THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Adherence to Guideline Recommendations and Clinical Outcomes of Different Stenting Techniques in Non-Left Main Bifurcation Lesions

ORIGINAL INVESTIGATION

Serkan Kahraman[1]
Muzaffer Değertekin[2]
Can Yücel Karabay[3]
Mehmet Akif Erdöl[4]
Hasan Arı[5]
Eser Durmaz[6]
Ertuğrul Okuyan[7]
Regayip Zehir[8]
Ali Rıza Akyüz[9]
Çağrı Yayla[4]
İrfan Şahin[7]
Cansu Ebren[2]
Gökhan Demirci[1]
Ahmet Güner[1]
Yunus Emre Erata[1]
Mustafa Ali Yavaş[1]
Ahmet Göktuğ Ertem[4]
Mustafa Azmi Sungur[3]
Bilal Mete Ülker[5]
Ahmet Ceyhun Cebeci[3]
Ali Nural[3]
Büşra Güvendi[8]
Ahmet Oğuz Aslan[9]
İshak Yılmaz[7]
Ali Kemal Kalkan[1]
Mehmet Ertürk[1]

[1]*Department of Cardiology, University of Health Sciences, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Center, Training and Research Hospital, İstanbul, Türkiye*
[2]*Department of Cardiology, Yeditepe University Medical Faculty Hospital, İstanbul, Türkiye*
[3]*Department of Cardiology, University of Health Sciences, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye*
[4]*Department of Cardiology, University of Health Sciences, Ankara City Hospital, Ankara, Türkiye*
[5]*Department of Cardiology, University of Health Sciences, Bursa Yuksek İhtisas Training and Research Hospital, Bursa, Türkiye*
[6]*Department of Cardiology, Cerrahpaşa School of Medicine, İstanbul University-Cerrahpaşa, İstanbul, Türkiye*

ABSTRACT

Background: Percutaneous coronary intervention (PCI) for coronary bifurcation lesions (CBLs) is a challenging procedure. The optimal stenting technique is still debated. The importance of adherence to current guideline recommendations on clinical outcomes has not yet been clarified. The authors' aim is to investigate the impact of guideline recommendations on clinical outcomes in PCI of CBL.

Methods: This was a retrospective, multicenter, observational registry that enrolled patients with true CBL undergoing PCI with provisional or 2-stent techniques. All techniques were evaluated according to the current guideline recommendations. The primary endpoint of the study was target lesion failure (TLF) as a composite endpoint of target lesion revascularization (TLR), target vessel myocardial infarction (TVMI), and cardiac death.

Results: A total of 1407 patients were enrolled, and the incidence of TLF, TLR, TVMI, and cardiac death were similar in provisional and 2-stent techniques. However, the incidence of TLF was higher in 2-stent (16.1%) compared to provisional (9.1%) if the guideline recommendations were not followed (HR:1.779; 95%CI: 1.187-2.668, $P = .005$). The incidence of TLF was lower in 2-stent (4.7%) compared to provisional (9.1%) if the guideline recommendations were followed (HR:0.501; 95% CI: 0.306-0.821, $P = .005$), mainly driven by reduced TLR (8.1% vs. 3.4%) (HR: 0.398; 95% CI: 0.228-0.696, $P = .001$) and TVMI (4.5% vs. 2.4%) (HR: 0.503; 95% CI: 0.250-1.011, $P = .049$).

Conclusion: Adherence to current guideline recommendations is the main determinant of clinical outcomes in the PCI of CBLs rather than the selected techniques.

Keywords: Bifurcation lesion, guideline recommendations, percutaneous coronary interventions

INTRODUCTION

Coronary bifurcation lesion (CBL) is an intriguing topic among interventional cardiologists with an incidence of almost 15%-20% of all percutaneous coronary interventions (PCIs).[1] Despite the advances in technology and increased operator's experience, the optimal percutaneous treatment strategy is still debated. Due to the complex structure and different anatomical variations of bifurcation lesions, it is difficult to provide optimal results for the same treatment procedure in every patient. While the provisional side branch stenting is the ultimate therapy for the majority of patients, 2-stent strategies are still necessary, especially in complex bifurcations. In recent years, it has been shown that the double kissing (DK) crush stenting has better results than provisional stenting and other 2-stent strategies.[2-4] However, it remains unclear whether these results are due to the crush technique being superior to other techniques or because DK crush is an optimally performed technique according to current guideline recommendations.[5]

Since 2-stent strategies involve many complex steps and technical difficulties, they are recommended to be performed by experienced operators.[5] The important point is to increase technical success and improve clinical outcomes in bifurcation lesions. What is important for this is to aim for procedural success in line with the guideline recommendations rather than what the strategy is. It is known

[7]Department of Cardiology, University of Health Sciences, Bağcılar Training and Research Hospital, İstanbul, Türkiye
[8]Department of Cardiology, University of Health Sciences, Koşuyolu Kartal Heart Training and Research Hospital, İstanbul, Türkiye
[9]Department of Cardiology, University of Health Sciences, Trabzon Ahi Evren Cardiovascular and Thoracic Surgery Research and Application Center, Trabzon, Türkiye

Corresponding author:
Serkan Kahraman
✉ serkankahraman_86@outlook.com

Received: February 18, 2025
Accepted: May 20, 2025
Available Online Date: July 9, 2025

Cite this article as: Kahraman S, Değertekin M, Karabay CY, et al. Adherence to guideline recommendations and clinical outcomes of different stenting techniques in non-left main bifurcation lesions. *Anatol J Cardiol.* 2025;XX(X):1-11.

DOI:10.14744/AnatolJCardiol.2025.5258

that the commonly performed 2-stent bifurcation techniques may result in imperfect stent configurations that may result in adverse clinical outcomes. On the other hand, adherence to guideline recommendations might reduce suboptimal stent configurations.[6] However, there is no data are yet available to demonstrate the importance of following guideline recommendations on cardiovascular outcomes. The authors' aim in this study is to evaluate the clinical outcomes of different bifurcation stenting techniques in terms of compliance with guideline recommendations.

METHODS

The present study was a retrospective, multicenter, observational registry that was conducted in 9 heart centers. Patients undergoing percutaneous revascularization for true CBL were enrolled into the study. Each participant had to be followed for the clinical outcomes. This trial was approved by the local ethic committee and conducted in accordance with the principles of the Declaration of Helsinki. Additionally, artificial intelligence (AI)–assisted technologies were not used in this manuscript or its contents.

