Catheterization and Cardiovascular Interventions

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ORIGINAL ARTICLE - CLINICAL SCIENCE

Impact of Isolated Side Branch Lesions on Procedural Techniques and Outcomes of Bifurcation Percutaneous Coronary Intervention

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Received: 25 March 2025 | **Revised:** 29 April 2025 | **Accepted:** 6 May 2025

ABSTRACT

Background: There is limited information on the impact of the isolated side branch lesions (ISBL) on the procedural techniques and outcomes of bifurcation percutaneous coronary intervention (PCI).

Aims: To examine the clinical, procedural and long-term outcomes of ISBL.

Methods: We examined the clinical, angiographic characteristics, and procedural outcomes of 1719 bifurcation PCIs in 1501 patients between 2014 and 2023 from the PROGRESS-BIFURCATION registry. A propensity score matched (PSM) Cox proportional hazards model was used to assess long-term outcomes.

Results: ISBL (Medina class 0,0,1) was present in 80 patients (5.3%). ISBL patients had similar baseline characteristics to the remaining patients, except for hypertension (90.0% vs. 79.2%, $p = 0.020$), prior PCI (66.3% vs. 44.5%, $p < 0.001$), and prior MI (50.6% vs. 35.2%, $p = 0.006$) that were more common in ISBL patients. ISBL had a median side branch diameter of 2.5 mm (interquartile range [IQR] 2.5–3.0), a median length of 10 mm (IQR 5–12), and a median side branch stenosis of 90% (IQR 80–95). The most common stenting strategies were side branch stenting (41.8%) and inverted provisional (25.5%). Technical and procedural success and in-hospital major adverse cardiovascular events (MACE) were similar in patients with and without ISBL. At 3-year follow-up, the incidence of MACE was higher in ISBL patients (36.3% vs. 26.4%, $p = 0.043$), driven by higher repeat target vessel PCI (26.8% vs. 12.0%; $p = 0.003$). On PSM adjusted Cox analysis, ISBL were independently associated with higher follow-up MACE (hazard ratio 1.58, 95% confidence intervals 1.13–2.20, $p = 0.008$).

Conclusions: PCI of ISBL was infrequent and was associated with similar technical and procedural success with non-ISBL but higher long-term MACE driven by higher TVR.

1 | Introduction

Approximately 15%–20% of all coronary lesions involve a bifurcation [1]. The Medina classification, a widely adopted system, assigns a binary value (1, 0) to each of the three components of a bifurcation (proximal main vessel, distal main vessel, and side branch) depending on whether they have more than (1) or less than (0) fifty percent diameter stenosis [2].

Isolated side branch ostial lesions (ISBL), defined as Medina class 0,0,1 lesions, are relatively uncommon with a prevalence of approximately 5% of all coronary bifurcation lesions [3]. However, they have been associated with worse clinical outcomes following bifurcation percutaneous coronary interventions (PCI) [4]. Despite this, limited data exist on procedural techniques and long-term outcomes of ISBL bifurcation PCI [1] that was the focus of the present study.

2 | Methods

2.1 | Patient Population

We analyzed the procedural characteristics and outcomes of bifurcation PCIs performed between 2014 and 2023 at six centers participating in the Prospective Global Registry for the Study of Bifurcation Lesion Interventions (PROGRESS-BIFURCATION, Clinicaltrials.gov Identifier: NCT05100992) registry (Figure 1). The PROGRESS-BIFURCATION registry collects patient-level baseline characteristics, procedural/angiographic characteristics, treatment strategies, in-hospital and long-term outcomes in patients undergoing bifurcation PCI. The Research Electronic Data Capture (REDCap) web-based application was used to capture anonymized data [5]. The study was approved by the institutional review board of all participating sites.

2.2 | Definitions

Bifurcation stenoses were defined according to the Bifurcation Academic Research Consortium (ARC) recommendations as coronary artery narrowings occurring adjacent to and/or involving the origin of an SB with a diameter greater than 2.0 mm [6]. The Medina classification was used to characterize bifurcation lesions, with ISBL defined as class 0,0,1 [2]. Technical success was defined as thrombolysis in myocardial infarction (TIMI) 3 flow and residual stenosis $< 30\%$ in both the main vessel (MV) and SB (when SB stenting was attempted) or as TIMI 3 flow and residual stenosis $< 30\%$ in the main vessel with TIMI 3 flow and either residual stenosis $\leq$ initial stenosis or residual stenosis $< 50\%$ or normal physiology in the SB (when SB stenting was not attempted) [6].

In-hospital major adverse cardiovascular events (MACE) were defined as the composite of death, myocardial infarction (MI), stroke, urgent repeat revascularization, or major bleeding [6]. Major bleeding was defined according to the Bleeding ARC Classification as Class 3 or higher [7]. Procedural success was defined as technical success without in-hospital MACE. The Fourth Universal Definition of MI (type 4a MI) was used to define MI [8]. Follow-up MACE was defined as the composite of death, MI, stroke, and target vessel revascularization. Target vessel revascularization was defined as any repeat PCI or coronary artery bypass graft surgery (CABG) performed on any portion of the target vessel, including the target bifurcation lesion [6].

