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Side Branch Additional Treatment for Coronary Bifurcation Lesion Revascularization

Insights From the KISS Randomized Trial

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ABSTRACT

BACKGROUND Although provisional stenting is the recommended strategy for most coronary bifurcation lesions, the clinical benefit of additional side branch (SB) intervention remains debated.

OBJECTIVES The aim of this study was to determine whether a conservative strategy without systematic SB intervention (SBI) is noninferior to systematic SB intervention regarding periprocedural events.

METHODS The multicenter, international KISS (Keep Bifurcation Single Stenting Simple) trial randomized patients with non–left main bifurcation lesions to 2 groups: no SBI or SBI following main branch stenting with the Resolute Onyx drug-eluting stent and a proximal optimization technique without impairment of SB flow. The primary endpoint was periprocedural myocardial infarction (MI) or myocardial injury, according to the Academic Research Consortium 2 definition. Secondary endpoints included procedural complications and 12-month clinical outcomes, including target lesion failure, defined as the composite of cardiac death, target vessel MI, and target lesion revascularization.

RESULTS Among the 616 included patients, 81% were treated for chronic coronary disease, and the bifurcation mainly involved was between the left anterior descending coronary artery and the diagonal. In the no-SBI group, an intervention on the SB was required in 2.0% of patients (n = 6). Periprocedural MI or myocardial injury occurred in 4.1% (n = 11) in the no-SBI group vs 5.7% (n = 16) in the SBI group ($P < 0.001$ for noninferiority; $P = 0.38$ for superiority). There was no significant interaction with age, sex, Medina classification, or SB residual stenosis. Procedure time, radiation dose, and contrast use were significantly lower in the no-SBI group. Procedural complications were rare, but SB dissection was more frequently observed in the SBI group (2.9% vs 0.0%; $P = 0.004$). There was no difference in target lesion failure at 1 year (4.9% [n = 15] vs 6.4% [n = 20] in the no-SBI and SBI groups respectively; $P = 0.442$).

CONCLUSIONS The KISS trial demonstrates that a conservative strategy without systematic SB intervention is associated with very rare procedural complications and is noninferior to a systematic SB intervention regarding periprocedural MI and myocardial injury. (JACC Cardiovasc Interv. 2026;19:961-972) © 2026 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ARC-2 = Academic Research Consortium-2

CAD = coronary artery disease

KBI = kissing balloon inflation

LM = left main

MB = main branch

MI = myocardial infarction

PCI = percutaneous coronary intervention

POT = proximal optimization technique

SB = side branch

SBI = side branch intervention

TLR = target lesion revascularization

Percutaneous coronary intervention (PCI) for coronary revascularization plays a central role in the therapeutic management of symptomatic coronary artery disease (CAD). A coronary bifurcation is involved in 15% to 20% of patients[1] and induces some technical challenges, including artery diameter incongruency, risk for stent malapposition leading to higher risk for stent thrombosis,[2] and particularly risk for side branch (SB) impairment due mainly to bifurcation carina shift or dissection. To maintain SB patency, many techniques have been proposed,[3] but provisional stenting has been established as a standard of care for most bifurcation lesions.[4]

To comply with the fractal law of the coronary tree,[5] it is recommended to select a stent sized to the distal reference diameter and to systematically perform a proximal optimization technique (POT), allowing correct apposition of the proximal part of the stent and scaffolding of the SB ostium.[4,6-8] Once these steps are completed, the clinical benefit of an additional intervention on the SB ostium is a matter of debate. SB intervention (SBI) is expected to decrease the risk for occlusion and, subsequently, for periprocedural myocardial injury and related worse outcomes.[9,10] SBI could be also expected to improve angina relief by reducing the risk for SB lesion evolution and the need for future reintervention. In contrast, the absence of SBI could reduce procedure time, contrast media volume, and x-ray exposure. This strategy might also mitigate the risk for SB dissection and second stent implantation, leading to potential higher risk for stent thrombosis.[6]

Several registries and small randomized clinical trials have addressed this issue, but most of them did not take into account the modern strategy of provisional stenting, including the absence of systematic SB predilatation, stenting of the main branch (MB) sized to the distal reference, and systematic POT.[11-14] In these studies, SBI was mainly a traditional kissing balloon inflation (KBI),[15] without considering the recent strategy of a sequence of POT, SB ballooning, and POT, proposed as an alternative because of its quicker execution and potential benefit on outcomes.[16,17]

As a consequence, the impact on procedural success and long-term outcomes of systematic SBI on the basis of the contemporary optimized coronary bifurcation revascularization is unknown. The main objective of the present randomized multicenter KISS (Keep Bifurcation Single Stenting Simple) trial was to determine whether a conservative strategy only, based on revascularization of the MB, is noninferior to systematic SBI.

METHODS

STUDY OVERSIGHT. The KISS trial was approved by national regulatory authorities and ethics committees or Institutional Review Boards as required in the participating countries. The study was conducted at 20 centers in 6 countries (France, Italy, Spain, the United Kingdom, Portugal, and Switzerland). The study is registered at ClinicalTrials.gov (NCT04285372). All patients included in this study provided written informed consent.