Patient Population

Consecutive patients older than 18 years of age with de novo true non-left main CBL were evaluated in this study. Coronary bifurcation lesion was classified according to the Medina classification. Briefly, coronary bifurcation region was divided into 3 segments: proximal main vessel (PMV), distal main vessel (DMV), and side branch (SB). The absence and presence of lesion in each segment are indicated as 0 and 1, respectively. Thus, patients with true CBL according to the Medina classification (Medina 1,1,1 or 0,1,1 or 1,0,1) were included. Patients with chronic coronary syndrome or acute coronary syndrome (unstable angina pectoris or non-ST segment elevation myocardial infarction) were evaluated in this study. The DMV reference diameter and SB reference diameter had to be at least 2.5 mm and 2.25 mm, respectively. Additionally, the difference between the main vessel (MV) and SB diameters had to be ≤1 mm. Patients with a history of coronary artery bypass grafting surgery, heart failure with ejection fraction <40%, chronic total occlusion or calcification requiring calcium modification, and patients undergoing PCI for stent restenosis and patients presented with cardiogenic shock and ST segment elevation myocardial infarction were excluded from the study. On the other hand, patients with hematological disorder or malignancy, end-stage renal or liver disease, active bleeding, pregnancy, and life-expectancy of <1 year were also excluded.

Revascularization Techniques

Patients who underwent percutaneous revascularization of CBL with provisional or 2-stent techniques were evaluated in this study. All techniques were evaluated according to the European Bifurcation Club (EBC) guideline recommendations.[5-7] The bifurcation stenting techniques were briefly described as follows. For the provisional stenting technique, after the MV stent was implanted, proximal optimization technique (POT) was performed with a non-compliant coronary balloon (NCB). The further SB intervention was performed if the SB TIMI (Thrombolysis in Myocardial Infarction) flow grade was <3 or severe SB ostial stenosis (70%<) or SB dissection (type A<) or SB ischemia (fractional flow reserve <0.80 or instantaneous wave-free ratio <0.89).[7-10] For the T technique and T and small protrusion (TAP) technique, after the MV stenting and POT, the SB was rewired and first kissing balloon dilatation (KBD) and second POT were performed. Then, the SB stent was implanted while a NCB was positioned uninflated in the MV at the level of carina. After the side branch optimization (SBO) technique was performed, second KBD was performed. The procedure was terminated with the final POT. For the culotte technique, the first stent was implanted from the PMV to the SB with a minimal

HIGHLIGHTS

- The optimal percutaneous treatment strategy of CBLs is still controversial.
- Provisional stenting is the appropriate strategy for the majority of patients.
- Planned 2-stent strategy is also important in complex bifurcation lesions.
- Adherence to guideline recommendations is the main determinant of clinical outcomes of stenting techniques.

protrusion (2-3 mm). Then, the SBO was performed. First POT was performed, before the MV rewiring. After the first KBD with NCBs, the MV stent was implanted. Then, the second POT was performed. The final KBD was performed with NCBs following with the SB rewiring. The procedure was terminated with the final POT. For the crush technique, SB stent was implanted with minimal protrusion (2-3 mm) while the MV NCB was positioned uninflated in the MV. Then, the SBO was performed. The SB stent was crushed with the NCB, after which the POT crush was encouraged with the NCB. After SB rewiring, first KBD was performed with NCBs. The MV stent was implanted and then POT was performed. After SB rewiring, final KBD and final POT was performed. The MV and SB stents were sized 1:1 to the reference DMV and SB diameters, respectively. The POT balloon was sized 1:1 to the PMV diameter. The KBD was performed with balloons sized 1:1 to the DMV and SB reference diameters. Non-compliant coronary balloons were preferred to be used at all stages. Procedural steps of standardized techniques were evaluated by independent cardiologists from high volume tertiary heart centers. All techniques were also classified according to whether they were performed in accordance with the guidelines, the steps of which were briefly explained above.[5,7] If the technical steps were not performed appropriately, it was considered that the technique was not performed in accordance with guideline recommendations. Intravenous or intracoronary unfractionated heparin (70-100 IU/kg) was given immediately after the guiding catheter cannulation. All patients received dual antiplatelet therapy with 81-100 mg/day acetylsalicylic acid and P2Y12 receptor inhibitor (clopidogrel 75 mg/day or ticagrelor 90 mg bid or prasugrel 10 mg/day) for at least 6 months according to the operator's decision. The use of glycoprotein IIb/IIIa receptor inhibitors and intravascular ultrasound (IVUS) imaging were at the discretion of the operators. Additionally, the use of quantitative coronary analysis (QCA) was not available in all centers and mandatory while it has been evaluated in selected patients. Quantitative coronary analysis was obtained by using CAAS bifurcation software (Pie Medical Imaging, Maastricht, the Netherlands). Two angiographic orthogonal views were obtained for analysis without vessel overlaps or foreshortening and with the widest bifurcation angle. Minimum lumen area, reference vessel diameters, bifurcation angle, and percent diameter stenosis were evaluated for each segments of PMV, DMV, and SB.[11]

Study Outcomes

The primary endpoint of the study was target lesion failure (TLF) as a composite endpoint of target lesion revascularization (TLR), target vessel myocardial infarction (TVMI), and cardiac death. The patient follow-up visits were done at the hospital admission or telephone contact. If a patient had an exact reason of cardiac mortality, it was accepted as a cardiac death in addition with any death without clear non-cardiac reasons. Target vessel myocardial infarction was defined as peri-procedural or spontaneous myocardial infarction (MI) unless there was clear evidence that they were attributable to a non-target vessel according to the the Academic Research Consortium.[11] Protocol defined peri-procedural MI and spontaneous MI were defined according to the fourth universal definition of MI (2018).[12] Ischemia driven TLR was defined as ischemia-related revascularization of MV or SB with a repeat percutaneous intervention or surgery.[11]

The DEFINITION (Definitions and impact of complEx biFurcation leslons on clinical outcomes after PCI using drug-eluting steNts) criteria were used to define whether a CBL was complex or not.[13] Complex bifurcation lesion was defined in the presence of both major criterion and additional 2 minor criteria. Major criterion for non-left main coronary artery (LMCA) bifurcation was SB lesion length ≥10 mm and SB diameter stenosis ≥ 90%. Minor criteria were as follows: mild calcification, multiple lesions, bifurcation angle <45° or >70°, MV reference diameter <2.5 mm, MV lesion length ≥25 mm, thrombus-containing lesions. Additionally, the Syntax (Synergy between PCI with Taxus and Cardiac Surgery) score calculator (www.syntaxscore.com) was used to obtain Syntax score of each patient.

