

A new sequential two-stent strategy for treating true distal left main trifurcation lesion

Yu-Xiang DAI*, Chen-Guang LI*, Jia HUANG*, Ren-De XU, Shu-Fu CHANG, Hao LU, Dao-Yuan REN, Lei GE, Ju-Ying QIAN, Feng ZHANG✉, Jun-Bo GE✉

Department of Cardiology, Zhongshan Hospital, Fudan University, Shanghai Institute of Cardiovascular Diseases, Shanghai, China

*The authors contributed equally to this manuscript

✉ Correspondence to: zhang.feng@zs-hospital.sh.cn; jbge@zs-hospital.sh.cn

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The incidence of significant left main (LM) coronary artery stenosis identified by coronary angiography was 5%–17.5% in various clinical presentations; about 80% of stenosis involved the LM bifurcation (LMB).^[1] Although percutaneous coronary intervention (PCI) is an appropriate alternative to coronary artery bypass graft in LM disease with low-to-intermediate anatomical complexity,^[2] PCI for LMB lesions remains the most technically challenging for interventional cardiologists with higher rates of acute periprocedural complications and higher risk of long-term major adverse cardiac events in the era of drug-eluting stent (DES).

The optimal technique for LMBs remains uncertain, particularly in the case of LM trifurcation (LMT), a specific type of bifurcation lesions with a significant ramus intermedius (RI). In general, initial provisional stenting technique is considered the standard method for simple LMBs on the basis of the criteria in the DEFINITION study,^[3] while two stents strategy should be considered for complex LMBs.^[4] The true LMT with three or more branches are highly challenging for interventional cardiologists because of the extreme complex anatomical features and poor long-term prognosis.^[5] To date, the data for PCI in true LMTs are limited and the optimal strategy remains unknown.

From January 2017 to June 2018, eighteen patients with a true distal LMT lesion (Medina type: 1,1,1,1 or 0,1,1,1), reference vessel diameter (RVD) of the left circumflex artery (LCX) > 2.5 mm and

RVD of RI \geq 2 mm at baseline angiography were enrolled in our study. Among these patients, all lesions met the criteria of complex LMBs in the DEFINITION study (LCX ostial stenosis \geq 70% with a lesion length \geq 10 mm). Baseline clinical and angiographic characteristics are shown in Table 1. Seven patients (38.9%) were left coronary dominant and fifteen patients (83.3%) without right-to-left collaterals were considered to have unprotected LMT lesions. The mean SYNTAX I and SYNTAX II scores were 29.1 ± 1.9 and 25.9 ± 5.0 , respectively. The RVD of LM, left anterior descending artery (LAD), LCX and RI was 4.5 ± 0.5 mm, 3.5 ± 0.3 mm, 2.8 ± 0.3 mm and 2.2 ± 0.2 mm, respectively. Meanwhile, the plaque burdens of distal LM, ostial LAD, LCX and RI were $64.4\% \pm 7.0\%$, $74.9\% \pm 7.8\%$, $65.1\% \pm 7.6\%$ and $41.6\% \pm 10.7\%$, respectively.

All patients were treated with a sequential two-stent strategy combined with double-kiss crush (DK-crush) and jailed balloon technique under intravascular ultrasound (IVUS) guidance. Detailed description of the strategy: (1) after wiring to distal LAD, LCX and RI, IVUS was performed for confirmation of each vessel; (2) LAD and LCX were predilated with compliant balloons; (3) LCX stent was implanted protruding minimally into the LM with a balloon placed at ostial of LAD for crush; (4) LCX stent was crushed with a large non-compliant balloon; (5) the LCX was then rewired through a proximal stent cell; (6) first kissing balloon inflation (KBI) was performed after rewiring to LCX; (7) LM-LAD stent was implanted with a jailed semi-inflated bal-

Table 1 Baseline clinical and angiographic characteristics of patients with true left main distal trifurcation lesion.