2.3 | Statistical Analysis

Categorical variables were presented as percentages and compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Continuous variables were presented as mean ± standard deviation or median (interquartile range [IQR]) and compared using the independent-samples *t*-test for normally distributed variables and the Mann–Whitney *U* test for non-parametric variables, as appropriate. The normality of distribution was assessed using the Shapiro–Wilk test and Q–Q plots. The risk of MACE was evaluated with time-to-event analysis using Kaplan–Meier and Cox proportional hazards methods.

Propensity score matching (PSM) analysis was utilized to overcome potential confounding factors. A total of 16 variables including clinical and angiographic characteristics were

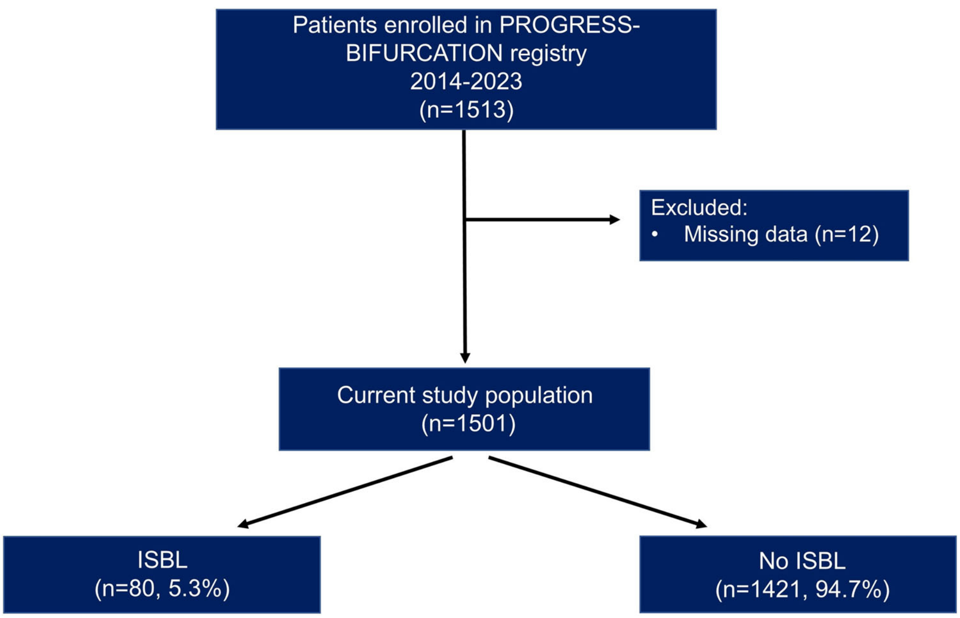


FIGURE 1 | Study flowchart. [Color figure can be viewed at wileyonlinelibrary.com]

included in the analyses: age, gender, diabetes mellitus, hypertension, family history of premature coronary artery disease, prior PCI, congestive heart failure, chronic kidney disease, peripheral arterial disease, smoking, proximal main vessel diameter, distal main vessel diameter, side branch diameter, bifurcation angle, main vessel moderate/severe calcification, and intravascular imaging use.

Five multiply imputed data sets were created and analyzed using multiple imputations to overcome the incomplete data limitation. Incomplete data were imputed under the fully conditional specification method, applying the default settings of the "mice" package (version 3.16.0) for R [9]. The percentage of missing data for the variables was 2.1%. PSM was performed using the "within" methodology due to the less bias risk as suggested by Granger et al. [10]. The nearest pair matching method was used, with a matching ratio of 1:1. The distribution of propensity scores within each treatment group was visually examined with a kernel density plot. Baseline, PSM adjustment balance between covariates were assessed by absolute standardized mean differences (SMD). SMDs before and after covariate balancing were demonstrated to have a good balance (Figure 2) [11]. The weights derived from the initial model were applied for adjustment to the Cox proportional hazard model to assess long-term MACE. Variables included in the model were selected according to their clinical relevance, prior research, and plausible relationship with the studied outcomes [12–14]. After the Cox proportional hazards model was performed in each of the imputed data sets, the results were pooled using the "pool ()" function of the "mice" package. All statistical analyses were performed using R Statistical Software, version 4.4.1 (R Foundation for Statistical Computing) with "MatchThem," "ggplot," "mice," "cobalt," "rms," and "survival" packages. All tests were two-tailed with p-value of < 0.05 indicated statistical significance.

3 | Results

3.1 | Clinical Characteristics

During the study period, 1719 bifurcation PCIs were performed in 1501 patients, of whom 80 underwent ISBL PCI (5.3%) (Figure 1). The baseline characteristics of the study population are shown in Table 1. Mean age was 67.0 ± 13.2 years and 82.5% of the patients were men in the ISBL group. The baseline characteristics of ISBL patients were similar to the remaining patients, except for hypertension (90.0% vs. 79.2%, $p = 0.020$), prior PCI (66.3% vs. 44.5%, $p < 0.001$), and prior MI (50.6% vs. 35.2%, $p = 0.006$) that were more common in ISBL patients. The most common presentation in ISBL patients was non-ST-segment elevation MI (NSTEMI) (34.0%) vs. stable angina in non-ISBL patients (34.2%). The primary indication of bifurcation PCI in ISBL patients was acute coronary syndrome (63.8%), followed by symptom relief (23.8%), and ischemia reduction (6.3%).