Statistical Analysis

Fisher's exact and Pearson chi-square tests were used to analyze the categorical variables. The Kolmogorov-Simirnov test was used to analyze to distribution of variables. Data was expressed as "mean ± standard deviation (SD)" and "median (25th-75th percentiles)" for variables with and without normal distribution, respectively and "n (%)" categorical variables. Kruskal-Wallis test was used for variables without normal distribution while one-way-ANOVA was used for variables with normal distribution and intergroup analyses were performed using post-hoc analyses. The statistical analyses of the endpoints were analyzed using the Kaplan-Meier method (with the log-rank test) and Cox regression analysis was used to to analyze outputs of hazard ratio (HR) and 95% CI. Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York, USA). A *P*-value <.05 was considered statistically significant.

RESULTS

A total 1407 consecutive patients with true CBL (Medina 1,1,1 or 0,1,1 or 1,0,1 classification) undergoing PCI were enrolled in this multicenter study. Patients were divided into 4 groups: provisional group (n=397), T/TAP group (n=168), culotte group (n=297), and crush (n=545) group. Baseline demographic and clinical variable were demonstrated in Table 1. All patients were followed-up up to 60 months. The mean age of provisional group was 61 ± 11, while it was 60 ± 10 in culotte and crush groups and 59 ± 10 in T/TAP group. Seventy patients (17.6%) was female in provisional group, while 33 patients (19.6%) in T/TAP, 59 patients (19.9%) in culotte, and 116 patients (21.3%) in crush groups. About 248 patients (62.5%) presented with acute coronary syndrome in provisional group, while it was 94 patients (56.0%) in T/TAP group, 1151 patients (50.8%) in culotte group, and 321 patients (58.9%) in crush group. There were no differences in terms of diabetes mellitus, hypertension, previous cerebrovascular accident, smoking status, laboratory parameters, and ejection fraction between groups.

Table 1. Clinical and Demographic Parameters

	Provisional (n=397)	T/TAP (n=168)	Culotte (n=297)	Crush (n=545)	*P*
Age (years)	61 ± 11	59 ± 10[a]	60 ± 10	60 ± 10	.018
Gender (female) n (%)	70 (17.6)	33 (19.6)	59 (19.9)	116 (21.3)	.586
Diabetes mellitus, n (%)	158 (39.8)	68 (40.5)	103 (34.7)	214 (39.3)	.472
Hypertension, n (%)	230 (57.9)	84 (50.0)	167 (56.2)	330 (60.6)	.104
Previous CVA, n (%)	12 (3.0)	1 (0.6)	3 (1.0)	13 (2.4)	.138
Smoking, n (%)	192 (48.4)	73 (43.5)	151 (50.8)	267 (49.0)	.490
Previous PCI, n (%)	87 (21.9)	39 (23.2)	61 (20.5)	123 (22.6)	.893
Hemoglobin (g/dl)	15 (13-15)	14 (13-15)	14 (12-15)	13 (12-15)	.080
Thrombocyte × 10^3/mm^3	231 (202-272)	243.5 (207.5-284)	245 (207-286)	247 (230-292)	.099
Leukocyte × 10^3/mm^3	8490 (7010-10760)	7970 (6450-10 520)	10 000 (7000-12 040)	8990 (6350-10 000)	.286
Creatinine (mg/dL)	0.98 ± 0.77	1.0 ± 0.96	0.92 ± 0.46	0.94 ± 0.57	.530
Total cholesterol (mg/dL)	191 ± 45	188 ± 48	190 ± 52	188 ± 51	.714
LDL cholesterol (mg/dL)	118 ± 39	120 ± 42	117 ± 43	113 ± 43	.278
HDL cholesterol (mg/dL)	38 (32-45)	41 (35-47)	40 (33-48)	38 (32-46)	.078
Triglyceride (mg/dL)	155 (110-239)	162 (109-232)	142 (107-200)	147 (108-222)	.397
Glucose (mg/dL)	112 (100-153)	111 (97-165)	113 (97-156)	117 (99-156)	.925
Acetylsalicylic acid, n (%)	385 (97.0)	165 (98.2)	296 (99.7)	531 (97.4)	.082
P2Y12 receptor inhibitors, n (%)					
Clopidogrel	249 (62.7)	102 (60.7)	152 (51.2)[a]	271 (49.7)[a]	<.001
Prasugrel	17 (4.3)	13 (7.7)	22 (7.4)	17 (3.1)	
Ticagrelor	131 (33.0)	53 (31.5)	123 (41.4)	257 (47.2)	
Betablocker, n (%)	337 (84.9)[b]	145 (86.3)	266 (89.6)	499 (91.6)[c]	.010
ACEI or ARB, n (%)	337 (84.9)	147 (87.5)	266 (89.6)	471 (86.4)	.336
Statin, n (%)	365 (91.9)	149 (88.7)	281 (94.6)	510 (93.6)	.086
Calcihum channel blocker, n (%)	101 (25.4)	47 (28.0)	73 (24.6)	155 (28.4)	.575
Clinical presentation, n (%)					
Chronic coronary syndrome	149 (37.5)	74 (44.0)	146 (49.2)	224 (41.1)	.019
USAP/NONSTEMI	248 (62.5)[c]	94 (56.0)	151 (50.8)[c]	321 (58.9)	
Syncope, n (%)	0 (0)	1 (0.6)	1 (0.3)	0 (0)	.207
Ejection fraction, (%)	53 ± 8	55 ± 9	54 ± 9	54 ± 9	.419

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCS, Canadian cardiovascular society; CVA, cerebrovascular accident; HDL, high density lipoprotein; LDL, low-density lipoprotein; NONSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; TAP, T and small protrusion; USAP, unstable angina pectoris. [a]Lower than provisional. [b]Lower than others. [c]Higher than others.

Angiographic and Procedural Features

Angiographic and procedural characteristic of patients were demonstrated in Table 2. The incidence of left anterior descending artery (LAD) artery as a culprit vessel in the provisional group was higher while the circumflex artery (CXA) was higher in the culotte group. The right coronary artery (RCA) revascularization was lower in the crush group than other groups. The incidence of radial access was lower in the culotte group. Acute SB occlusion was more frequent in the provisional and T/TAP groups. The SB reference vessel diameter was lower in the T/TAP group. The length of MV and SB lesions were lower in the provisional group. Final kissing and DK balloon dilatations, final POT, adherence to guideline recommendations were lower in the crush technique. The number of patients with complex lesion was lower in the provisional group. There were no differences in terms of bifurcation angle, diameter stenosis of PMV, DMV, and SB, the use of intra-aortic balloon pump, intra-vascular ultrasound imaging, glycoprotein IIb/IIIa inhibitors, between groups.