STUDY DESIGN AND POPULATION. The KISS trial was a randomized (1:1), prospective, open-label, multicenter, international study whose aim was to demonstrate the noninferiority of a non-SBI strategy after main vessel stenting in the treatment of a non-left main (LM) coronary bifurcation lesion. Any patient with CAD requiring coronary revascularization was considered to be eligible, except for patients with ST-segment elevation myocardial infarction (MI) with signs of ongoing ischemia. The main inclusion criteria were as follows: 1) non-LM coronary bifurcation with de novo significant lesion in the main vessel requiring stenting of the MB vessel (angiographic coronary stenosis ≥70% and/or coronary stenosis with significant hemodynamic impairment [fractional flow reserve ≤0.8]); 2) SB diameter ≥2.25 mm and compatibility with potential stent implantation; and 3) absence of SB occlusion or SB slow flow associated with ongoing ischemia (either acute chest pain or dynamic ST-segment changes) after POT in the main vessel.

The main exclusion criteria were as follows: 1) LM coronary lesion; 2) coronary lesion bifurcation requiring a planned double-stenting strategy; 3) Medina type 0,0,1 bifurcation without planned MB

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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stenting; 4) unsuccessful non-target vessel intervention prior to treatment of the target lesion; 5) chronic total occlusion of any target vessel; 6) SB TIMI flow grade <III; 7) SB predilatation before randomization; 8) ST-segment elevation MI or cardiogenic shock; and 9) left ventricular ejection fraction <20%.

STUDY PROCEDURES AND RANDOMIZATION. All patients underwent clinical assessment and blood tests, including troponin level, within 24 hours prior to the index intervention, as well as 12-lead electrocardiography. All patients received dual antiplatelet therapy before PCI. Treatment of a single non-bifurcation lesion in a non-target vessel during the same procedure and prior to target bifurcation PCI was acceptable if successful. Anticoagulation therapy with unfractionated heparin or enoxaparin was administrated during procedure. Access choice was left to the operator's discretion. Systematic wiring of the MB and SB was performed at the beginning of the PCI procedure. After appropriate preparation of the MB lesion (left to the operator's discretion), a Resolute Onyx drug-eluting stent (Medtronic) was implanted using a 1:1 diameter ratio calculated on the distal MB reference diameter. A systematic POT was performed after stenting using a 1:1 balloon/artery ratio and according to the fractal law.[18] After the POT, and in the absence of SB occlusion or SB slow flow, patients were randomized to no intervention on the SB or SBI. In the SBI group, the SBI was left to the operator's discretion: SB balloon inflation, KBI, or the POT-SB dilatation-POT technique.[17] A guidewire should remain jailed in the nonstented vessel until randomization. A final POT was recommended in case of the KBI technique and mandatory in case of the POT-SB dilatation-POT technique. Systematic similar angiographic views were recommended at the end of the intervention after guidewire removal.

ANGIOGRAPHIC CORE LABORATORY ANALYSIS. All procedures were independently reviewed by a core laboratory (Cardiovascular European Research Center). An exhaustive angiographic analysis using 3D QCA Bifurcation (Medis Medical Imaging) was performed, including a detailed description of coronary lesions, the PCI procedure, and results. A double reading was performed by 2 independent experienced observers. In case of discrepancies, additional expert advice was requested (E. Barbato, Y. Louvard, F. Mauri).

FOLLOW-UP. Clinical assessment, electrocardiography, and blood tests were repeated within 24 hours, with at least 1 troponin level measurement later than 6 hours after PCI and not later than 48 hours for the evaluation of periprocedural MI and myocardial injury.

Dual antiplatelet therapy duration was left to the operator's discretion, with a recommendation of 6-month treatment in case of stable CAD and 12-month treatment in case of acute coronary syndrome and in the absence of high bleeding risk in accordance with international guidelines.[19,20]

Clinical follow-up was conducted at 1 month and 12 months. Data were collected in an anonymized electronic case report form and assessed by an independent monitoring board regarding the collection of data and an independent adjudication committee regarding clinical endpoints evaluation, according to the monitoring plan (CERC).

STUDY ENDPOINTS. The primary endpoint was defined as the rate of periprocedural MI or significant periprocedural injury according to the Academic Research Consortium-2 (ARC-2) definition.[21] Periprocedural MI was defined as an absolute rise in high-sensitivity cardiac troponin from baseline ≥35 times the upper reference limit and 1 or more of the following criteria within 48 hours: new significant Q waves or flow-limiting angiographic complications or new substantial loss of myocardium on imaging. Significant periprocedural myocardial injury was defined as an absolute rise in high-sensitivity cardiac troponin from baseline ≥70 times the upper reference limit without clinical symptoms or electrocardiographic or angiographic complications.[22]

Procedural secondary endpoints were as follows: 1) technical success, defined as deployment of the MB stent with <20% angiographic residual stenosis and a patent SB at the end of procedure, as evaluated by the core laboratory; 2) the proportion of crossovers and required SB stenting in the no-SBI group; 3) total procedure time; 4) acute diameter gain in the SB and MB as measured using dedicated quantitative coronary angiographic software; 5) fluoroscopy time; 6) total radiation dose (air kerma); and 7) total contrast dose.

Clinical endpoints at 1 and 12 months were: 1) target lesion failure, defined as the composite of cardiac death, target vessel MI, clinically driven target lesion revascularization (TLR); 2) MB TLR and SB TLR; 3) definite or probable stent thrombosis (ARC-2 criteria)[23]; and 4) angina status according to the Canadian Cardiovascular Society classification. An improvement of angina status was considered in case of a reduction of at least 1 Canadian Cardiovascular Society class between baseline and follow-up visits.