3.2 | Angiographic and Procedural Characteristics

In the ISBL group, the most common proximal main vessel was the left main coronary artery (LMCA) (38.8%), followed by the left anterior descending artery (LAD) (30.6%), and the left circumflex (LCX) (19.4%) (Table 2). The most common side branch segment was the proximal LCX (26.5%), followed by the first diagonal (25.5%), and the first (13.3%) and second marginal (7.1%) arteries (Central Figure 1). ISBL were more likely to be in larger proximal (3.50 [3.25–4.00] vs. 3.50 [3.00–4.00] mm; $p = 0.001$), distal main (3.00 [2.75–3.50] vs. 3.00 [2.70–3.25] mm; $p = 0.018$), and side branch vessels (2.50 [2.50–3.00] vs. 2.50 [2.25–2.80] mm; $p = 0.001$). ISBL had a median length of 10.0 mm (IQR 5.0–12.0), a median side branch stenosis of 90% (IQR 80–95), and 33.7% had moderate to severe calcification.

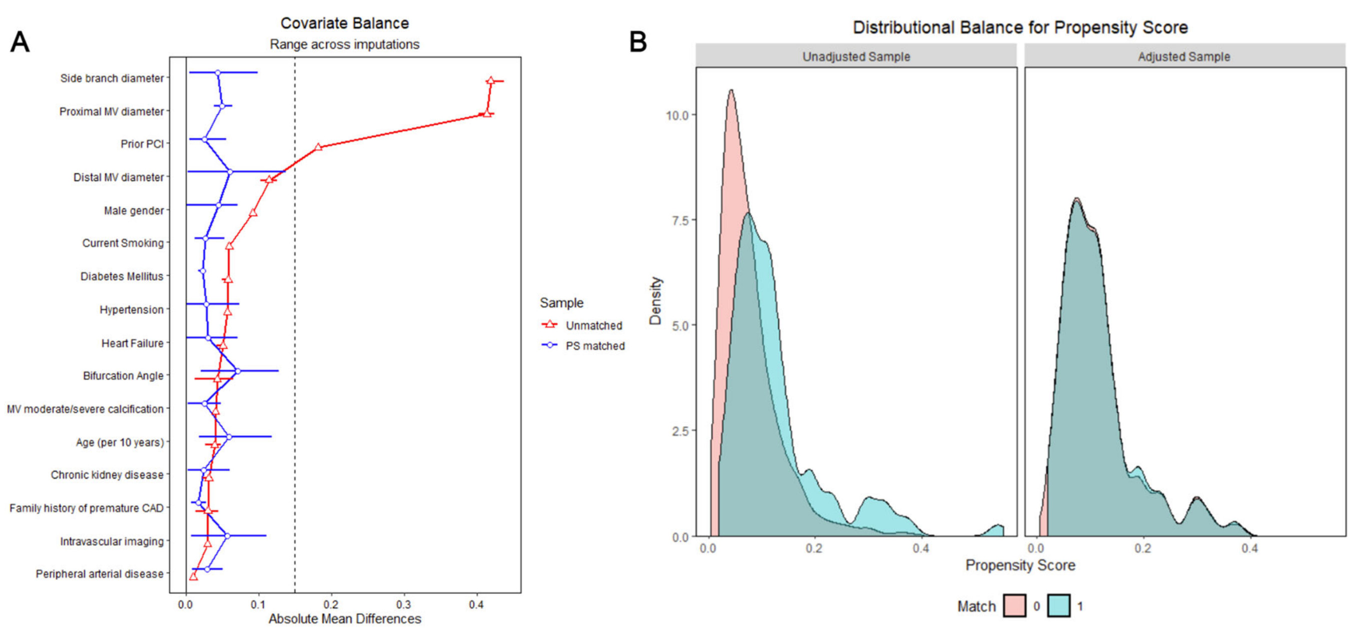


FIGURE 2 | (A) Covariate balance graph in the unmatched and matched study population. (B) Kernel density plot for distribution balance. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 | Baseline clinical characteristics of the study patients, classified according to whether they underwent PCI of a ISBL versus non-ISBL lesion.