Clinical Outcomes

The primary clinical endpoint of the study was TLF as a composite endpoint of TLR, TVMI, and cardiac death (Table 3). The incidence of TLF, TLR, TVMI, and cardiac death were similar in both groups. The incidence of TLF was 9.1% in the provisional technique, while it was 12.5% in the T/TAP technique, 9.8% in the culotte technique, and 8.3% in the crush technique ($P = .417$). The incidence of TLR was 8.1%, 10.1%, 5.4%, and 6.1% in the provisional, T/TAP, culotte and crush techniques, respectively ($P = .161$). The incidence of TVMI was 4.5%, 8.3%, 4.7%, and 3.7% in the provisional, T/TAP, culotte and crush techniques, respectively ($P = .099$). The incidence of cardiac death was also 1.5%, 0%, 2.0%, and 1.5% in the provisional, T/TAP, culotte and crush techniques, respectively ($P = .360$). Then, the study groups were categorized according to the adherence of the guideline recommendations. 2-stent techniques performed in accordance with guideline recommendations and those performed without guideline recommendations

Table 2. Angiographic and Procedural Characteristics

	Provisional (n=397)	T/TAP (n=168)	Culotte (n=297)	Crush (n=545)	*P*
Vessel, n (%)					<.001
LAD	314 (79.1)[a]	115 (68.5)	191 (64.3)	418 (76.7)	
CXA	64 (16.1)	46 (27.4)	96 (32.3)[b]	123 (22.6)	
RCA	19 (4.8)	7 (4.2)	10 (3.4)	4 (0.7)[c]	
CAD severity, n (%)					.031
1-vessel disease	191 (48.1)	74 (44.0)	118 (37.9)	267 (49.0)	
2-vessel disease	137 (34.5)[c]	63 (37.5)	133 (44.8)[d]	210 (38.5)	
3-vessel disease	69 (17.4)	31 (18.5)	46 (15.5)	68 (12.5)	
SYNTAX score	18±5	18±6	17±4[c]	18±8	.003
IABP, n (%)	4 (1.0)	2 (1.2)	3 (1.0)	3 (0.6)	.798
Arterial access, n (%)					.002
Femoral	368 (92.7)	151 (89.9)	291 (98.0)[e]	515 (94.5)	
Radial	29 (7.3)	17 (10.1)	6 (2.0)	30 (5.5)	
Acute SB occlusion, n (%)	17 (4.3)	12 (7.1)	1 (0.3)[g]	1 (2.0)[f]	<.001
Glycoprotein IIb/IIIa inhibitors, n (%)	19 (4.8)	11 (6.5)	7 (2.4)	24 (4.4)	.173
Bifurcation angle (°)	59±15	60±14	60±14	59±14	.771
Medina classification, n (%)					<.001
1,1,1	269 (67.8)	123 (73.2)	204 (68.7)	452 (82.9)[d]	
0,1,1	104 (26.2)	40 (23.8)	76 (25.6)	73 (13.4)[c]	
1,0,1	24 (6.0)	5 (3.0)	17 (5.7)	20 (3.7)	
Diameter stenosis of PMV (%)	67 ± 29	67 ± 30	65 ± 27	68 ± 22	.368
Diameter stenosis of DMV (%)	79 ± 20	78 ± 16	76 ± 17	77 ± 17	.271
Diameter stenosis of SB (%)	83 ± 14	81 ± 14	82 ± 13	83 ± 10	.491
DMV reference diameter (mm)	2.94 ± 0.33	2.94 ± 0.31	2.90 ± 0.29	2.89 ± 0.29	.084
SB reference diameter (mm)	2.61 ± 0.35	2.53 ± 0.22[c]	2.60 ± 0.24	2.60 ± 0.22	.007
Final POT, n (%)	377 (95.0)	158 (94.0)	292 (98.3)	527 (69.7)	.049
Lesion length of MV (mm)	22 ± 8[g]	24 ± 7	23 ± 9	24 ± 8	.018
Lesion length of SB (mm)	9 ± 4[c]	13 ± 7	12 ± 6	13 ± 5	<.001
Final kissing balloon dilatation, n (%)	101 (25.4)[h]	161 (95.8)	287 (96.6)	410 (75.2)[h]	<.001
Pre-procedural TIMI flow of MV, n (%)					<.001
TIMI 0	19 (4.8)	5 (3.0)	15 (5.1)	230 (42.2)[d]	
TIMI 1	8 (2.0)	4 (2.4)	10 (3.4)	45 (8.3)	
TIMI 2	32 (8.1)	9 (5.4)	44 (14.8)[d]	33 (6.1)	
TIMI 3	338 (85.1)	150 (89.3)	228 (76.8)[c]	237 (43.5)[c]	
Post-procedural TIMI flow of MV, n (%)					.148
TIMI 1	0 (0)	1 (0.6)	0 (0)	0 (0)	
TIMI 2	4 (1.0)	3 (1.8)	7 (2.4)	11 (2.0)	
TIMI 3	393 (99.0)	164 (97.6)	290 (97.6)	534 (98.0)	
Pre-procedural TIMI flow of SB, n (%)					<.001
TIMI 0	7 (1.8)	6 (3.6)	10 (3.4)	226 (41.5)[d]	
TIMI 1	4 (1.0)	4 (2.4)	15 (5.1)	47 (8.6)	
TIMI 2	3 (3.3)	8 (4.8)	37 (12.5)	27 (5.0)	
TIMI 3	373 (94.0)	150 (89.3)	235 (79.1)	245 (45.0)[c]	
Post-procedural TIMI flow of SB, n (%)					<.001
TIMI 0	10 (2.5)	0 (0)	0 (0)	0 (0)	
TIMI 1	4 (1.0)	1 (0.6)	0 (0)	0 (0)	
TIMI 2	12 (3.0)	2 (1.2)	4 (1.3)	12 (2.2)	
TIMI 3	371 (93.5)[c]	165 (98.2)	293 (98.7)	533 (97.8)	
Use of IVUS, n (%)	5 (1.3)	8 (4.8)	12 (4.0)	14 (2.6)	.053
Appropriate number of POT, n (%)	302 (76.1)	132 (78.6)	229 (77.1)	399 (73.2)	.410
Double kissing balloon dilatations, n (%)		122 (72.6)	224 (75.4)	272 (49.9)[c]	<.001
Guideline recommendations followed, n (%)	302 (76.1)	120 (71.4)	213 (71.7)	262 (48.1)[c]	<.001
Complex lesion*, n (%)	52 (13.1)[c]	61 (36.3)	111 (37.4)	237 (43.5)	<.001