STATISTICAL ANALYSES. Analyses were done in the intention-to-treat and per-protocol data sets.

Continuous variables are presented as mean ± SD or median (Q1-Q3) depending on their distribution. Categorical variables are expressed as n (%). We used chi-square testing or the Fisher test for frequency comparisons according to distribution. The statistical method to assess normal distribution was based on the central limit theorem, considering a sufficient sample size of the population. For independent data, characteristics were compared between the 2 treatment groups (no SBI and SBI) by means of unpaired Student's *t*-tests or the Wilcoxon test for continuous variables and the chi-square test or Fisher exact test for categorical variables, as appropriate.

Assuming an expected 15% rate of MI or myocardial injury as defined by the ARC-2 criteria in the control group, taking a 6% drop-out rate into account, and using an absolute noninferiority limit of 7.5%, 596 subjects randomized equally between the 2 arms would have 80% power to show noninferiority at a 1-sided significance level of 0.05. The sample size calculation was based on an unpooled variance estimator of a *z*-test. The hypothesis with regard to the primary clinical endpoint was formulated as follows: H_0: pA - pB ≥ δ H_1: pA - pB < δ, where pA and pB are the risks for periprocedural MI at discharge or 48 hours postprocedure without SBI and with SB ballooning, respectively; and δ represents the noninferiority margin, set to 7.5%. The null hypothesis (H_0) states that the risk for periprocedural MI at discharge or 48 hours postprocedure is higher without SBI vs with SB ballooning by at least δ. Rejection of the null hypothesis was needed to conclude noninferiority. If noninferiority was statistically reached, superiority was tested. The hypothesis test was performed using a Farrington-Manning test. Reported *P* values are 2-sided and considered to indicate statistical significant if <0.05. The between-group comparisons of clinical endpoints was done by presenting the risk differences with a 2-sided 95% CI and a *z*-test. SAS version 9.4 (SAS Institute) was used for all analyses.

RESULTS

STUDY PATIENTS. From October 2020 to November 2022, 616 patients were enrolled and randomized in the 2 study groups: 303 patients in the no-SBI group and 313 patients in the SBI group. Group crossover was observed in 9 patients (Figure 1).

Baseline clinical characteristics of the studied population listed in the Table 1. The mean age was 67.7 ± 10.9 years, with a male predominance. The majority of enrolled patients were treated for chronic coronary disease (81%). The different clinical characteristics were well balanced between the 2 groups, except for history of previous MI and previous PCI, more frequently observed in the SBI group. Antithrombotic treatment prescribed at baseline before the PCI procedure is reported in Table 1, including 11.2% of patients with indications for chronic oral anticoagulation therapy.

ANGIOGRAPHIC AND PROCEDURAL CHARACTERISTICS. Radial access was the preferred access for the majority of procedures, without a significant difference between the 2 groups. The bifurcation between the left anterior descending coronary artery and diagonal was mainly involved (81.2% of patients). There was no significant difference between the 2 studied groups for the angiographic characteristics of the treated bifurcation, including diameters of the SB and MB, Medina classification, bifurcation tortuosity, or technique of stenting preparation (Table 2).

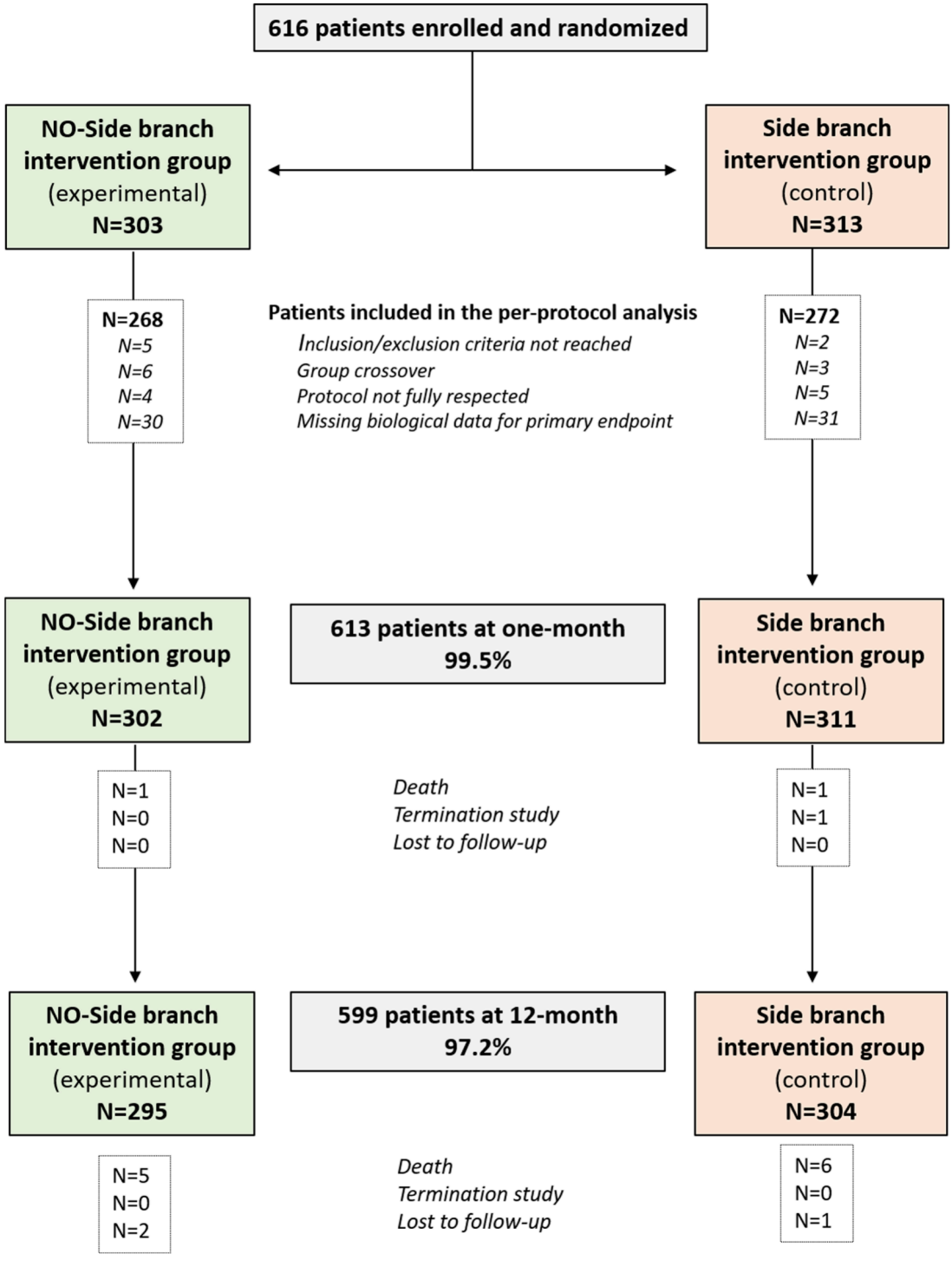
After stenting of the MB, a POT was performed in 94.4% in the no-SBI group and 95.2% in the SB group ($P = 0.635$). In the no-SBI group, an intervention on the SB was performed in 2.0% of patients (n = 6), including KBI (n = 4), SB ballooning (n = 1), and SB stenting (n = 1) because of SB flow compromise associated with ischemic clinical symptoms after randomization. In the SBI group, intervention on the SB was represented by isolated balloon inflation in 57% of the patients (n = 175) and KBI in 43% of the patients (n = 132). SB stenting was required in 5.8% of patients (n = 18) (Table 2).