Variables	ISBL ($n = 80$)	Non-ISBL ($n = 1421$)	p value
Age (years)	67.05 ± 13.25	66.54 ± 11.74	0.526
Gender, male	82.5% (66)	73.6% (1035)	0.078
BMI	29.20 ± 6.20	30.23 ± 6.11	0.176
Hypertension	90.0% (72)	79.2% (1115)	0.020
Dyslipidemia	82.5% (66)	78.8% (1109)	0.432
Smoking, current	21.3% (17)	20.0% (284)	0.784
Diabetes mellitus	42.3% (33)	35.2% (494)	0.201
Left ventricular ejection fraction (%)	54.91 ± 11.66	53.48 ± 12.82	0.809
Family history of CAD	20.3% (16)	19.2% (261)	0.821
Heart failure	19.0% (15)	22.5% (316)	0.461
Prior PCI	66.3% (53)	44.5% (623)	< 0.001
Prior MI	50.6% (39)	35.2% (492)	0.006
Cerebrovascular disease	13.9% (11)	10.8% (152)	0.392
Peripheral arterial disease	10.1% (8)	10.2% (144)	0.974
CAD presentation			0.010
Stable angina	20.5% (16)	34.2% (474)	
Unstable angina	30.8% (24)	18.8% (260)	
NSTEMI	37.2% (29)	28.4% (393)	
STEMI	6.4% (5)	12.3% (170)	
No symptoms	3.8% (3)	5.6% (78)	
Nonischemic symptoms	1.3% (1)	0.7% (10)	
Bifurcation PCI indication			0.380
Symptom relief	23.8% (19)	28.6% (396)	
Ischemia reduction	6.3% (5)	6.1% (85)	
ACS	63.8% (51)	52.1% (722)	
Arrhythmia/VT/VF/SCD	0.0% (0)	1.2% (16)	
Staged for complete revascularization stable angina	1.3% (1)	3.6% (50)	
High-risk stress test	2.5% (2)	4.8% (67)	
Reduced EF	2.5% (2)	1.2% (17)	
Avoidance of transplant	0.0% (0)	2.4% (33)	
Baseline creatinine (mg/dL)	1.00 [0.84, 1.20]	0.99 [0.82, 1.18]	0.432

Abbrevaitions: CAD = coronary artery disease, MI = myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction, STEMI = ST-segment elevation myocardial infarction.

The prevalence of in-stent restenosis and stent thrombosis were similar between the two groups (Table 2).

Intravascular imaging was similarly used in both groups (Table 2). The most common ISBL stenting strategy was side branch stenting (41.8%), followed by inverted provisional (25.5%), T-stenting (14.3%), and mini-crush (12.2%) (Supporting Information S1: Table 1) (Central Figure 1).

3.3 | Procedural Outcomes

ISBL patients had shorter fluoroscopy time (16 [10–26] vs. 21 [13–32] min; $p = 0.004$), but similar procedure time (69 [45−105] vs. 78 [53−122] min; $p = 0.067$), air kerma radiation dose (1.40 [0.97−2.20] vs. 1.37 [0.90−2.15] Gray; $p = 0.499$), and contrast volume (175 [120−230] vs. 170 [125−220] mL; $p = 0.943$). Technical (96.9% vs. 94.3%, $p = 0.383$) and procedural (96.3% vs. 90.0%, $p = 0.066$) success and in-hospital MACE (1.3% vs. 4.7%, $p = 0.260$) were similar in both groups (Table 3).

In the subgroup of ISBL only treated with side branch stenting, ostial miss occurred in 5 patients (12.2%). Main vessel occlusion occurred in 4 patients (9.8%), all of whom were successfully treated mainly with main vessel ballooning (9.8%). Only 1 (2.4%) patient required conversion to a two-stent strategy (Supporting Information S1: Table 2). Technical and procedural success and in-hospital MACE were similar in inverted

TABLE 2 | Angiographic characteristics of the study lesions, classified according to whether they were ISBL versus non-ISBL.

Variables	ISBL ($n = 98$)	Non-ISBL ($n = 1621$)	p value
LM stenosis (%)	0 [0, 20]	0 [0, 45]	0.002
Proximal LAD stenosis (%)	30 [0, 40]	70 [30, 90]	< 0.001
Mid-distal LAD, diagonal stenosis (%)	80 [40, 95]	80 [50, 90]	0.899
CIRC, OM, LPDA, LPL branches stenosis (%)	80 [50, 95]	70 [30, 90]	0.036
RCA, RPDA, RPL branches stenosis (%)	55 [30, 100]	70 [30, 99]	0.647
Proximal main vessel			0.019
LMCA	38.8% (38)	24.0% (387)	
LAD	30.6% (30)	41.8% (675)	
RCA	10.2% (10)	14.5% (234)	
Circumflex	19.4% (19)	18.3% (296)	
Bypass graft	1.0% (1)	1.4% (22)	
Proximal main vessel diameter (mm)	3.50 [3.25, 4.00]	3.50 [3.00, 4.00]	0.001
Proximal main vessel lesion length (cm)	0.30 [0.00, 0.50]	0.80 [0.50, 1.00]	< 0.001
Proximal main vessel diameter stenosis (%)	0 [0, 30]	80 [50, 90]	< 0.001
Distal main vessel diameter (mm)	3.00 [2.75, 3.50]	3.00 [2.70, 3.25]	0.018
Distal main vessel lesion length (cm)	0.50 [0.00, 1.00]	1.00 [0.50, 1.50]	< 0.001
Distal main vessel diameter stenosis (%)	20 [0, 40]	80 [70, 90]	< 0.001
Calcification			0.106
None	30.6% (30)	31.9% (516)	
Mild (spots)	35.7% (35)	28.5% (461)	
Moderate (≤ 50% reference lesion diameter)	23.5% (23)	20.5% (332)	
Severe (> 50% reference lesion diameter)	10.2% (10)	19.2% (311)	
Proximal main vessel tortuosity			0.952
Straight (< 70 degrees, 1 bend)	52.0% (51)	52.8% (856)	
Slight (> 70 degrees, 1 bend)	30.6% (30)	27.9% (453)	
Moderate (2 bends > 70 degrees or 1 bend > 90 degrees)	14.3% (14)	15.4% (249)	
Severe (2 bends > 90 degrees or 1 bend > 120 degrees)	3.1% (3)	3.9% (63)	
Side branch diameter (mm)	2.50 [2.50, 3.00]	2.50 [2.25, 2.80]	0.001
Side branch lesion length (cm)	1.00 [0.50, 1.20]	0.50 [0.30, 1.00]	< 0.001
Side branch diameter stenosis (%)	90 [80, 95]	60 [20, 90]	< 0.001
Bifurcation angle (degrees)	60 [42, 80]	60 [45, 80]	0.953
ISR lesion	13.3% (13)	12.1% (189)	0.855
Stent thrombosis	2.1% (2)	1.0% (16)	0.277
IVUS for treatment	23.5% (23)	25.5% (414)	0.648
OCT for treatment	0.0% (0)	2.7% (44)	0.174
Technical success	96.9% (95)	94.3% (1529)	0.383