CAD, coronary artery disease; CXA, circumflex artery; DMV, distal main vessel; IABP, intra-aortic balloon pump; IVUS, intra-vascular ultrasound imaging; LAD, left anterior descending artery; LMCA, left main coronary artery; MV, main vessel; PMV, proximal main vessel; POT, proximal optimization technique; RCA, right coronary artery; SB, side branch; TAP, T and small protrusion; TIMI, thrombolysis in myocardial infarction.
*According to the DEFINITION criteria. [a]Higher than T/TAP and culotte; [b]higher than provisional and crush; [c]lower than others; [d]higher than others; [e]higher than provisional and T/TAP; [f]lower than provisional and T/TAP; [g]lower than crush; [h]lower than T/TAP and culotte.

Table 3. Clinical Outcomes of Bifurcation Stenting

	Provisional (n=397)	T/TAP (n=168)	Culotte (n=297)	Crush (n=545)	*P*
TLF, n (%)	36 (9.1)	21 (12.5)	29 (9.8)	45 (8.3)	.417
TLR, n (%)	32 (8.1)	17 (10.1)	16 (5.4)	33 (6.1)	.161
TVMI, n (%)	18 (4.5)	14 (8.3)	14 (4.7)	20 (3.7)	.099
Cardiac ex, n (%)	6 (1.5)	0 (0)	6 (2.0)	8 (1.5)	.360

TAP, T and small protrusion; TLF, target lesion failure; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

were compared separately with the provisional technique (Table 4). The incidence of TLF was higher in the 2-stent techniques (16.1%) compared to provisional technique (9.1%) if the guideline recommendations not followed (HR:1.779; 95%CI: 1.187-2.668, *P*=.005). There were no differences in TLR (8.1% in the provisional technique and 11.1% in the 2-stent techniques) (HR: 1.352; 95%CI: 0.861-2.123, *P*=.188), TVMI (4.5% vs. 8.2% in the provisional and 2-stent techniques, respectively, *P*=.050), and cardiac death (1.5% vs. 2.4% in the provisional and 2-stent techniques, respectively, *P*=.404) (Figure 1). The incidence of TLF was lower in the 2-stent techniques (4.7%) compared to provisional technique (9.1%) if the guideline recommendations followed (HR:0.501; 95%CI: 0.306-0.821, *P*=.005) that was mainly driven by TLR (8.1% in the provisional technique and 3.4% in the 2-stent techniques) (HR: 0.398; 95%CI: 0.228-0.696, *P*=.001) and TVMI (4.5% in the provisional technique and 2.4% in the 2-stent techniques) (HR: 0.503; 95%CI:0.250-1.011, *P*=.049). There was no difference in cardiac death (1.5% vs. 0.7% in the provisional and 2-stent techniques, respectively, *P*=.176) (Figure 1). The 2-stent techniques had a lower TLF, TLR, TVMI, and cardiac death if guideline recommendations followed (Table 5).

Additionally, the patients were divided into 2 groups according to the absence and presence of the primary composite endpoint (TLF). The predictors of TLF were demonstrated in Table 6. Adherence to guideline recommendations (67.4% vs. 28.2%; HR: 0.212, 95% CI: 0.145-0.310; *P* < .001), double KBD for 2-stent techniques (63.8% vs. 35.8%; HR: 0.341, 95% CI: 0.224-0.519; *P* < .001), and appropriate number of POT (78.9% vs. 42.0%; HR: 0.219, 95% CI: 0.155-0.309; *P* < .001) had improved clinical outcomes. On the other hand, the presence of complex bifurcation lesions (31.9% vs. 41.2%; HR: 1.454, 95% CI: 1.027-2.059; *P* = .034) had a higher ratio of TLF, while the IVUS usage had a lower TLF ratio (3.1% vs. 0%; HR: 0.048, 95% CI: 0.0-4.562; *P* = .048) (Figure 2).

DISCUSSION

In this multicenter, observational study, the clinical outcomes of the provisional stenting and 2-stent techniques were evaluated in true CBLs. Although the clinical outcomes of the provisional technique and 2-stent techniques were similar, it has been shown that the main factor influencing TLF was adherence to current guideline recommendations. Adherence to guideline recommendations was associated with a lower rate of TLF that was mainly driven by reduced TLR and TVMI. On the other hand, DK balloon dilations, appropriate number of POTs, and non-complex lesions were associated with a lower ratio of TLF.

Bifurcation lesions have become increasingly important in recent years and are treated more frequently with PCI. The incidence of CBL is almost 15%-20% in all PCIs.[1] Although there are numerous studies on bifurcation stenting techniques in CBL, the optimal treatment strategy still remains unclear.[14-19] The provisional side branch stenting is still the optimal treatment strategy in patients with bifurcation lesions, even if true CBL is present. There is still no randomized trial showing the superiority of 2-stent techniques over provisional stenting in non-LMCA bifurcations. Provisional stenting should be the initial strategy for non-LMCA bifurcations. On the other hand, if the bifurcation lesion is complex with extensive SB disease and the SB occlusion risk is high, the up-front 2-stent strategy may be performed in selected patients according to the guideline recommendations (Figure 3). In the distal LMCA bifurcations, recent 2 trials compared provisional stenting with 2-stent strategies.[3,14] In the EBC-MAIN trial, fewer major adverse cardiac events (MACE) occurred with provisional stenting

Table 4. Comparison of Clinical Outcomes of Provisional and 2-Stent Strategies Based on Adherence to Guideline Recommendations