PROCEDURES AND COMPLICATIONS. Technical success rates, as determined by the core laboratory, were similar between the 2 groups at 80.2% (n = 243) and 82.1% (n = 257) for the MB ($P = 0.544$) and 100% (n = 303) and 99% (n = 310) for the SB ($P = 0.249$) in the no-SBI and SBI groups, respectively. Procedural complications were rare, but SB dissection was more frequently observed in the SBI group (2.9% vs 0.0%; $P = 0.004$) (Table 3).

Procedure time was shorter (median 34 minutes vs 45 minutes; $P < 0.001$), as well as fluoroscopy time (median 10 minutes vs 13 minutes; $P < 0.001$), in the no-SBI group in comparison with the SBI group. Consequently, radiation dose was also reduced (453 mGy vs 629 mGy; $P < 0.001$) in the no-SBI group, in association with a significant reduction of total contrast media volume (130 mL vs 150 mL; $P < 0.001$) (Table 3).

In-stent acute gain in the MB was 1.17 ± 0.54 mm in the no-SBI group vs 1.1 ± 0.49 mm in the SBI group ($P = 0.1$). In-lesion acute gain in the SB was - 0.04 ± 0.36 mm in the no-SBI group vs 0.1 ± 0.41 mm in the SBI group ($P < 0.01$).

FIGURE 1 Study Flowchart



Distribution of included patients in the different study arms: no-side branch intervention (experimental group; green boxes) and side branch intervention (control group; orange boxes).

TABLE 1 Baseline Clinical Characteristics and Medications

	No Side Branch Intervention (n = 303)	Side Branch Intervention (n = 313)	*P* Value
Age, y	67.4 ± 11.2	68 ± 10.5	0.473
Male	230 (75.9)	246 (78.6)	0.426
Hypertension	191 (63)	191 (61)	0.607
Diabetes mellitus	82 (27.1)	85 (27.2)	0.979
Dyslipidemia	160 (52.8)	180 (57.5)	0.241
Current smoking	67 (22.1)	63 (20.1)	0.546
BMI, kg/m^2	28.3 ± 14.9	28.5 ± 19.8	0.891
Family history of CAD	80 (26.4)	64 (20.5)	0.081
History of stroke	23 (7.6)	14 (4.5)	0.103
Peripheral vascular disease	30 (9.9)	14 (14.1)	0.113
History of congestive heart failure	14 (4.6)	7 (2.2)	0.103
Chronic renal failure	11 (3.6)	19 (6.1)	0.160
Previous myocardial infarction	41 (13.5)	86 (27.5)	<0.001
Previous PCI	85 (28.1)	116 (37.1)	0.017
Previous CABG	2 (0.7)	1 (0.3)	0.618
Left ventricular ejection fraction, %	55.8 ± 11.2	56.5 ± 10.7	0.516
Systolic blood pressure, mm Hg	131.5 ± 22.1	136.1 ± 25.8	0.019
Diastolic blood pressure, mm Hg	74.7 ± 13.1	74.4 ± 14.3	0.806
Heart rate, beats/min	70.6 ± 16.9	69.9 ± 14.5	0.569
Clinical presentation			0.892
Silent ischemia	162 (53.6)	159 (50.8)	
Stable angina	85 (28.2)	93 (29.7)	
Unstable angina	27 (8.9)	28 (8.9)	
Acute coronary syndrome	28 (9.3)	33 (10.5)	
Angina class (CCS)			0.364
1	34 (32.1)	41 (34.8)	
2	47 (44.3)	52 (44.1)	
3	22 (20.8)	17 (14.4)	
4	3 (2.8)	8 (6.8)	
Medications at baseline			
Aspirin	273 (90.4)	266 (85)	0.041
Clopidogrel	181 (59.9)	182 (58.2)	0.652
Ticagrelor	44 (14.6)	46 (14.7)	0.964
Prasugrel	13 (4.3)	11 (3.5)	0.613
Oral anticoagulation	33 (10.9)	36 (11.5)	0.821
Statins	214 (70.9)	211 (67.4)	0.355