Clinical characteristics		Angiographic characteristics	
Age, yrs	57.6 ± 8.5	Dominant left coronary artery	7 (38.9%)
Male	15 (83.3%)	Unprotected left main coronary artery	15 (83.3%)
Body mass index, kg/m ²	25.2 ± 2.4	SYNTAX I score	29.1 ± 1.9
Hypertension	15 (83.3%)	SYNTAX II score	25.9 ± 5.0
Diabetes mellitus	6 (33.3%)	Medina type: 1,1,1,1	16 (88.9%)
Hypercholesterolemia	10 (55.6%)	Pre-reference vessel diameter by IVUS, mm	
Smoker	12 (66.7%)	LM	4.5 ± 0.5
Acute myocardial infarction	1 (5.6%)	LAD	3.5 ± 0.3
Old myocardial infarction	1 (5.6%)	LCX	2.8 ± 0.3
Unstable angina	10 (55.6%)	RI	2.2 ± 0.2
History of coronary artery bypass graft	0	Pre-plaque burden, %	
Left ventricular ejection fraction, %	57.8 ± 6.5	Distal LM	64.4 ± 7.0
Estimated glomerular filtration rate, mL/min per 1.73 m ²	79.11 ± 13.99	Ostium of LAD	74.9 ± 7.8
Hemoglobin A1c, %	5.8 ± 1.0	Ostium of LCX	65.1 ± 7.6
C-reactive protein, mg/L	6.9 (3.4–9.8) [*]	Ostium of RI	41.6 ± 10.7

Data are presented as means ± SD or n (%). ^{*}Presented as median (interquartile range). IVUS: intravascular ultrasound; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main; RI: ramus intermedius.

loon in RI; (8) the LCX then was rewired again through a proximal stent cell; (9) alternating post-dilations with non-compliant balloons to LAD and LCX were performed followed by final KBI; and (10) finally, the proximal optimization technique (POT) was performed with a short non-compliant balloon post-dilating just proximal to the carina (Figures 1 & 2).

DESs were implanted in all patients and mean total stent length was 61.3 mm ± 5.4 mm. Minimum stent area (MSA) of LM, polygon of confluence, LAD and LCX measured by IVUS were 13.0 ± 2.2 mm², 11.2 ± 1.7 mm², 9.7 ± 1.4 mm² and 5.8 ± 0.8 mm², respectively. Angiographic success was achieved in all patients. Clinical follow-up was completed for all patients at discharge and at twelve months, with seventeen patients (94.4%) undergoing angiography at twelve-month follow-up. One patient who had not suffered any cardiac events as assessed by telephone interview and refused to undergo angiographic follow-up. The procedural success rate was 94.4% (17/18) and only one patient was diagnosed with periprocedural myocardial infarction. The rate of target lesion failure (TLF) was 5.6% (1/18), with one case of ischemia-driven revascularization at LCX ostium by angioplasty with drug-eluting balloon and final kissing.

Because distal LMBs is the largest bifurcation of the coronary tree, stenting techniques should consider the risk of potential complications to the large branches such as acute occlusion and long-term adverse outcomes of TLF. Stenting strategy of distal LMT is even more challenging because of their more complex anatomical features. Ielasi, *et al.*^[5] reported that the rate of long-term major adverse cardiac events was 37.7% in forty true LMT disease at three-year follow-up, while Kubo, *et al.*^[6] reported a 14.5% incidence of TLF which was even higher in the multi-stent group (31.3%), in a series of seventy-two patients with trifurcation lesions (44.4% true trifurcation) at three-year follow-up. However, in these studies, IVUS guidance was used in 65% and 77.8% of cases, respectively. The strategy for two or multiple stents consisted of several kinds of technique including V-stent, T-stent, Culotte and Crush. The POT was not mandatory and only 41.7% of cases was performed in Kubo's study.^[6] Thus, the limited knowledge on the optimal PCI strategy resulted in the poor long-term outcome of true LMTs.^[5] In our study, the primary endpoint occurred in 5.6% of patients at one-year follow-up, which seem much lower than other LMT studies and comparable to DK-crush two-stent strategy in DKCRUSH-V study.^[7]



