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Original article

Optimal strategy for side branch treatment in patients with left main coronary bifurcation lesions

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ABSTRACT

Introduction and objectives: There are no guidelines regarding the most appropriate approach for provisional side branch (SB) intervention in left main (LM) bifurcation lesions.

Methods: The present prospective, randomized, open-label, multicenter trial compared conservative vs aggressive strategies for provisional SB intervention during LM bifurcation treatment. Although the trial was designed to enroll 700 patients, it was prematurely terminated due to slow enrollment. For 160 non-true bifurcation lesions, a 1-stent technique without kissing balloon inflation was applied in the conservative strategy, whereas a 1-stent technique with mandatory kissing balloon inflation was applied in the aggressive strategy. For 46 true bifurcation lesions, a stepwise approach was applied in the conservative strategy (after main vessel stenting, SB ballooning when residual stenosis > 75%; then, SB stenting if residual stenosis > 50% or there was a dissection). An elective 2-stent technique was applied in the aggressive strategy. The primary outcome was a 1-year target lesion failure (TLF) composite of cardiac death, myocardial infarction, or target lesion revascularization.

Results: Among non-true bifurcation lesions, the conservative strategy group used a smaller amount of contrast dye than the aggressive strategy group. There were no significant differences in 1-year TLF between the 2 strategies among non-true bifurcation lesions (6.5% vs 4.9%; HR, 1.31; 95%CI, 0.35-4.88; *P* = .687) and true bifurcation lesions (17.6% vs 21.7%; HR, 0.76; 95%CI, 0.20-2.83; *P* = .683).

Conclusions: In patients with a LM bifurcation lesion, conservative and aggressive strategies for a provisional SB approach have similar 1-year TLF rates.

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Estrategia óptima para el tratamiento de lesiones en bifurcación del tronco coronario izquierdo

Palabras clave:
Enfermedad del tronco coronario izquierdo
Rama secundaria
Intervención coronaria percutánea
Resultados

RESUMEN

Introducción y objetivos: No hay directrices sobre el tratamiento óptimo de la rama secundaria (RS) en lesiones en bifurcación del tronco coronario izquierdo (TCI).
Métodos: Ensayo clínico aleatorizado, multicéntrico y abierto que comparó una estrategia conservadora frente a una agresiva para el abordaje de la RS durante la intervención percutánea en lesiones bifurcadas del TCI. Aunque se diseñó para incluir a 700 pacientes, se terminó prematuramente debido a la baja tasa de reclutamiento. Se trataron 160 lesiones en bifurcación no verdaderas mediante implante de 1 *stent* sin inflado simultáneo de balones (técnica conservadora) o con la técnica de 1 *stent* con inflado simultáneo de balones obligatorio (estrategia agresiva). En 46 bifurcaciones verdaderas del TCI, se realizó un abordaje escalonado con estrategia conservadora (colocación del *stent* en el vaso principal y dilatación con balón de la RS si la estenosis residual era > 75%, y después implante de *stent* en la RS si la estenosis residual era > 50% o disección). El tratamiento electivo de 2 *stents* se usó como estrategia agresiva. El objetivo primario de fallo en la lesión diana fue el compuesto de muerte cardiaca, infarto de miocardio o revascularización de la lesión diana.
Resultados: Entre las bifurcaciones no verdaderas, en el grupo tratado mediante estrategia conservadora, se utilizó una cantidad de contraste significativamente menor que con la estrategia agresiva. No hubo diferencias en el objetivo primario al año entre las 2 estrategias en las lesiones en bifurcación no verdaderas (el 6,5 frente al 4,9%; HRa = 1,31; IC95%, 0,35-4,88; p = 0,687) y las bifurcaciones verdaderas (el 17,6 frente al 21,7%; HRa = 0,76; IC95%, 0,20-2,83; p = 0,683).
Conclusiones: En pacientes con lesiones del TCI en bifurcación, la estrategia conservadora en el tratamiento provisional de la RS tuvo un riesgo de fallo en la lesión diana al año similar al de una estrategia agresiva.

Abbreviations

FKB: final kissing balloon
LM: left main
MV: main vessel
PCI: percutaneous coronary intervention
SB: side branch
TLF: target lesion failure

INTRODUCTION

Despite recent advances in drug-eluting stents and interventional techniques, percutaneous coronary intervention (PCI) of lesions at bifurcations remains a challenging procedure. Intervention of bifurcation lesions carries a risk of side branch (SB) closure, which can lead to periprocedural myocardial infarction and adverse clinical outcomes.[1] Prior studies have investigated the optimal strategy for bifurcation lesions. The accepted standard treatment for bifurcation lesions is a simple 1-stent technique with a provisional SB approach.[2–4] However, there are limited data regarding left main (LM) bifurcation lesions because most previous studies have been conducted on non-LM bifurcation lesions.