Values are mean ± SD or n (%). Data are based on intention-to-treat analysis.

BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; PCI = percutaneous coronary intervention; SB = side branch.

PERIPROCEDURAL MI AND MYOCARDIAL INJURY (PRIMARY ENDPOINT). Periprocedural MI or significant myocardial injury occurred in 4.1% (n = 11) in the no-SBI group vs 5.7% (n = 16) in the SBI group ($P < 0.001$ for noninferiority; $P = 0.38$ for superiority) in the intention-to-treat cohort and respectively in 4.1% (n = 11) and 5.9% (n = 16) ($P < 0.001$ for noninferiority; $P = 0.34$ for superiority) in the per-protocol analysis (**Table 4**, **Central Illustration**).

There was no significant interaction considering the occurrence of the primary endpoint with age, sex, Medina classification of the lesion, or residual SB stenosis degree (Supplemental Table 1).

FOLLOW-UP AND SECONDARY CLINICAL ENDPOINTS. Only 2 patients (0.7%) in the no-SBI group and 1 patient (0.3%) in the SBI group were lost to follow-up. At 1 year, death occurred in 2.0% (n = 6) and 2.3% (n = 7) of the patients in the no-SBI and SBI groups, respectively ($P = 0.795$). There was no difference in target lesion failure at 1 year (4.9% [n = 15] vs 6.4% [n = 20] in the no-SBI and SBI groups, respectively; $P = 0.442$) (**Table 5**, **Central Illustration**). At 1 year, improvement in angina status was observed in 99.0% and 93.7% of patients in the no-SBI and SBI groups, respectively ($P = 0.039$) (**Table 5**, Supplemental Table 2).

Considering only the SBI group, a complementary analysis was performed to evaluate the impact of SBI technique. The use of only SB ballooning was associated with a lower rate of the primary endpoint in comparison with a KBI technique (3.4% [n = 5] vs 8.9% [n = 11], respectively; $P < 0.001$ for noninferiority) but without a significant difference considering clinical secondary endpoints (Supplemental Table 3).

All patients were prescribed dual antiplatelet therapy after PCI or single antiplatelet therapy in association with oral anticoagulation for patients requiring long-term anticoagulation therapy, without a significant difference between the 2 studied groups. The detailed antithrombotic treatment during follow-up is described in Supplemental Table 4.

DISCUSSION

The KISS trial is the first randomized study to investigate the impact of no SBI in a common population of coronary patients treated for non-LM bifurcation coronary lesions. The main findings can be summarized as follows. First, the absence of SBI was associated with simpler procedures, as demonstrated by a significant reduction of procedure time, x-ray dose, and volume contrast. Second, in a contemporary cohort of bifurcation PCI, the rate of procedural complications remained very low and without a significant difference between the 2 stenting strategies, while a higher rate of SB dissection was observed in the case of systematic SBI. Likewise, the rates of major adverse clinical events and mortality were very low, without a difference according to PCI strategy. Third, although it is a surrogate and subjective endpoint, significant angina improvement at 1 year was observed in the group of patients without systematic SBI. Finally, the absence of SBI was associated with a lower rate of periprocedural myocardial injury and MI, which was the primary endpoint of the present KISS trial, confirming the noninferiority of this strategy in comparison with systematic SBI regardless of the type of SBI. Even if there is continuing debate over definitions, and although they are often asymptomatic, these periprocedural complications can delay hospital discharge. More important, several studies and meta-analyses have shown that periprocedural myonecrosis, even of limited magnitude, is associated with late adverse cardiac events and all-cause mortality.[9,10] Thus, even if the present study was not powered to evaluate long-term clinical events, the significant reduction of periprocedural myocardial injuries and infarctions associated with the