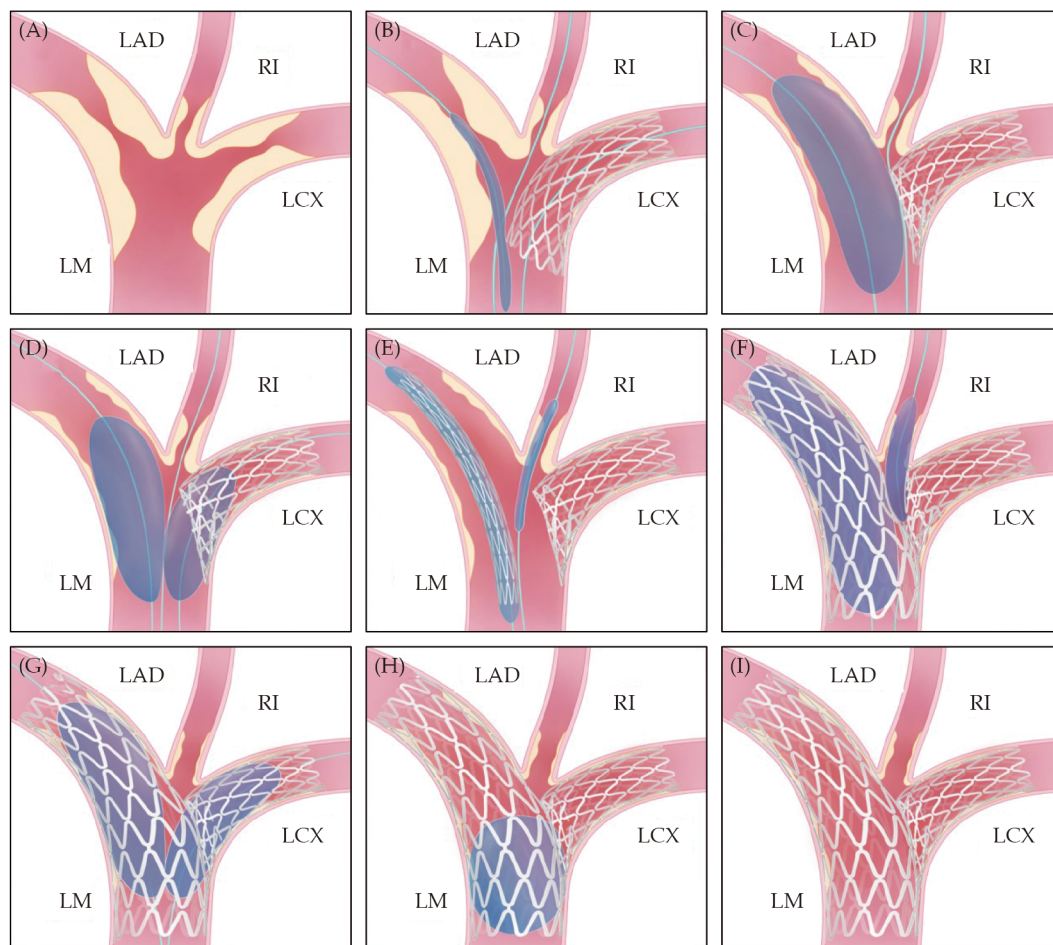


Figure 1 Step by step of the sequential strategy. (A): Patients with true complex distal LM trifurcation lesions (Medina type: 1,1,1,1 or 0,1,1,1) and reference diameter of LCX ≥ 2.5 mm and RI ≥ 2 mm were included; (B): after pre-dilation of LAD and LCX, LCX stent was implanted protruding minimally into the LM with a balloon placed at ostial of LAD for crush; (C): LCX stent was crushed with a large non-compliant balloon; (D): after the LCX rewired through a proximal stent cell, first KBI was performed; (E & F): LM-LAD stent was implanted with a jailed semi-inflated balloon in RI; (G): after LCX rewired again through a proximal stent cell, alternating post-dilations with non-compliant balloons to LAD and LCX were performed followed by final KBI; (H): final proximal optimization technique was performed with a short non-compliant balloon post-dilating just proximal to the carina; and (I): final result. KBI: kissing balloon inflation; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main; RI: ramus intermedius.

For complex bifurcation lesions following to the DEFINITION criteria,^[3] one-stent strategy resulted in a higher rate of in-hospital myocardial infarction and one-year cardiac death compared with two-stent strategy. Thus, in current practice, LMBs are recommended to be classified as simple or complex to stratify one-stent or two-stent strategy according to the DEFINITION criteria. Similar to LMBs, numbers of patients with true LMTs cross over to multi-stent strategy due to acute occlusion, exacerbated stenosis or flow limiting dissection in the side branch (SB) after provisional stenting in previous studies. Even after two-stent strategy with guide-wire protection in the minor SB, a portion of patients suffered from

suboptimal results in the minor SB and had to undergo three-stent techniques. However, the long-term prognosis of LMTs with three-stent strategy are particularly unsatisfactory due to extremely high rates of in-stent restenosis.^[5]

All the patients in our study belonged to complex trifurcation lesions according to the DEFINITION criteria. Therefore, LCXs have higher rate of acute occlusion in one-stent strategy. Furthermore, the RVD of LCX is larger than that of RI, so LCXs should be intervened with stenting rather than RIs in these cases. In the DKCRUSH-III study,^[8] when the LAD-LCX bifurcation angle $> 70^\circ$, DK-crush strategy for the LMBs was superior to the Culotte technique. Therefore,

