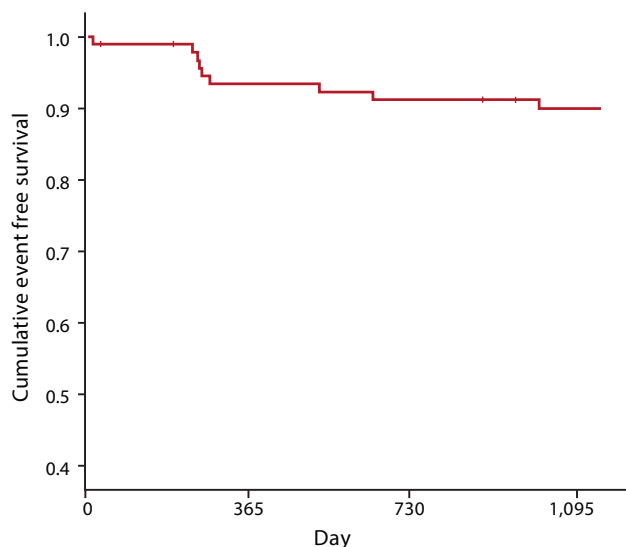
survival is shown in Fig. 3. Upon univariate analysis, all of clinical presentation, left ventricular ejection fraction, reference vessel diameter, and stent size, were associated with MACEs. However, no independent predictor of MACE was evident upon multivariate regression analysis.



**Figure 1.** Incidences of 3-year major adverse cardiac events and stent thrombosis. MI, myocardial infarction; TLR, target lesion revascularization; MACE, major adverse cardiovascular event.



**Figure 2.** Locations of restenosis. LM, left main coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex artery.



**Figure 3.** Three-year Kaplan-Meier event-free survival after simple left main crossover stenting.

## DISCUSSION

The major findings of our current study were: 1) the long-term outcomes of LM-to-LAD simple crossover stenting in patients with *de novo* distal LM or ostial LAD disease (without significant ostial LCX disease) were good; and 2) it was safe to not open a strut on the LCX ostium after crossover stenting. Thus, additional complex LM bifurcation strategies increasing the risk of procedural complications are not necessary. Our results should be confirmed in future large-scale randomized studies.

Coronary bifurcation lesions are regarded as challenging by coronary intervention specialists even in the present era of DESs [11,12]. The unique characteristics of bifurcation lesions render complex procedures no more effective than simple procedures, and the restenosis rate at the ostium of the side branch is high after performance of complex procedures [2,5,13]. A better understanding of this lesional subset is required before complex procedures are applied. A provisional approach, thus selective side-branch intervention after main vessel stenting, is currently regarded as preferred when non-LM bifurcation lesions require treatment [5,14]. Such a strategy was supported by an elegant series of investigations of FFR-guided interventional strategies used to treat jailed side branches [11,15,16]. The cited studies imparted two important messages. First, angiographic evaluation frequently overestimated the functional severity of a jailed side branch lesion. Second, the functional status of such lesions was stable during follow-up. However, use of such a strategy to treat a jailed LCX after LM-to-LAD simple crossover stenting was not explored. Such work was required, because a large amount of myocardium may be in jeopardy after LCX jailing. Coronary Bifurcation Stenting (COBIS) registry II data demonstrate the possible harmful effects associated with use of two-stent strategies to treat LM bifurcation lesions [17]. A small pilot study revealed discrepancies between angiographic stenosis and FFR data on jailed LCX lesions, and that use of an FFR-guided PCI strategy to treat the jailed LCX reduced the need for additional PCI [8]. However, the long-term safety of a residual strut placed on the LCX ostium was not assured. In our current study, we explored the long-term clinical outcomes of LM-to-LAD simple crossover

stenting, without opening of a strut on the LCX ostium. The 3-year MACE rate was acceptable, being 9.7%.

Another important finding is that no additional procedure was required by 88.6% of patients (93/105) who underwent successful simple crossover stenting. Only 11.4% patients required an additional kissing balloon dilation procedure (for carinal modification) after simple crossover stenting, or a two-stent procedure after LM-to-LAD stenting. Therefore, as was previously found in studies on non-LM bifurcation PCI, the use of a simple strategy reduces the need for additional procedures to treat LM bifurcations. Such lesions are not only complex, but are also associated with poor prognoses.

Although the requirement for additional procedures was lower than that of a previous study [18], a careful approach is warranted when using provisional LM bifurcation procedures. Such lesions may have a greater plaque burden, and be at higher risk of carinal shifting, than non-LM bifurcation lesions [16,19].

Our present study had several limitations. First, although over 100 patients with a specific subset of lesions were enrolled, no single-center observational study is entirely free from selection bias. We excluded patients who received any PCI as an index procedure to treat LCX. As our study population was restricted to those exhibiting good angiographic morphology, caution is required when interpreting our results, which need confirmation in a future randomized study with higher numbers of patients. Also, although we collected 3-year clinical follow-up data, the longer-term safety of our chosen strategy is not assured. Finally, we did not perform additional imaging, or gather physiological data, which would have yielded additional valuable information.

In conclusion, although no strut on the ostial LCX was opened after LM-to-LAD simple crossover stenting, such a strategy was safe and effective in the long term.

### Conflict of interest

No potential conflict of interest relevant to this article was reported.

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## KEY MESSAGE

1. The long-term clinical outcomes of left main-to-left anterior descending coronary artery simple crossover stenting, without opening of a strut on the left circumflex coronary ostium, were acceptable.
2. Use of such a strategy reduces the need for additional complex left main bifurcation procedures, which may increase the risk of complications.

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