TABLE 2 Procedural Characteristics

	No Side Branch Intervention (n = 303)	Side Branch Intervention (n = 313)	*P* Value
Radial approach	263 (86.8)	284 (90.7)	0.098
Periprocedural anticoagulant therapy			0.716
Heparin	237 (78.2)	241 (77.0)	
LMWH	66 (21.8)	72 (23.0)	
Any nontarget lesion successfully treated before treatment of targeted bifurcation	58 (19.1)	74 (23.6)	0.174
Main branch of the treated bifurcation			0.708
Left anterior descending coronary artery	240 (79.2)	260 (83.1)	
Circumflex coronary artery	41 (13.5)	39 (12.5)	
Right coronary artery	17 (5.6)	12 (3.8)	
Medina classification			0.229
1,1,1	61 (20.1)	77 (24.6)	
1,1,0	115 (37.9)	93 (29.7)	
1,0,1	5 (1.7)	10 (3.2)	
1,0,0	26 (8.6)	25 (8.0)	
0,1,1	26 (8.6)	34 (10.9)	
0,1,0	70 (23.1)	74 (23.6)	
Bifurcation tortuosity			0.913
None	153 (50.5)	156 (49.8)	
Mild	115 (37.9)	115 (36.7)	
Moderate	27 (8.9)	33 (10.5)	
Severe	8 (2.6)	9 (2.9)	
Main branch characteristics			
Lesion length, mm	22.2 ± 8.8	22.3 ± 9.2	0.993
Proximal reference vessel diameter, mm	3.4 ± 0.5	3.3 ± 0.5	0.108
Distal reference vessel diameter, mm	2.9 ± 0.4	2.9 ± 0.4	0.092
Proximal stenosis preprocedure, %	68.7 ± 32	70.3 ± 31.7	0.590
Distal stenosis preprocedure, %	74.7 ± 25	72.7 ± 26.5	0.272
Side branch characteristics			
Lesion length, mm	3.8 ± 5.7	4.8 ± 5.9	0.019
Reference vessel diameter, mm	2.5 ± 0.3	2.5 ± 0.3	0.034
Stenosis preprocedure, %	26 ± 31	33 ± 34	0.029
Preparation of main branch			
Noncompliant balloon	255 (84.2)	256 (81.8)	0.434
Cutting balloon	6 (2)	3 (1)	0.261
Atherectomy	4 (1.3)	4 (1.3)	0.963
Intravascular lithotripsy	1 (0.3)	1 (0.3)	0.982
Number of study stents implanted			–
Main branch	347	355	
Side branch	1	14	
Main branch stenting			
1 stent	278 (91.8)	297 (94.0)	0.460
>1 stent	22 (7.3)	17 (5.4)	
Side branch stenting			
1 stent	1 (0.3)	14 (4.4)	<0.0001
>1 stent	0 (0.0)	1 (0.3)	
Proximal optimization technique	286 (94.4)	300 (95.2)	0.635
Maximum postdilatation diameter, mm	3.4 ± 0.5	3.4 ± 0.6	0.081
Maximum postdilatation length, mm	10.5 ± 3.8	10.9 ± 4.5	0.408
Maximum pressure in main branch, atm	16.2 ± 4.0	15.6 ± 3.9	0.021
Side branch intervention	6 (2.0)	308 (98.4)	–
Kissing balloon	4 (66.7)	132 (43.0)	
Side branch ballooning	2 (33.3)	175 (57.0)	
Stent implanted	1 (16.7)	18 (5.8)	
Side branch stenosis postprocedure, %	28 ± 33	18 ± 26	0.001

Values are n (%) or mean ± SD. Data are based on intention-to-treat analysis.
LMWH = low-molecular weight heparin.

TABLE 3 Procedural Secondary Endpoints

	No Side Branch Intervention (n = 303)	Side Branch Intervention (n = 313)	Difference (95% CI)	*P* Value
Main branch technical success	243 (80.2)	257 (82.1)	- 1.9 (- 8.1 to 4.3)	0.544
Side branch technical success	303 (100)	310 (99.0)	1.0 (- 0.3 to 2.8)	0.249
Need for crossover	6 (2.0)	5 (1.6)	0.4 (- 1.7 to 2.5)	0.720
Procedural complications				
Main branch dissection	4 (1.3)	3 (0.9)	–	0.721
Side branch dissection	0 (0.0)	9 (2.9)	–	0.004
Side branch acute occlusion	3 (1.0)	0 (0.0)	–	0.118
Side branch perforation	0 (0.0)	0 (0.0)	–	–
Side branch thrombus	0 (0.0)	0 (0.0)	–	–
Procedure time, min	34.0 (25.0-50.0)	45.0 (33.0-62.0)	- 10.0 (- 13.0 to - 7.0)	<0.001
Fluoroscopy time, min	10.0 (6.3-15.8)	13.2 (9.0-20.0)	- 3.3 (- 4.4 to - 2.3)	<0.001
X-ray dose (air kerma), mGy	453.4 (240.0-872.0)	629.0 (332.0-1025)	- 113 (- 180 to - 50.3)	<0.001
Contrast volume, mL	130 (100.0-170.0)	150 (120.0-190.0)	- 23 (- 30.0 to - 15.0)	<0.001

Values are n (%) or median (Q1-Q3). Data are based on intention-to-treat analysis.

conservative treatment of SB without systematic intervention appears relevant, with a clinical impact.

Consequently, as supported by our results, the POT is the only recommended intervention to treat coronary bifurcation after stenting of the main vessel,[6,8] and intervention on the SB appears optional only in case of flow impairment or acute occlusion of the SB. In these cases, the optimal revascularization strategy remains uncertain. The present study suggests a better result of only SB ballooning in comparison with KBI, with a significant reduction of periprocedural MI and myocardial injury (significant *P* value for noninferiority and a trend for superiority). It is still important to note that this was a subgroup analysis, and the choice of SBI technique was left to the discretion of the practitioner, without randomization. Although only hypothesis generating, these data are consistent with a previous observational study that underlined the safety and efficacy of SB ballooning, with a 1-year target lesion failure rate of only 2%.[24]