Several observational studies have found that the 1-stent strategy with a provisional SB approach obtains favorable results in LM bifurcation lesions.[5–8] The SMART-STRATEGY study reported that the provisional SB approach was safe and effective in the treatment of 114 patients with a LM bifurcation lesion.[9] However, given the large amount of subtended myocardium in SBs, the need for additional SB dilatation after main vessel (MV) stenting is a challenging issue. Although routine use of a final kissing balloon (FKB) after MV stenting has been discouraged in non-LM bifurcation lesions,[10,11] it has not been established whether routine FKB would be beneficial in the provisional SB approach for LM bifurcation lesions.[12] Therefore, we compared clinical outcomes among patients with a LM bifurcation lesion treated with conservative vs aggressive strategies for SB intervention. In doing so, we sought to determine the optimal criteria for the provisional SB approach.

METHODS

Study design and patients

The SMART-STRATEGY II study was a prospective, randomized, open-label, multicenter trial comparing conservative vs aggressive strategies for provisional SB intervention during LM bifurcation PCI at 15 centers in Korea between March 2013 and December 2016 (ClinicalTrials.gov, NCT01798433). The study protocol was approved by the local institutional review boards. Written informed consent was obtained from all participants. Inclusion criteria were as follows: *a)* age ≥ 20 years; *b)* a LM bifurcation lesion on coronary angiography with a reference diameter of the main branch (left anterior descending artery) and SB (left circumflex artery) ≥ 2.5 mm by visual estimation; *c)* significant myocardial ischemia in the main branch or SB diameter stenosis > 75% or 50%-75% with angina and/or objective evidence of ischemia in the noninvasive stress test; and *d)* patients who voluntarily signed the written informed consent form. Exclusion criteria were as follows: *a)* patients with coronary artery stenosis only in the SB ostium of the LM bifurcation lesion (Medina 0.0.1 lesion); *b)* patients with known hypersensitivity or contraindication to heparin, aspirin, clopidogrel, or biolimus; or *c)* patients who previously underwent stent implantation in the target lesion prior to enrollment. All of the study patients in this trial met the inclusion criteria and none of the exclusion criteria.

Patients were stratified according to whether they had a non-true bifurcation lesion (SB stenosis diameter < 50%) or true bifurcation lesion (SB stenosis diameter ≥ 50%). Patients were then randomized 1:1 to a conservative or aggressive strategy group for provisional SB intervention after MV stenting (figure 1). For

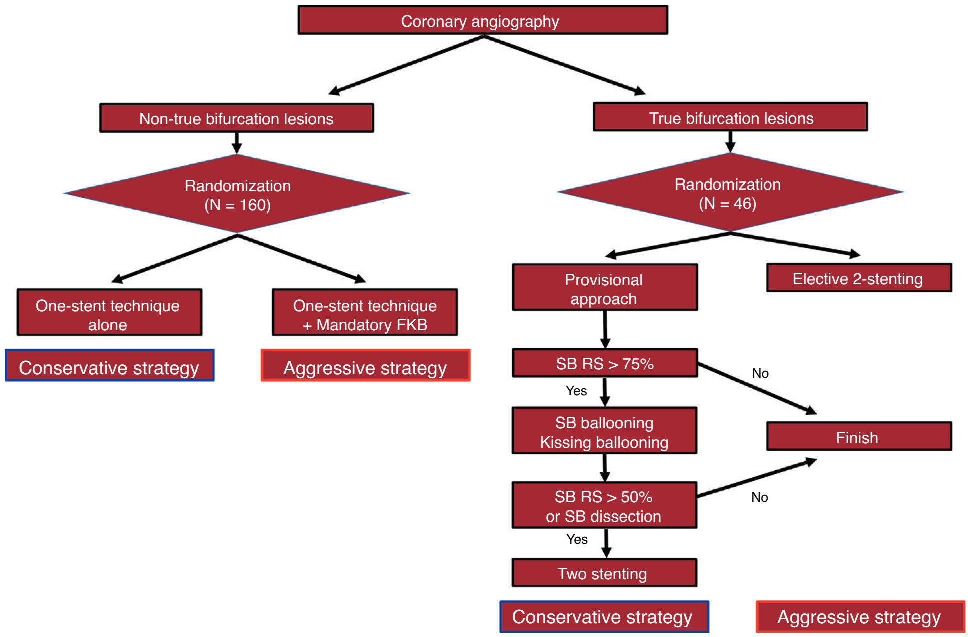

Figure 1. Study protocol. FKB, final kissing balloon; RS, residual stenosis; SB, side branch.