	Provisional	2-Stent (Guideline Recommendations not Followed)	HR (95% CI)	*P*
TLF, n (%)	36 (9.1)	67 (16.1)	1.779 (1.187-2.668)	.005
TLR, n (%)	32 (8.1)	46 (11.1)	1.352 (0.861-2.123)	.188
TVMI, n (%)	18 (4.5)	34 (8.2)	1.757 (0.992-3.111)	.050
Cardiac ex, n (%)	6 (1.5)	10 (2.4)	1.533 (0.557-4.218)	.404
	Provisional	**2-Stent (Guideline Recommendations Followed)**	**HR (95% CI)**	***P***
TLF, n (%)	36 (9.1)	28 (4.7)	0.501 (0.306-0.821)	.005
TLR, n (%)	32 (8.1)	20 (3.4)	0.398 (0.228-0.696)	.001
TVMI, n (%)	18 (4.5)	14 (2.4)	0.503 (0.250-1.011)	.049
Cardiac ex, n (%)	6 (1.5)	4 (0.7)	0.429 (0.121-1.519)	.176

HR, hazard ratio; TLF, target lesion failure; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

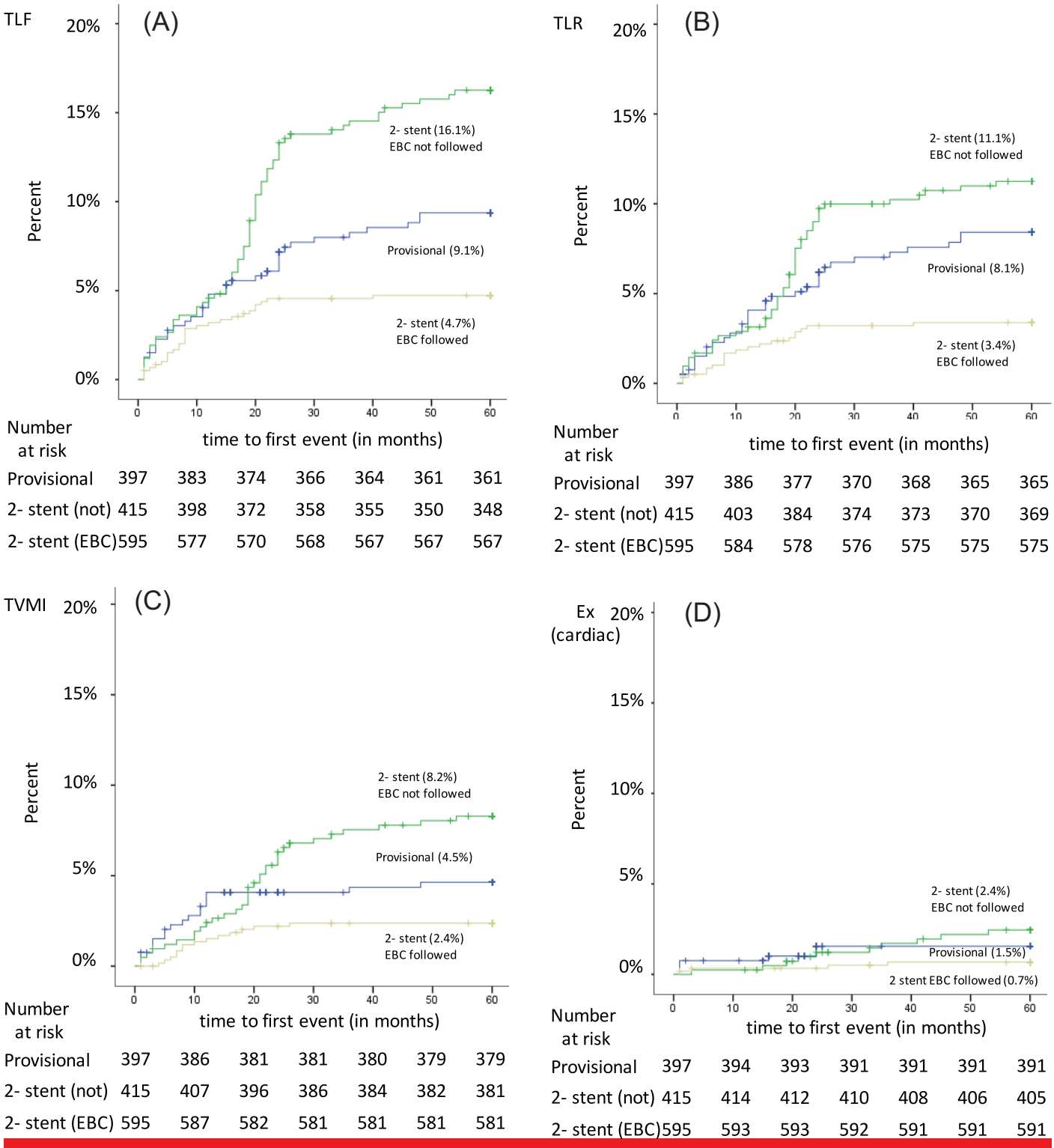

Figure 1. Kaplan-Meier time-to-first event curves according to the guideline recommendations. (A) Target lesion failure; (B) target lesion revascularization; (C) target vessel myocardial infarction; (D) cardiac death. HR, hazard ratio.

compared to planned 2-stent strategies, although without statistical significance.[14] In this trial, the culotte stenting strategy was the most commonly preferred 2-stent strategy according to the operator's decision. On the other hand, in the DK crush V trial, DK crush stenting had a lower rate of TLF compared to provisional stenting in patients with more complex and extensive side branch disease.[3] Additionally, some meta-analyses showed that DK crush stenting had more favorable outcomes than provisional stenting and other 2-stent techniques in both LMCA and

Table 5. Clinical Outcomes of 2-Stent Strategies According to the Guideline Recommendations

	T/TAP	*P*	Culotte	*P*	Crush	*P*
TLF, n (%)		<.001		.003		<.001
Guideline not followed	15 (31.3)		15 (17.9)		37 (13.1)	
Guideline followed	6 (5.0)		14 (6.6)		8 (3.1)	
TLR, n (%)		<.001		.049		.001
Guideline not followed	12 (25.0)		8 (9.5)		26 (9.2)	
Guideline followed	5 (4.2)		8 (3.8)		7 (2.7)	
TVMI, n (%)		.001		.173		.001
Guideline not followed	10 (20.8)		6 (7.1)		18 (6.4)	
Guideline followed	4 (3.3)		8 (3.8)		2 (0.8)	
Cardiac ex, n (%)				.056		.169
Guideline not followed	0 (0)		4 (4.8)		6 (2.1)	
Guideline followed	0 (0)		2 (0.9)		2 (0.8)	

TAP, T and small protrusion; TLF, target lesion failure; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