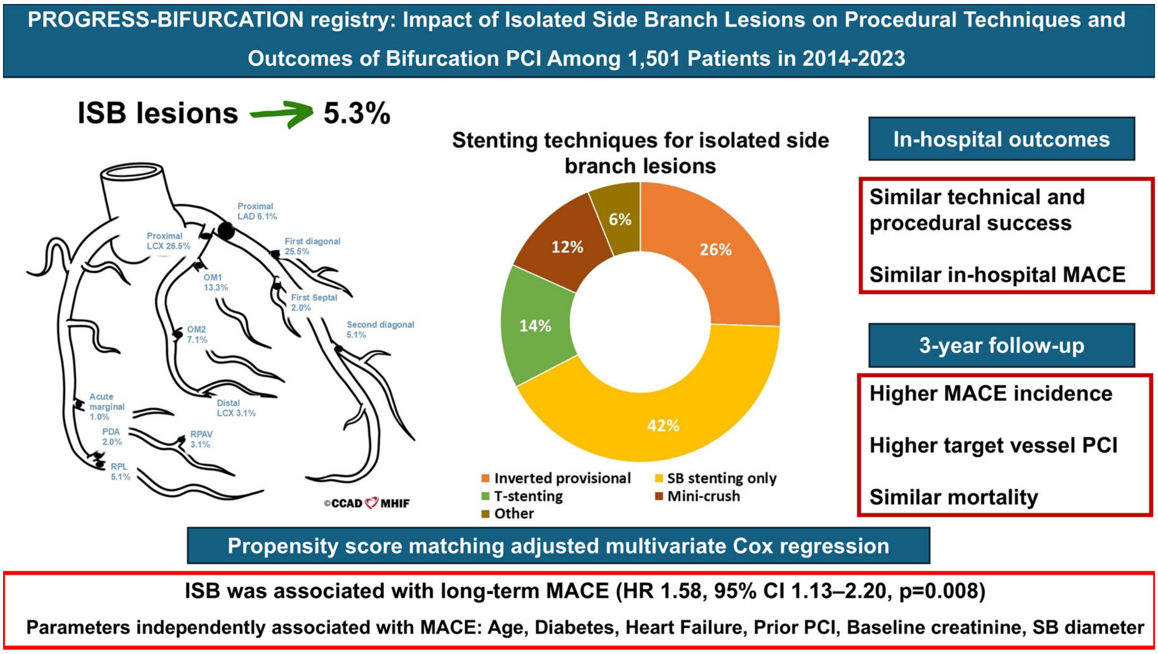
Abbreviations: CIRC = circumflex, IQR = interquartile range, ISR = in-stent restenosis, IVUS = intravascular ultrasound, LAD = left anterior descending, LM = left main, LPDA = left posterior descending artery, LPL = left posterolateral, OCT = optical coherence tomography, OM = obtuse marginal, RCA = right coronary artery, RPDA = right posterior descending artery, RPL = right posterolateral.

provisional and side branch only stenting (Supporting Information S1: Table 3).

3.4 | Long-Term Outcomes

During a median follow-up of 36 (IQR 14–67) months, the incidence of MACE was higher in ISBL patients, driven by higher repeat target vessel PCI, and revascularization with CABG (Table 4, Figure 3).