non-true bifurcation lesions, the conservative strategy included MV stenting alone without FKB. The aggressive strategy included MV stenting followed by mandatory FKB. For true bifurcation lesions, the conservative strategy was SB ballooning followed by kissing ballooning for an SB stenosis diameter $\geq$ 75% after MV stenting. SB stenting was only performed when the SB stenosis diameter was $\geq$ 50% or there was a SB dissection. The aggressive strategy included an elective 2-stent approach for the MV and SB. In all cases, the choice of the 2-stenting technique was made at the operator's discretion. Intravascular ultrasound use was recommended, but not mandatory. For the stent implantation, the BioMatrix stent (Biosensors Interventional Technologies Pte. Ltd, Singapore) was used except when it was clinically unavailable. After the index procedure, measurement of the myocardial band fraction of creatine kinase was mandatory.

Quantitative coronary analysis and follow-up angiography

Angiograms were obtained in the 15 participating centers using portable storage devices and sent to the core laboratory (Cardiac and Vascular Center, Samsung Medical Center, Korea). All cine coronary angiograms were reviewed and quantitatively analyzed at the Core Laboratory by 2 independent experienced staff members. Quantitative coronary analysis was performed for LM bifurcation lesions before and after the intervention using the same projections with the optimal view. Routine follow-up angiography was recommended at 9 months after the index procedure. However, the rate of follow-up angiography was 54.9% (113 out of 206 patients).

Study end points and follow-up

The primary end point was the occurrence of target lesion failure (TLF), a composite of cardiac death, myocardial infarction, or target lesion revascularization at 1 year of follow-up. The secondary end points included the individual components of the primary end point: cardiac death or myocardial infarction, stent thrombosis, and target vessel revascularization at 1 year of follow-up. All deaths were considered cardiac unless a definite noncardiac cause could be established. Myocardial infarction was defined as elevated cardiac enzymes (troponin or the myocardial band fraction of creatine kinase) greater than the upper limit of normal that occurred with ischemia symptoms or electrocardiogram findings indicative of ischemia that were unrelated to the index procedure. Procedure-related myocardial infarction was defined as an elevated myocardial band fraction of creatine kinase more than 3 times above the upper limit of normal within 48 hours of the index procedure. Target lesion revascularization was defined as repeat PCI of the lesion within 5 mm of stent deployment. Target vessel revascularization was defined as repeat PCI or bypass graft surgery of the target vessel. Stent thrombosis was defined as definite or probable stent thrombosis according to the definitions of the Academic Research Consortium.[13]

Data regarding the primary and secondary end points were obtained through office visits or by telephone contact 1, 6, 9, and 12 months after the index procedure. For validation, information regarding vital status was obtained until September 2018 from the National Population Registry of the Korea National Statistical Office using a unique personal identification number. When available, each participating center was encouraged to collect additional follow-up information up to 3 years after the index procedure.

Statistical analysis

The expected rate of TLF was 5% in the conservative strategy group and 14% in the aggressive strategy group in patients with a non-true LM bifurcation lesion; the corresponding rates in those with a true bifurcation lesion were 7% in the conservative strategy group and 14% in the aggressive strategy group .[5,14,15] With 5% type I error, 80% power, and a 5% drop-out rate, a total of 700 patients were needed (350 with a non-true bifurcation lesion and 350 with a true bifurcation lesion) to show that the conservative strategy was superior to the aggressive strategy. However, the SMART-STRATEGY II study was terminated early due to slow enrollment.

All data were analyzed according to the intention-to-treat principle. Categorical variables are summarized as numbers with percentages and were compared using Pearson chi-square or Fisher exact test. Continuous variables are presented as means with standard deviations and were compared using an independent *t*-test or Wilcoxon rank-sum test according to distribution normality. Time-to-event hazard curves were plotted using Kaplan-Meier estimates and were compared using a log-rank test. To ascertain variables independently associated with 1-year TLF, multivariable Cox regression was performed using clinically relevant covariates, including age, male sex, dyslipidemia, current smoking, diabetes, hypertension, chronic kidney disease, previous myocardial infarction, left ventricular ejection fraction, performance of follow-up angiography, treatment strategy, type of bifurcation lesion (true or non-true), bifurcation angle, length of MV disease, and presence of significant SB ostial stenosis ($\geq$ 50%) after the index procedure.

All of the probability values are 2-tailed and *P* values $<$ .05 were considered statistically significant. R software version 3.4.3 (R Foundation for Statistical Computing) was used for all statistical analyses.