Table 6. Clinical Endpoints

	Primary Composite Endpoint* (−) (n = 1276)	Primary Composite Endpoint* (+) (n = 131)	HR (95% CI)	*P*
Provisional strategy, n (%)	361 (28.9)	36 (27.5)	1.010 (0.688-1.483)	.958
Guideline recommendations followed, n (%)	860 (67.4)	37 (28.2)	0.212 (0.145-0.310)	<.001
Double kissing balloon dilatations,** n (%)	584 (63.8)	34 (35.8)	0.341 (0.224-0.519)	<.001
Appropriate number of POT, n (%)	1007 (78.9)	55 (42.0)	0.219 (0.155-0.309)	<.001
IVUS usage, n (%)	39 (3.1)	0 (0)	0.048 (0.0-4.562)	.048
Complex lesion, n (%)	407 (31.9)	54 (41.2)	1.454 (1.027-2.059)	.034

HR, hazard ratio; IVUS, intravascular ultrasound; POT, proximal optimization technique. *Primary composite endpoint (target lesion failure) was defined as a composite endpoint of target lesion revascularization, target vessel myocardial infarction and cardiac ex. **For only 2-stent techniques.

non-LMCA bifurcations.[4] These findings raise the question of whether DK crush stenting is better than all other bifurcation techniques. On the other hand, it will be necessary to examine why this success, which could not be achieved with the crush stenting strategy, was obtained with the DK crush technique.

In the contemporary bifurcation stenting era, optimal stent apposition and expansion in the bifurcation vessels, as well as optimal 2-stent placement in the polygon of confluence and minimal metallic overlap are aimed for, besides as little metallic burden as possible in the neocarina. For this reason, all current guideline recommendations include multiple complex steps and recommendations for stent optimization, regardless of the 2-stent strategy chosen.[5] This success with DK crush, one of the optimal 2-stent strategies performed in accordance with current guideline recommendations, is not a surprise in this context, especially in true CBLs and complex SB lesion anatomy. Following this success achieved with DK crush, studies began to examine the results of other commonly used 2-stent strategies when performed in accordance with the guideline recommendations. In a bench test, it was demonstrated that the DK culotte stenting had a shorter metal carina length, smaller area stenosis of SB, and lower ratio of stent malapposition compared to mini-culotte stenting.[15] In another bench test, DK culotte had a lower rate of stent malapposition than the DK crush technique.[16] A recent study showed that the DK culotte was associated with a lower rate of 5-year MACE and TLR compared to mini-culotte technique.[17] It was also demonstrated that patients with unprotected LMCA disease had 1-year MACE rates achieved with the DK culotte technique that were approximately 7.4 times better than the results previously observed with the Culotte in the DK crush III study.[2,18] These results actually show us that clinical outcomes are better when DK-mini culotte stenting is performed in accordance with current guidelines. Supporting these results, in the MOBBEM study, it was demonstrated that commonly performed 2-stent techniques may result in imperfect stent configurations.[6] Adherence to current guideline recommendations with an appropriate number of POT and KBD may reduce these suboptimal results. It can provide better clinical outcomes and improved event-free survival. Additionally, in a recent trial, it was demonstrated that the DK culotte technique was associated with a lower rate of TLF compared to the DK crush technique in a 1-year follow-up period.[19] All these results show us that what is more important than the selected stenting technique is that the performed technique is in full compliance with current guideline recommendations. In light of the foregoing data, several modifications of culotte and crush techniques have been implemented to develop contemporary DK culotte and DK crush techniques. Thus, as mentioned above, contemporary techniques have better outcomes