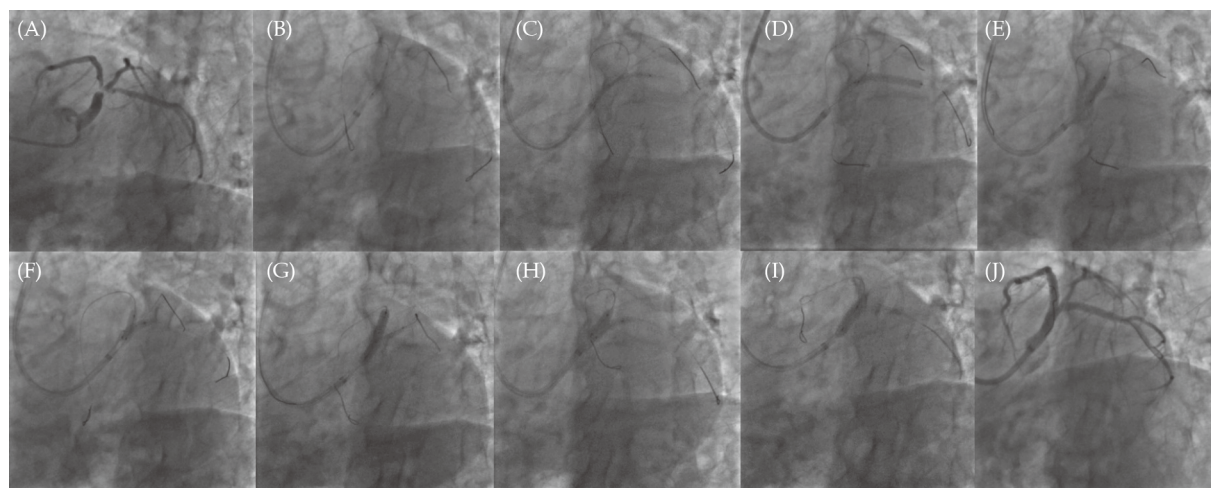


Figure 2 One typical case of the new sequential two-stent strategy. (A): The patient has a true LM trifurcation lesion (Medina type: 1,1,1,1); after wiring to distal LAD, LCX and RI, intravascular ultrasound was performed for confirmation; (B & C): predilation of LAD and LCX with a 2.5 mm × 20 mm compliant balloons; (D): a 3.0 mm × 28 mm DES was implanted in proximal LCX protruding minimally into the LM with a 3.5 mm × 15 mm balloon placed at ostial LAD for crush; (E): LCX stent was crushed with a 3.5 mm × 15 mm non-compliant balloon; (F): first KBI was performed after rewiring to LCX with 3.25 mm × 15 mm and 3.0 mm × 15 mm non-compliant balloons; (G): a 3.5 mm × 24 mm DES stent was implanted in LM-LAD with a 2.0 mm × 15 mm compliant balloon jailed inflated in RI with inflation to 6 atmospheres; (H): after LCX was rewired again through a proximal stent cell, alternating post-dilations with a 3.25 mm × 15 mm and 3.0 mm × 15 mm non-compliant balloons to LAD and LCX were performed followed by final KBI; (I): proximal optimization technique was performed with a 3.75 mm × 8 mm non-compliant balloon; and (J): final result showed thrombolysis in myocardial infarction 3 flow for LAD, LCX and RI. DES: drug-eluting stent; KBI: kissing balloon inflation; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main; RI: ramus intermedius.

for the relatively wider angles between the LAD and LCX in LMTs, DK-crush technique seems the ideal two-stent strategy. More importantly, DK-crush technique was used uniformly instead of Culotte technique to minimize the layers of stents covering the ostium of RI.

The jailed semi-inflated balloon technique when treating LAD and RI bifurcation would provide a high rate of procedural success and preservation of RI blood flow after LM-LAD stenting mainly because it prevents carina or plaque shift into the RI ostium. With the jailed semi-inflated balloon protection in the RIs, all of cases in our study completed revascularization with satisfactory acute result, and no one subjected to three-stent strategy. All patients completed the second KBI in our study, while