RESULTS

Baseline clinical and procedural characteristics

A total of 206 patients with a LM bifurcation lesion (160 non-true bifurcation lesions and 46 true bifurcation lesions) were included in this study. The baseline clinical characteristics are shown in table 1 and were well-matched between the conservative and aggressive strategy groups. Regarding the procedural characteristics, there were no significant differences in vascular access, number of diseased vessels, Medina classification of the LM lesion, and intravascular ultrasound use between the 2 strategies in patients with non-true and true bifurcation lesions (table 2). All study patients were receiving dual antiplatelet therapy at the index procedure, and the rate of 1-year dual antiplatelet therapy did not differ between the conservative and aggressive strategy groups (97.0% vs 97.1%, *P* = .962).

Procedural outcomes are shown in table 3. Among patients with a non-true bifurcation lesion, the mean amount of contrast dye used was significantly smaller in the conservative than aggressive strategy group (221.1 $\pm$ 77.7 mL vs 259.9 $\pm$ 117.9 mL, *P* = .017). The mean fluoroscopic time and the rate of procedure-related myocardial infarction were not significantly different between the 2 strategies. During the procedure, 7 patients (9.0%) in the conservative strategy group underwent kissing balloon inflation due to SB compromise during the procedure. Among patients with a true bifurcation lesion, there were no significant differences in the fluoroscopic time, amount of contrast dye, and rate of procedure-related myocardial infarction between the conservative and aggressive strategy groups.

Baseline characteristics and procedural outcomes according to treatment strategy in the overall population are presented in table 1 of the supplementary data, table 2 of the supplementary data, and table 3 of the supplementary data.

Quantitative coronary analysis

Quantitative coronary analysis was possible in 200 patients (97.1%) at baseline and in 113 patients at 9 months (54.5% of the conservative strategy group and 55.2% of the aggressive strategy group, *P* = .910) (figure 2 and table 4 of the supplementary data). Among non-true bifurcations lesions, there were no significant differences in the minimal lumen diameter of the SB or in binary (re)stenosis between the conservative and aggressive strategy groups after the index procedure and at follow-up. There were no significant differences in the MV in quantitative coronary analysis.

Among true bifurcation lesions, the conservative strategy had a lower minimal lumen diameter of the SB (2.1 $\pm$ 0.9 vs 2.9 $\pm$ 0.5 mm; *P* = .001) after the index procedure than the aggressive strategy. SB (re)stenosis occurred in 6 patients (40.0%) in the conservative strategy group and in 3 patients (25.0%) in the aggressive strategy group; the difference was not significant (*P* = .681). There were no significant differences in the MV in quantitative coronary analysis.

Clinical outcomes

The median follow-up duration was 1028 days. Of a total of 206 patients, 200 (97.1%) completed the planned 1-year clinical follow-up (figure 2 and table 4). One-year TLFs were not significantly different between the conservative and aggressive strategies among patients with a non-true bifurcation lesion (6.5% vs 4.9%; hazard ratio [HR], 1.31; 95% confidence interval [95%CI],

Table 1
Baseline clinical characteristics

	Non-true bifurcation lesions			True bifurcation lesions		
	Conservative (N = 78)	Aggressive (N = 82)	*P*	Conservative (N = 23)	Aggressive (N = 23)	*P*
Age, y	63.7 ± 8.8	65.3 ± 9.4	.263	65.5 ± 8.7	66.3 ± 10.6	.783
Male sex	60 (76.9)	64 (78.0)	.865	15 (65.2)	16 (69.6)	.757
Body mass index, kg/m^2	24.6 ± 2.6	24.1 ± 3.1	.255	25.1 ± 3.6	25.2 ± 2.8	.991
Hypertension	48 (61.5)	56 (68.3)	.373	18 (78.3)	17 (73.9)	.734
Diabetes mellitus	27 (34.6)	31 (37.8)	.676	10 (43.5)	11 (47.8)	.771
Dyslipidemia	32 (41.0)	33 (40.2)	.920	11 (47.8)	9 (39.1)	.559
Current smoker	22 (28.2)	25 (30.5)	.753	6 (26.1)	5 (21.7)	.734
Peripheral artery disease	3 (3.8)	5 (6.1)	.516	1 (4.3)	2 (8.7)	.558
Cerebrovascular accident	5 (6.4)	10 (12.2)	.213	0 (0.0)	4 (17.4)	.038
Chronic kidney disease	7 (9.0)	3 (3.7)	.168	2 (8.7)	4 (17.4)	.391
Previous myocardial infarction	6 (7.7)	5 (6.1)	.692	1 (4.3)	2 (8.7)	.558
Previous PCI	16 (20.5)	12 (14.6)	.331	5 (21.7)	4 (17.4)	.715
Previous CABG	0 (0.0)	1 (1.2)	.329	0 (0.0)	1 (4.3)	.318
LVEF, %	62.0 ± 8.2	62.1 ± 8.0	.982	59.1 ± 10.9	61.5 ± 9.3	.445

CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.
Values are presented as No. (%) or mean ± standard deviation.