ISBL patients who underwent side branch only stenting had similar follow-up MACE ($p = 0.960$), mortality ($p = 0.690$), and TVR ($p = 0.690$) to the other stenting strategies (Figure S1). ISBL patients who underwent intravascular imaging had similar follow-up MACE ($p = 0.650$), mortality



CENTRAL FIGURE 1 | Study summary and findings of the impact of isolated side branch lesions on procedural techniques and outcomes. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 | In-hospital outcomes of the study patients, classified according to whether they underwent PCI of a ISBL versus non-ISBL lesion.

Variables	ISBL ($n = 80$)	Non-ISBL ($n = 1421$)	p value
Procedural success	96.3% (77)	90.0% (1263)	0.066
MACE	1.3% (1)	4.7% (66)	0.260
Death	0.0% (0)	1.2% (17)	1.000
Acute MI	0.0% (0)	1.5% (22)	0.627
Repeat PCI	0.0% (0)	1.4% (20)	0.621
Stroke	0.0% (0)	0.6% (9)	1.000
Emergency CABG	0.0% (0)	0.1% (2)	1.000
Bleeding	0.0% (0)	0.6% (9)	1.000
Side branch occlusion	0.0% (0)	0.1% (1)	1.000
Equipment loss	0.0% (0)	0.4% (6)	1.000
Pericardiocentesis	0.0% (0)	0.1% (2)	1.000
Perforation	0.0% (0)	1.3% (18)	0.620
Dissection	1.3% (1)	2.5% (35)	1.000
Thrombus	2.5% (2)	0.9% (13)	0.188
Tamponade	0.0% (0)	0.1% (2)	1.000
Contrast volume, mL	175.0 [120.0, 230.0]	170.0 [125.0, 220.0]	0.943
Fluoroscopy time	16.0 [10.0, 26.0]	21.0 [13.0, 32.0]	0.004
Air Kerma radiation dose (Gray)	1.40 [0.97, 2.20]	1.37 [0.90, 2.15]	0.499
Procedure time	68.7 [45.0, 105.0]	78.0 [53.0, 122.0]	0.067

Abbreviations: CABG = coronary artery bypass graft, MACE = major adverse cardiac events, MI = myocardial infarction, PCI = percutaneous coronary intervention.

($p = 0.120$), and TVR ($p = 0.770$) as those who did not have imaging (Figure S2).

The PSM-adjusted multivariate Cox proportional hazards regression model was used to identify predictors of MACE. Age (per 10 years) (hazard ratio [HR] 1.22, 95% confidence intervals [CI] 1.10–1.35, $p < 0.001$), diabetes (HR 1.47, 95% CI 1.18–1.84, $p = 0.001$), heart failure (HR 1.47, 95% CI 1.18–1.84, $p = 0.001$), prior PCI (HR 1.48, 95% CI 1.18–1.86, $p = 0.001$), baseline creatinine (per 0.5 mg/dL) (HR 1.08, 95%

TABLE 4 | Kaplan−Meier estimates for 3-year outcomes of the study patients, classified according to whether they underwent PCI of a ISBL versus non-ISBL lesion.

	1-year events		2-year events		3-year events		
Variables	**ISBL**	**Non-ISBL**	**ISBL**	**Non-ISBL**	**ISBL**	**Non-ISBL**	**Log rank *p* value**
Follow-up MACE	20.6% (15)	14.9% (140)	30.2% (21)	21.7% (195)	36.3% (24)	26.4% (226)	0.043
CABG	3.0% (2)	0.8% (7)	4.9% (3)	1.3% (11)	7.2% (4)	1.5% (12)	0.004
Death	5.6% (4)	5.0% (47)	10.5% (7)	9.1% (80)	12.8% (8)	12.2% (99)	0.680
Stroke	1.2% (1)	1.5% (14)	1.2% (1)	2.2% (19)	1.2% (1)	2.4% (20)	0.710
Spontaneous MI	5.0% (4)	4.0% (37)	6.2% (5)	5.3% (47)	7.5% (6)	6.9% (56)	0.730
Repeat target vessel PCI	15.7% (11)	7.0% (63)	22.4% (15)	9.6% (83)	26.8% (17)	12.0% (97)	0.003

Abbreviations: CABG = coronary artery bypass graft, MACE = major adverse cardiac events, MI = myocardial infarction, PCI = percutaneous coronary intervention.