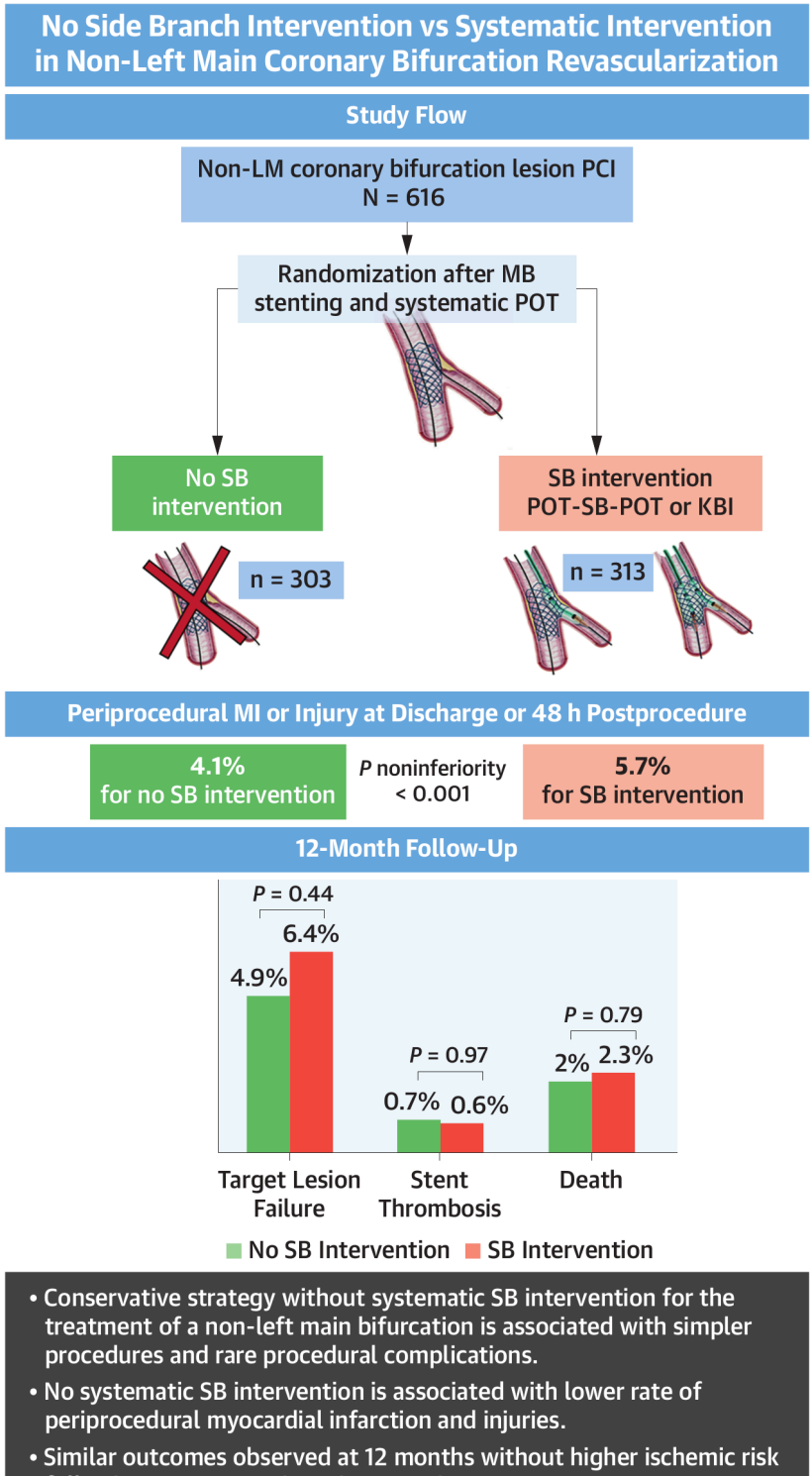
The population included in the present study appears representative of daily clinical practice and consistent with previous studies, with a predominance of left anterior descending coronary artery or diagonal bifurcation and limited disease of the SB, with a median SB lesion length <5 mm. The present findings may thus be particularly relevant to everyday practice, in which most bifurcations are noncomplex, but the results cannot be extrapolated for the management of LM, because of the exclusion of these patients in this study. Because of larger diameters and lower subsequent risk for in-stent restenosis or plaque shifting, but also the unacceptable compromise result for the "SB," PCI of the LM is commonly considered with specific management. However, the most recent studies that evaluated a PCI strategy for the LM

TABLE 4 Occurrence of the Primary Endpoint: Periprocedural Myocardial Infarction or Myocardial Injury at Discharge or 48 Hours Postprocedure

	No Side Branch Intervention	Side Branch Intervention	Difference (95% CI)	*P* Value	
				Noninferiority	Superiority
Intention-to-treat population	(n = 303)	(n = 313)			
Periprocedural MI or myocardial injury at discharge or 48 h postprocedure	11 (4.1)	16 (5.7)	- 1.6 (- ∞ to 1.4)	<0.001	0.384
Per protocol set population	(n = 268)	(n = 272)			
Periprocedural MI or myocardial injury at discharge or 48 h postprocedure	11 (4.1)	16 (5.9)	-1.8 (- ∞ to 1.3)	<0.001	0.345

Values are n (%).
MI = myocardial infarction.

CENTRAL ILLUSTRATION **Methodology and Main Results of the KISS Trial**



Chevalier B, et al. JACC Cardiovasc Interv. 2026;19(8):961-972.