Table 2
Procedural characteristics

	Non-true bifurcation lesions			True bifurcation lesions		
	Conservative (N = 78)	Aggressive (N = 82)	*P*	Conservative (N = 23)	Aggressive (N = 23)	*P*
General procedure						
Vascular access			.334			.771
Radial artery	56 (71.8)	53 (64.6)		11 (47.8)	10 (43.5)	
Femoral artery	22 (28.2)	29 (35.4)		12 (52.2)	13 (56.5)	
Extent of coronary artery disease			.160			.772
1-vessel disease	30 (38.5)	20 (24.4)		0 (0.0)	0 (0.0)	
2-vessel disease	31 (39.7)	41 (50.0)		12 (52.2)	11 (47.8)	
3-vessel disease	17 (21.8)	21 (25.6)		11 (47.8)	12 (52.2)	
Left main bifurcation lesions						
Medina classification						
Non-true bifurcation lesions			.727			
1.0.0	13 (16.7)	13 (15.9)				
0.1.0	23 (29.5)	29 (35.4)				
1.1.0	42 (53.8)	40 (48.8)				
True bifurcation lesions						.114
1.1.1				16 (69.6)	19 (82.6)	
1.0.1				3 (13.0)	4 (17.4)	
0.1.1				4 (17.4)	0 (0.0)	
IVUS-guided	65 (83.3)	61 (74.4)	.170	13 (56.5)	19 (82.6)	.064

IVUS, intravascular ultrasound.
Values are presented as No. (%).

Table 3
Procedural outcomes

	Non-true bifurcation lesions			True bifurcation lesions		
	Conservative (N = 78)	Aggressive (N = 82)	*P*	Conservative (N = 23)	Aggressive (N = 23)	*P*
General procedure						
Number of treated lesions	1.6 ± 0.9	1.7 ± 0.8	.571	2.6 ± 0.9	2.7 ± 0.7	.464
Total number of stents	1.7 ± 0.9	1.8 ± 0.9	.375	2.1 ± 0.7	2.8 ± 0.9	.005
Mean time of fluoroscopy, min	49.2 ± 30.4	55.1 ± 32.6	.247	63.3 ± 33.0	66.3 ± 35.0	.766
Mean amount of contrast dye, mL	221.7 ± 77.7	259.9 ± 117.9	.017	245.0 ± 85.2	286.9 ± 141.8	.233
Procedure-related myocardial infarction[a]	9 (11.5)	10 (12.2)	.898	3 (13.0)	2 (8.7)	.642
Main vessel						
Number of stents per lesion, mm	1.1 ± 0.3	1.1 ± 0.4	.406	1.1 ± 0.3	1.1 ± 0.4	.608
Total stent length, mm	24.7 ± 10.2	27.7 ± 12.5	.100	24.7 ± 12.5	24.8 ± 12.8	.993
Maximal stent diameter, mm	3.7 ± 0.4	3.7 ± 0.4	.710	3.4 ± 0.4	3.5 ± 0.4	.807
Side branch						
Balloon inflation	7 (9.0)	82 (100.0)	< .001	19 (82.6)	23 (100.0)	.116
Final kissing balloon inflation	7 (9.0)	82 (100.0)	< .001	16 (69.6)	22 (95.7)	.052
Stent implantation	1 (1.3)	2 (2.4)	.592	8 (34.8)	23 (100.0)	< .001
Number of stents per lesion, mm	2.0	1.0 ± 0.0	NA	1.0 ± 0.0	1.0 ± 0.2	.329
Total stent length, mm	28.0	14.0 ± 0.0	NA	17.4 ± 4.7	19.6 ± 8.6	.527
Maximal stent diameter, mm	3.5	3.1 ± 0.5	NA	3.2 ± 0.3	3.0 ± 0.5	.446
Treatment according to randomization[b]	78 (100.0)	82 (100.0)	NA	21 (91.3)	23 (100.0)	.470

NA, not available.
Values are presented as No. (%) or mean ± standard deviation.
[a] Procedure-related myocardial infarction was indicated by a myocardial band fraction of creatine kinase > 3 times the upper normal limit.
[b] In the conservative strategy group, 2 patients were not treated according to randomization by operator's clinical judgment.

0.35-4.88; *P* = .687) and among those with a true bifurcation lesion (17.6% vs 21.7%; HR, 0.76; 95%CI, 0.20-2.83; *P* = .683) (figure 3). The incidences of cardiac death, myocardial infarction, target lesion revascularization, and stent thrombosis were also not significantly different between the strategies. Out of 11 target lesion revascularizations during the first year after the index procedure, 3 events were due to angiographic restenosis incidentally found in follow-up angiography. Clinical outcomes according to treatment strategy in the overall population are presented in table 5 of the supplementary data.