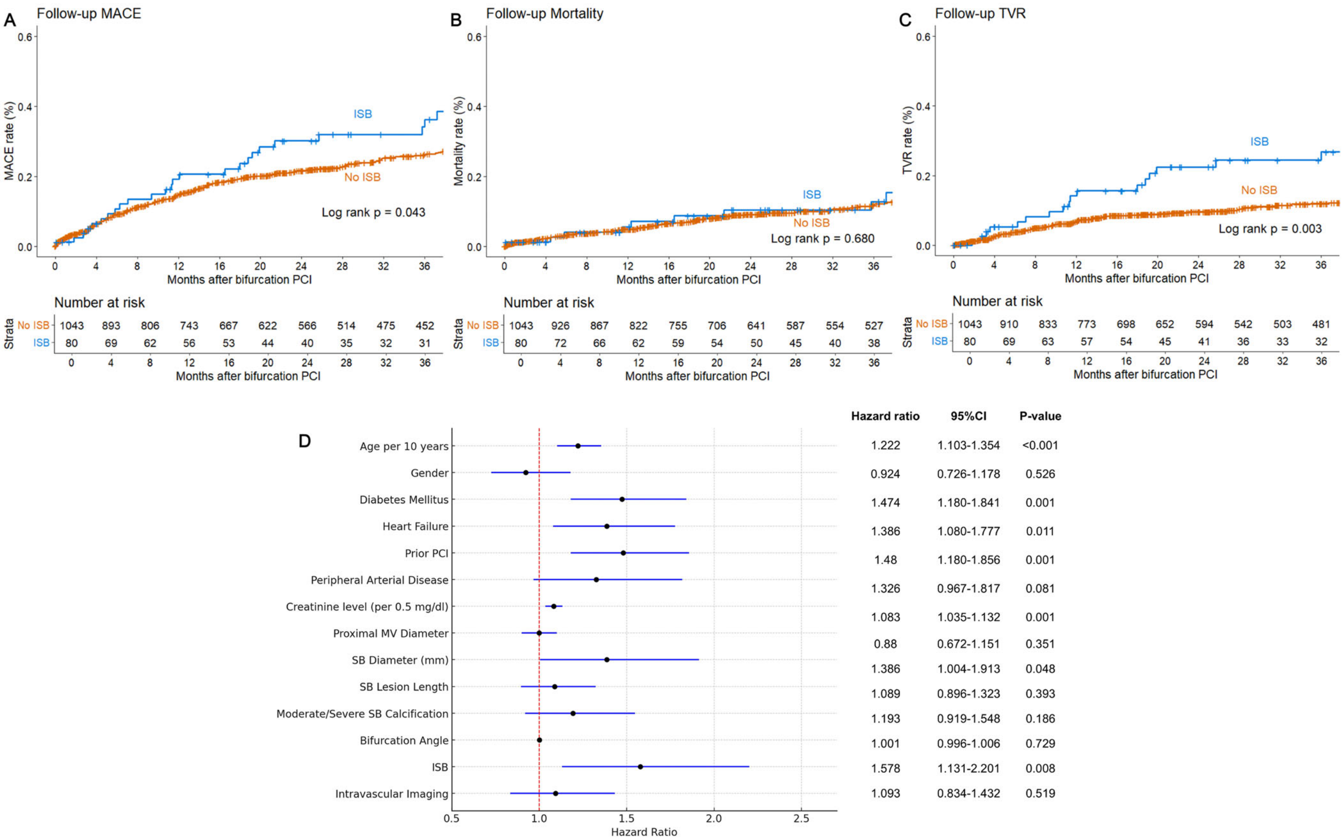


FIGURE 3 | Kaplan−Meier curves for (A) MACE, (B) mortality, (C) TVR for ISBL versus non-ISBL lesions undergoing bifurcation PCI. (D) Forest plot of parameters associated with follow-up MACE. ISBL, isolated side branch lesions; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention; TVR, target vessel revascularization. [Color figure can be viewed at wileyonlinelibrary.com]

CI 1.03–1.13, $p = 0.001$), SB diameter (HR 1.39, 95% CI 1.00–1.91, $p = 0.048$), and ISBL (HR 1.58, 95% CI 1.13–2.20, $p = 0.008$) were independently associated with higher follow-up MACE (Figure 3).

4 | Discussion

The major findings of our study are that: (1) ISBL were uncommon and (2) frequently located in proximal LCX and first diagonal coronary segments. Compared with non-ISBL, ISBL patients had (3) similar comorbidity burden; (4) similar technical and procedural success; but (5) higher TVR and long-term MACE.

There are several potential explanations for the worse outcomes of ISBL bifurcation PCI patients. Bifurcation PCI to the ostial side branch lesions can be challenging due to angulation and the severity of the stenosis [1, 15]. As previously demonstrated, mechanical trauma to the artery during the delivery of equipment may lead to accelerated disease progression [16]. Correct identification of the side branch ostium can be challenging, potentially resulting in geographical miss of the ostium, or compromise of the main vessel [17]. In our study, ostial miss occurred in 12.2% of ISBL patients. Moreover, the main vessel was compromised in 9.8%. However, all of them were successfully treated.

Consistent with our findings, in a recent study that assessed the impact of Medina classification in 778 intravascular imaging-guided bifurcation PCI on 1-year clinical outcomes, MACE was 18.2% in the Medina 0,0,1 group, which was higher than the remaining classes. Additionally, ISBL were independently associated with higher MACE (HR 4.04, 95% CI 1.31–13.45) and target lesion revascularization (TLR) (HR 6.19, 95% CI 1.69–22.74) [4]. However, only 21 ISBL cases were included in this study, and lesion segments were not reported.

In our study, the most common side branch segment was the proximal LCX. A recent study compared 47 ostial LCX and LAD lesions for bifurcation PCI using PSM analysis, showed that ostial LCX bifurcation PCI was associated with high TLR in both univariable and multivariable analysis (HR 7.5, 95% CI 2.1–26.4) [13].