KBI = kissing balloon inflation; KISS = Keep Bifurcation Single Stenting Simple; LM = left main; MB = main branch; PCI = percutaneous coronary intervention; POT = proximal optimization technique; SB = side branch.

TABLE 5 Clinical Secondary Endpoints at 1 Month and 1 Year

	No Side Branch Intervention (n = 303)	Side Branch Intervention (n = 313)	Difference (95% CI)	*P* Value
Clinical outcomes at 1 mo				
All-cause death	1 (0.3)	1 (0.3)	0.0 (- 0.9 to 0.9)	0.982
Cardiac death	0 (0.0)	0 (0.0)	–	–
Target lesion failure[a]	11 (3.6)	14 (4.5)	- 0.8 (- 0.4 to 2.3)	0597
Target vessel MI	10 (3.3)	14 (4.5)	- 1.2 (- 4.2 to 1.9)	0.452
Clinically driven target lesion revascularization	2 (0.7)	0 (0.0)	–	–
Definite/probable ST	1 (0.3)	1 (0.3)	0.0 (- 0.9 to 0.9)	0.982
Angina improvement	101/106 (95.3)	104/117 (88.9)	6.4 (- 0.6 to 13.4)	0.080
Clinical outcomes at 1 year				
All cause death	6 (2.0)	7 (2.3)	- 0.3 (- 2.6 to 2.0)	0.795
Cardiac death	1 (0.3)	0 (0.0)	–	–
Target lesion failure[a]	15 (4.9)	20 (6.4)	- 1.4 (- 5.1 to 2.2)	0.442
Target vessel MI	15 (4.9)	20 (6.4)	- 1.4 (- 5.1 to 2.2)	0.442
Clinically driven target lesion revascularization	4 (1.3)	6 (1.9)	- 0.6 (- 2.6 to 1.4)	0.556
Definite/probable ST	2 (0.7)	2 (0.6)	0.0 (- 1.3 to 1.3)	0.971
Angina improvement	102/103 (99.0)	104/111 (93.7)	5.3 (0.4-10.2)	0.040

Values are n (%) or n/N (%). Data are based on intention-to-treat analysis. [a]Target lesion failure was defined as the composite of cardiac death, target vessel MI, and clinically driven target lesion revascularization.

MI = myocardial infarction; ST = stent thrombosis.

provided similar conclusions regarding non-LM bifurcations, with fewer major adverse cardiac events and long-term TLR in case of a provisional stenting strategy.[25-27] Although no study has specifically addressed this issue, a "keep bifurcation stenting simple" strategy for LM may be beneficial, particularly given the lower risk for flow impairment in a large SB and the limited risk for SB rewiring in case of reintervention due to larger stent struts.

STUDY LIMITATIONS. First, although the study was based on a randomized, multicenter, international design, it remained open label, which may have introduced operator biases in procedural decisions and follow-up assessments. Nevertheless, as in the other previous studies on this setting, because of the evaluation of the intervention on the SB, a double-blind study appears not feasible. Moreover, all procedures were reviewed by a core laboratory with 2 independent physicians.

Second, the inclusion criteria, focused on bifurcation lesions with preserved SB flow, could potentially limit the generalizability of the findings to more complex or high-risk anatomies.

Third, the definition of periprocedural MI, although aligned with ARC-2 criteria, relies partly on a biomarker-based MI definition, which can be influenced by procedural variables and lacks standardization across centers.

Fourth, the trial follow-up duration and the lower rate of observed events than expected could have led to an underpowered trial considering the noninferiority margin and could have limited the detection of differences between the groups.

Finally, intracoronary imaging was not mandatory per the trial design to guide PCI, and its use was very limited despite the demonstrated significant reduction of major adverse cardiac events in complex PCI.[19,28,29] Nevertheless, the evidence of this clinical benefit, particularly for the treatment of bifurcation lesions, and the subsequent international guidelines were published after the design of the trial and the patients' inclusion. Moreover, intracoronary imaging could have been relevant to confirm the result on the MB after POT, but its impact on the SB and periprocedural MI and myocardial injury appears limited.

CONCLUSIONS

A conservative strategy without systematic SBI in case of normal SB flow is associated with very rare procedural complications and is noninferior to a systematic SBI regarding periprocedural MI and myocardial injury. These findings support a simplified "keep bifurcation stenting simple" approach in noncomplex and non-LM bifurcation PCI. Further studies are warranted to support these data and evaluate the impact of this conservative strategy on long-term clinical events.

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PERSPECTIVES

WHAT IS KNOWN? PCI of a coronary bifurcation induces some technical challenges, including management of the SB and subsequent risk for flow impairment. The provisional stenting strategy has been established as a standard of care with MB stenting and a POT, but the clinical benefit of additional SBI remains debated.

WHAT IS NEW? A conservative strategy without systematic SBI for the treatment of a non-LM bifurcation is associated with simpler procedures and very rare procedural complications and is noninferior to systematic SBI regarding periprocedural MI and myocardial injury as 1-year occurrence of target lesion failure.

WHAT IS NEXT? Further studies are warranted to evaluate the impact of this conservative strategy on long-term clinical events, the predictive factors of SB flow impairment, and the extrapolation of these data in all bifurcation lesions, including the LM.

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KEY WORDS bifurcation, KISS, myocardial infarction, myocardial injury, periprocedural complications, side branch

APPENDIX For a list of participating centers and investigators for the KISS trial as well as supplemental tables, please see the online version of this paper.