Of a total of 206 patients, 116 (56.3%) completed the 3-year follow-up. At 3 years, there were no significant differences in

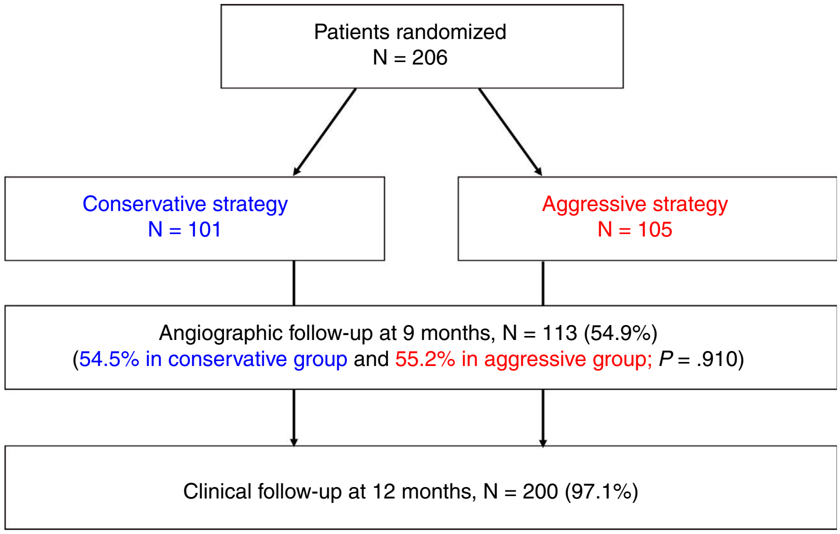

Figure 2. Study population.

Table 4
Clinical outcomes at 1 year

Outcome	Conservative	Aggressive	Hazard ratio (95%CI)	*P*
Non-true bifurcation lesions	N = 78	N = 82		
TLF	5 (6.5)	4 (4.9)	1.31 (0.35-4.88)	.687
Cardiac death	3 (3.9)	2 (2.6)	1.60 (0.27-9.58)	.606
MI	0 (0.0)	3 (2.7)	NA*	.091
TLR	2 (2.6)	2 (2.5)	1.06 (0.15-7.50)	.956
Cardiac death or MI	3 (3.9)	4 (4.9)	0.79 (0.18-3.52)	.755
Definite or probable ST	1 (1.3)	1 (1.2)	1.07 (0.07-17.03)	.964
Target vessel revascularization	3 (4.0)	3 (3.7)	1.06 (0.21-5.27)	.940
True bifurcation lesions	N = 23	N = 23		
TLF	4 (17.6)	5 (21.7)	0.76 (0.20-2.83)	.683
Cardiac death	1 (4.3)	1 (4.5)	1.00 (0.06-15.99)	>.999
MI	2 (8.9)	1 (5.3)	2.07 (0.19-22.81)	.553
TLR	3 (13.9)	4 (18.7)	0.74 (0.16-3.29)	.688
Cardiac death or MI	2 (8.9)	2 (8.7)	1.01 (0.14-7.18)	.991
Definite or probable ST	1 (4.3)	0 (0.0)	NA*	.317
Target vessel revascularization	3 (13.9)	4 (18.7)	0.74 (0.16-3.29)	.688

95%CI, 95% confidence interval; MI, myocardial infarction; NA, not available; ST, stent thrombosis; TLF, target lesion failure; TLR, target lesion revascularization.
Values are presented as No. (%).
TLF is a composite of cardiac death, MI, and TLR.
* *P* values were derived from the log-rank test.