the second KBI is considered the default strategy for the two-stent strategy because of the benefit in reducing the risk of SBs restenosis and repeat revascularization. However, KBI was shown to have several disadvantages in bench models including elliptical overexpansion and distortion of the main vessel stent with development of malapposition.^[9] Therefore, in our study, the final POT following the second

KBI was performed in all patients. The final POT would improve full expansion, maximal eccentricity and complete apposition of the proximal main vessel stent, which would also reduce the risk of inadvertent abluminal rewiring of the main vessel stent, optimize the final stent geometry and flow dynamics and open the stent cells overlying the SB ostium.^[10,11]

Intravascular imaging plays a key role in preparation and evaluation of intervention of left main coronary artery.^[12] Before intervention, IVUS would provide extra information of lesion severity and atherosclerosis distribution of the trifurcation, reference lumen diameter and length of lesion. After the procedure, IVUS would evaluate geometry of the trifurcation, strut malapposition, stent distortion, as well as associated arterial complication.^[13] Additionally, MSA measured by IVUS was considered to be an important predictor of in-stent restenosis at follow-up. The optimal IVUS-MSA criteria for predicting angiographic restenosis on a segmental basis were 5.0 mm² for the LCX ostium, 6.3 mm² for the LAD ostium, 7.2 mm² for the polygon of confluence, and 8.2 mm² for the proximal LM.^[11] The IVUS-MSA



of all patients in our study met the criteria above, which may account for the relatively low rate of TLF in such complex distal LMTs.

In summary, the new sequential strategy combined with DK-crush and jailed balloon technique for treating true distal LMTs was efficacious and safe. A step-by-step procedure and IVUS guidance are essential to ensure the success rate. A randomized clinical study with a larger study population is warranted to further evaluate long-term clinical outcomes of this strategy.

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