A single-arm multicenter registry of 273 patients with ISBL reported 16.9% 3-year MACE (composite of death, MI, TVR) mainly driven by TVR (14.4%). On univariable Cox analysis dyslipidemia, diabetes, prior PCI, and LM bifurcation were associated with 3-year MACE, however only diabetes was independently associated with 3-year MACE in multivariable analysis (HR 2.35, 95% CI 1.23–4.49) [12]. The 3-year MACE (composite of death, MI, stroke, TVR with PCI or CABG) incidence in ISBL patients was much higher in our study (36.3%). Composite endpoint definition differences could partially explain this variation, but diabetes was also an independent predictor. Additionally, in our study, age, heart failure, prior PCI, baseline creatinine, and side branch diameter were associated with a higher risk of long-term MACE.

The e-Ultimaster (Prospective, Single-Arm, Multi Centre Observations Ultimaster Drug Eluting Stent Registry) study demonstrated that ISBL were associated with higher 1-year cardiac death compared with the remaining Medina classes (HR 4.7, 95% CI 1.0–21.6; $p = 0.044$), which was not observed in our study [17]. A potential explanation could be that our study had a higher utilization of intravascular imaging for bifurcation PCI. This may lead to careful selection of cases and reduce unneeded treatment of ISB lesions. In a similar fashion, Murasoto et al. also did not demonstrate any mortality difference at 1-year follow-up compared with the remaining Medina classes [4].

In our study, the most common stenting strategy for ISB lesions was the only side branch stenting, followed by inverted provisional stenting. Subgroup analysis was performed to identify the impact of various stenting strategies on in-hospital and follow-up outcomes. Both techniques had similar technical and procedural outcomes and in-hospital MACE. Furthermore, we demonstrated no significant differences between only side branch stenting and residual stenting strategies for 3-year MACE, TVR, and mortality. In line with our results, Maurina et al. showed that inverted provisional and side branch stenting had similar in 3-year MACE and TLR [12].

Drug-coated balloons (DCB) are important tools for treating ISBL. In a recently published clinical trial, 784 patients were randomized to either the DCB group or the noncompliant (NC) balloon group [18]. At the 1-year follow-up, the DCB group had lower MACE compared with the NC balloon group (HR 0.56; 95% CI, 0.35–0.88; $p = 0.013$) [18]. However, DCBs were not used in our study, as FDA approval for the coronary use of DCBs occurred in 2024, whereas our most recent data collection was completed in 2023.

Kahraman et al. compared the outcomes after PCI versus medical therapy in 357 patients with ISBL lesions [19], showing similar incidence of the composite endpoint of TVR, MI, and mortality at 6 months of follow-up [19]. However, this study had several limitations: the lesions were restricted to diagonal and obtuse marginal branches, only a limited number of ACS patients were included in the medical therapy group, the follow-up duration was relatively short, and no multivariable adjustment was performed. In our study, we had a longer follow-up period, including more complex lesions, and used a more robust methodology.

Our study has limitations. The PROGRESS-Bifurcation is an observational bifurcation PCI registry with all inherent limitations. There was no independent adjudication of clinical events or core laboratory analysis of the study angiograms. Technique selection was at the operator's discretion. The included procedures were performed at centers with experienced bifurcation PCI operators, which may limit the generalizability of our results to centers with less experience.

5 | Conclusion

Although infrequent, ISBL PCI is associated with similar periprocedural outcomes but higher follow-up MACE compared with non-ISBL, driven by higher TVR.

Acknowledgments

The authors are grateful for the philanthropic support of our generous anonymous donors (2) and the philanthropic support of Drs. Mary Ann and Donald A Sens; Mrs. Diane and Dr. Cline Hickok; Mrs. Wilma and Mr. Dale Johnson; Mrs. Charlotte and Mr. Jerry Golinvaux Family Fund; the Roehl Family Foundation; the Joseph Durda Foundation; Ms. Marilyn and Mr. William Ryerse; Mr. Greg and Mrs. Rhoda Olsen. The generous gifts of these donors to the Minneapolis Heart Institute Foundation's Science Center for Coronary Artery Disease (CCAD) helped support this research project.

Conflicts of Interest

Dr. Yader Sandoval: Abbott (consultant, advisory board), Roche Diagnostics (consultant, advisory board, speaker), Philips (consultant, advisory board, speaker), Zoll (advisory board), GE Healthcare (consultant, advisory board), CathWorks (consultant), HeartFlow (speaker), Cleerly (speaker, research grant). He is an associate editor for JACC Advances. He and others hold patent 20210401347. Dr. M. Nicholas Burke: consulting and received speaker honoraria from Abbott Vascular and Boston Scientific. Dr. Emmanouil S. Brilakis: consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor, Circulation), Amgen, Asahi Intecc, Biotronik, Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), CSI, Elsevier, GE Healthcare, IMDS, Medicure, Medtronic, Siemens, and Teleflex; research support: Boston Scientific, GE Healthcare; owner, Hippocrates LLC; shareholder: MHI Ventures, Cleerly Health, Stallion Medical.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.