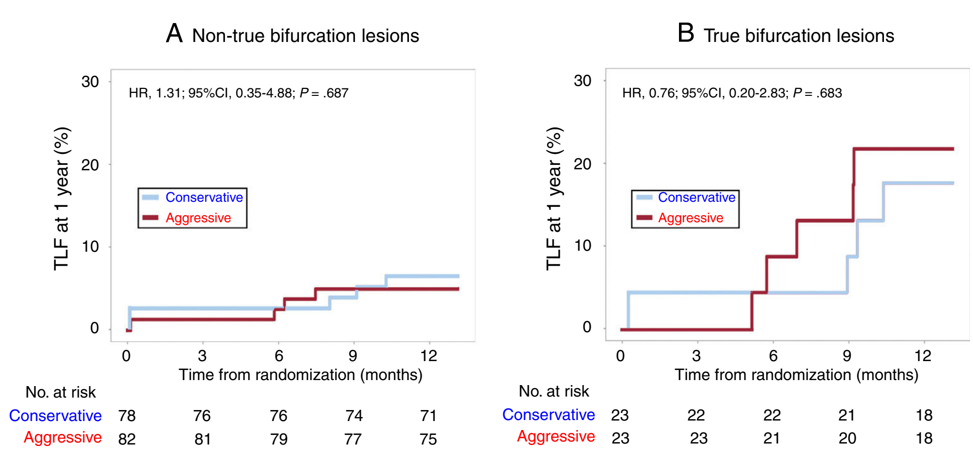

Figure 3. Target lesion failure at 1 year. A: non-true bifurcation lesion. B: true bifurcation lesion. 95%CI, 95% confidence interval; HR, hazard ratio; MI, myocardial infarction; TLF, target lesion failure.

clinical outcomes between the conservative and aggressive strategies (table 6 of the supplementary data).

Independent predictors of TLF

In multivariable Cox analysis, factors independently associated with 1-year TLF were a true bifurcation lesion (HR, 4.94; 95%CI, 1.60-15.21; $P = .005$), bifurcation angle (per 10°; HR, 0.78; 95%CI, 0.61-1.00; $P = .046$), and chronic kidney disease (HR, 5.45; 95%CI, 1.16-25.64; $P = .032$).

DISCUSSION

We compared 2 different strategies for provisional SB ballooning and stenting in patients undergoing LM bifurcation interventions using a prospective, randomized trial. The principal findings were as follows: *a)* among patients with a non-true bifurcation lesion, the conservative strategy had a similar 1-year TLF using a smaller amount of contrast dye to the aggressive strategy; *b)* among patients with a true bifurcation lesion, there was no significant difference in 1-year TLF between the conservative and aggressive strategies; and *c)* the independent predictors of 1-year TLF were a true bifurcation lesion, bifurcation angle, and chronic kidney disease.

Previous studies have demonstrated that a provisional SB approach is superior to an elective 2-stent strategy in non-LM coronary bifurcation lesions.[2–4,16] The provisional SB approach is also safe and feasible in LM bifurcation lesions.[5,7–9] However, it has not been well-established when and how to perform a SB intervention after MV stenting during the provisional approach to LM bifurcation lesions. Although 1 study suggested that residual SB stenosis > 75% should be a criterion for SB intervention after MV stenting, the SB approach by type of bifurcation lesion was not provided in that study.[9] The present study showed the feasibility of a conservative strategy for the provisional SB approach to both non-true and true bifurcation lesions.

FKB after MV stenting may improve SB ostial opening but requires SB rewiring. FKB after MV stenting also carries a risk of MV stent deformity or SB injury. Although FKB is considered mandatory in the elective 2-stent strategy, its role in the provisional SB approach is controversial. In non-LM bifurcation lesions, FKB during the provisional 1-stent strategy was associated with a longer procedural time, larger contrast volume, and similar clinical outcomes in a randomized study,[11] whereas conflicting outcomes are found in real-world data.[10,17] However, in LM bifurcation lesions, no randomized study has examined the role of FKB during the provisional SB approach, despite the significance of SBs with their large territory of subtended myocardium. One retrospective study found that the risk of adverse cardiac events was similar for MV stenting with and without FKB. However, the usefulness of this result was limited because the use of FKB was at the operator's discretion during the procedure.[12]

Among non-true bifurcation lesions in the present study, MV stenting alone without FKB had similar clinical outcomes to MV stenting with mandatory FKB. Our findings may be explained by the low risk of SB compromise, which limits the potential benefit of FKB. LM bifurcations have larger caliber vessels and a wider bifurcation angle than non-LM bifurcations.[6] These characteristics could be protective factors for plaque and carina shift, a known mechanism of SB ostial lumen loss after MV stenting.[18–20] In non-LM bifurcations, Koo et al.[21] demonstrated that only 37% of lesions were functionally significant among jailed SBs with > 75% stenosis and that no lesion with a jailed SB with < 75% stenosis was functionally significant. In LM bifurcations, a significant SB compromise occurs in only 7% of cases after MV stenting and in 17% when the SB has > 50% stenosis.[22,23] In the quantitative coronary analysis of our study, the observed rate of SB stenosis > 50% after MV stenting without FKB was just 9.3%. In addition, the minimal lumen diameter of the SB ostium was similar for MV stenting alone and MV stenting with FKB. Therefore, routine FKB may be an unnecessary procedure after MV stenting in LM non-true bifurcation lesions.

Among true bifurcation lesions, clinical outcomes were not significantly different between the 1-stenting strategy with a provisional SB approach and elective 2-stenting. SB ostial disease is a major predictor of SB compromise and adverse outcomes in bifurcation PCI.[8,20] In our study, a true bifurcation lesion was also an independent predictor of 1-year TLF. Several studies have compared the provisional 1-stent strategy and elective 2-stent strategy in the presence of significant SB ostial disease in LM bifurcation lesions. The DEFINITION study reported that the 2-stent strategy is required in lesions with SB stenosis > 70% and lesion length > 10 mm, although the study included a small proportion of LM bifurcation lesions.[24] The recent DKCRUSH-V randomized study[25] demonstrated that the elective 2-stent strategy with double kissing crush technique resulted in a lower rate of TLF than provisional SB stenting in LM true bifurcation lesions. However, the DKCRUSH-V study had a different criterion for additional SB stenting (residual SB stenosis > 75% after kissing balloon inflation) vs our study. The European Bifurcation Coronary TWO (EBC) study,[26] which included true bifurcation lesions with large-caliber SBs (≥ 2.5 mm), determined that provisional T stenting had similar outcomes with a shorter procedure time to the culotte technique, as well as lower costs. The results of the EBC study support our findings that the 1-stent strategy with a provisional SB approach may be feasible in patients with a true LM bifurcation lesion.

The rate of periprocedural MI was higher than that of previous trials.[27] A recent study reported that the rate of periprocedural MI varied substantially according to the MI definition applied, with periprocedural MI related to long-term adverse outcomes irrespective of its definition.[28] Therefore, the incidence of periprocedural MI in our study would be explained by the lower threshold of periprocedural MI[29] and have clinical implications.

This study has several limitations. First, the number of enrolled patients was much smaller than originally designed because patient enrollment was prematurely terminated due to slow enrollment. The statistical power was low because of the small study population, particularly patients with a true bifurcation lesion. Although there were no significant differences in 1-year TLF between the 2 different strategies, the application of the current results to real-world practice should be individualized based on patient and lesion characteristics. A large randomized study is needed to substantiate our findings. Second, operators possibly included patients with favorable anatomy for this study. However, because the quantitative coronary analytical results of the present study were not largely different from those of real-world data,[8] the current results would not be significantly biased by the population selection. Third, intravascular ultrasound parameters were not provided, despite its high use (76.7%). Although most bifurcation studies have provided quantitative coronary analytical results as a main parameter, quantitative coronary analysis is sensitive to several factors, such as angiogram quality and projection angle. Intravascular ultrasound identifies the exact vessel size, plaque burden, and stent optimization. However, functionally significant flow disturbance in SBs is poorly associated with both quantitative coronary analysis and intravascular ultrasound parameters.[23] Fourth, there was no information on the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score. However, considering the number of diseased vessels and treated lesions, the patients included in the present study appear to have been suitable candidates for PCI. Fifth, the fractional flow reserve measurement of SBs was at the operator's discretion and was not recorded. Given the controversy surrounding fractional flow reserve-guided PCI in bifurcation lesions,[30] a randomized trial is needed to investigate the clinical benefit of the fractional flow reserve-guided strategy in LM bifurcation lesions. Sixth, clinical outcomes might be affected by the scheduled follow-up angiography. However, this type of bias is unlikely to explain our results because only 3 target lesion revascularizations were performed due to restenosis incidentally found in follow-up angiography and there was no significant difference in the rate of follow-up angiography between the conservative and aggressive strategies. Seventh, this was an open-label trial. This lack of blinding may have introduced bias in the symptom assessment during follow-up and in the clinical outcomes. Finally, various 2-stenting techniques were used in this study, which might have affected the clinical outcomes. However, the primary purpose of this study was to compare the 2 different strategies, not to compare specific stenting techniques in LM bifurcation lesions. In addition, because the study protocol was not limited to specific stenting techniques, the operators would have used the most familiar techniques, as in real-world practice.

CONCLUSIONS

In patients with LM bifurcation lesions, a conservative strategy for SB intervention had similar clinical outcomes to that of an aggressive strategy. However, the study was underpowered and inconclusive due to premature termination of patient enrollment. Larger studies are required to establish the optimal treatment strategy for LM bifurcation lesions.

WHAT IS KNOWN ABOUT THE TOPIC?

- A 1-stent technique with provisional SB approach is considered the standard treatment for bifurcation lesions.
- However, in LM bifurcation lesions, when and how to perform SB intervention after MV stenting during the provisional approach have not been established.

WHAT DOES THIS STUDY ADD?

- In this prospective, randomized, multicenter trial, a conservative strategy for provisional SB intervention had similar clinical outcomes to an aggressive strategy for LM bifurcation lesions.
- Because this trial was underpowered due to a relatively small sample size, larger studies are required to establish the optimal treatment strategies for LM bifurcation lesions.

CONFLICTS OF INTEREST

There are no conflicts of interest.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.rec.2020.06.011

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