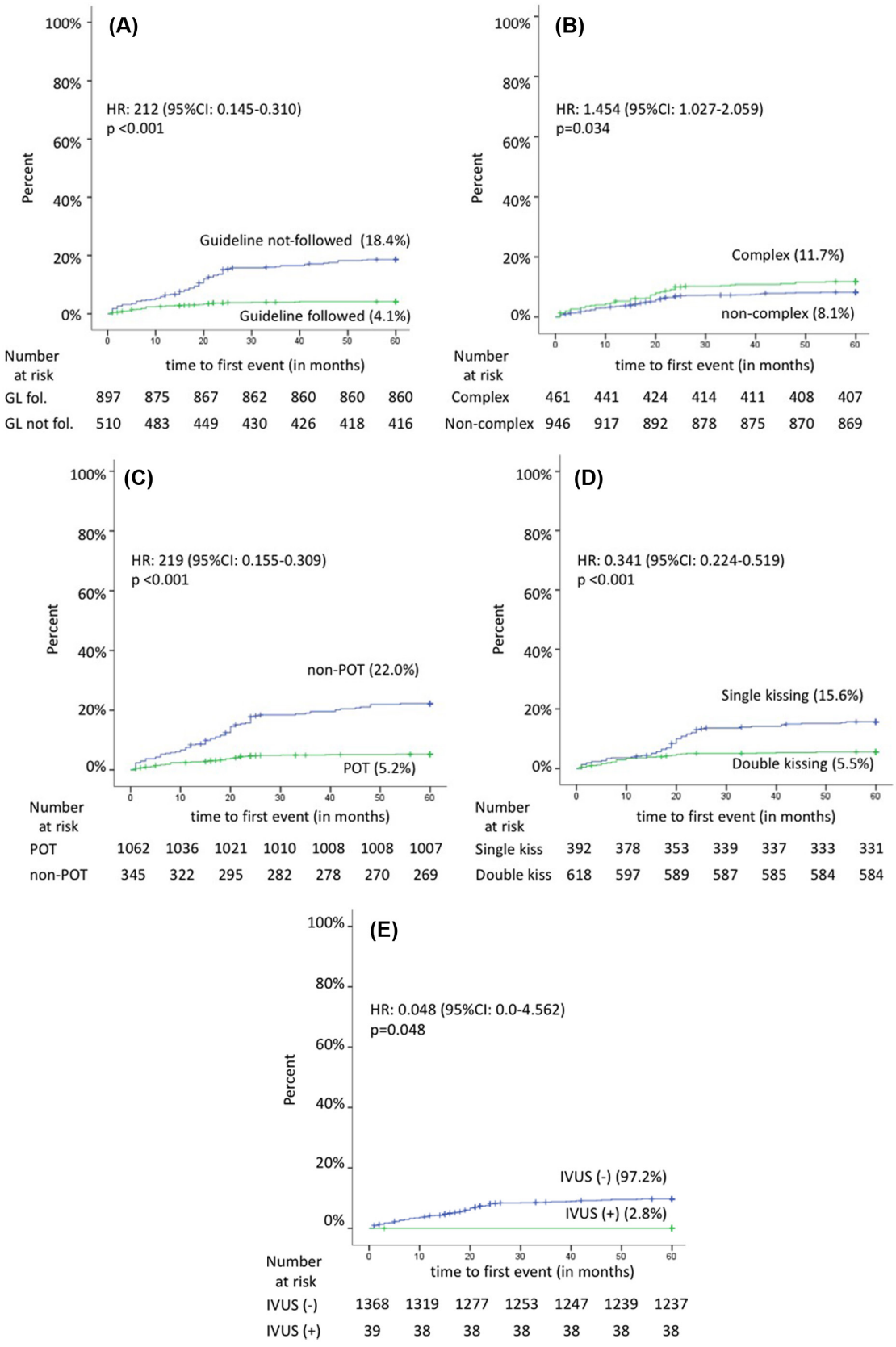

Figure 2. Kaplan-Meier time-to-first event curves for target lesion failure. (A) Guideline recommendations, (B) complex lesion, (C) appropriate number of POT, (D) double kissing balloon dilation,* (E) IVUS usage. HR, hazard ratio; IVUS, intravascular ultrasound; POT, proximal optimization technique; *based on 1010 patients with 2-stent techniques.

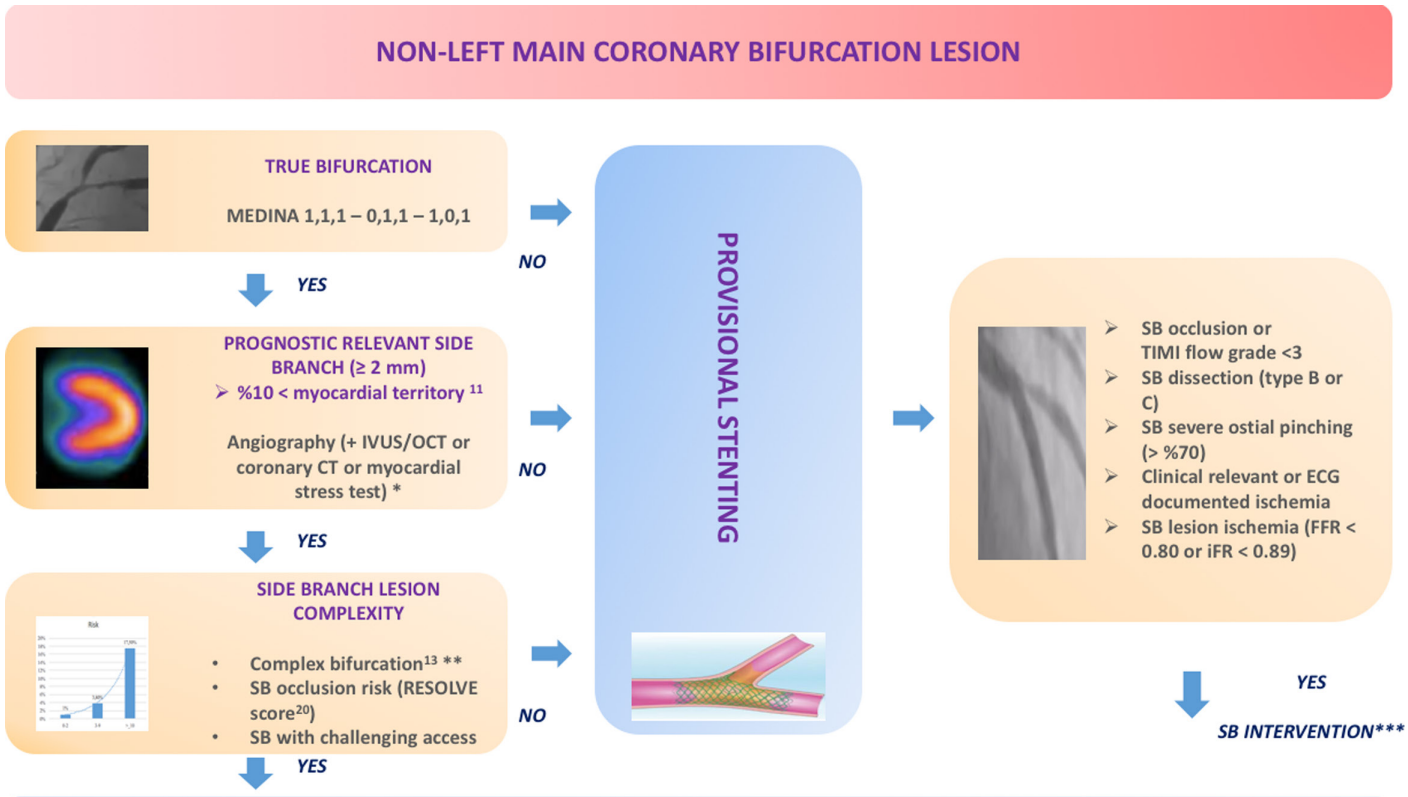

Figure 3. A percutaneous treatment algorithm for true non-left main coronary bifurcation lesions. Prognostic relevant side branches can be detected by multiple modalities;[11] (A) Angiography (+ IVUS/OCT): if an SB length >73 mm or SNUH score ≥2 (1 point each: reference vessel diameter >2.5 mm—number of SB ≤2—no SB below the target SB). (B) Coronary CT: if an SB length >73 mm or fractional myocardial mass on myocardial segmentation software >10%. (C) Myocardial stress test: ≥3 segments stress-induced moderate to severe hypokinesia or akinesia on stress echocardiography or ≥10 myocardial ischemia on SPECT or ≥2 contiguous reduced perfusion segments on cardiac magnetic resonance imaging. Side branch with ≥10 mm lesion length and diameter stenosis ≥90% as well as 2 minor criteria (>mild calcification, multiple lesions, bifurcation angle <45° or >70°, main vessel reference diameter <2.5 mm, main vessel lesion length ≥25 mm or thrombus containing) according to the DEFINITION criteria.[13] RESOLVE score[20] includes 6 parameters, each with a separate score (plaque distribution, main vessel TIMI flow, pre-procedural diameter stenosis of bifurcation core, bifurcation angle, diameter ratio of main vessel/SB, diameter stenosis of SB). High RESOLVE score: ≥10. Side branch intervention with or without bail-out 2-stent strategy. CT, computed tomography; ECG, electrocardiogram; IVUS, intravascular imaging; iFR, instantaneous wave-free ratio; FFR, fractional flow reserve; OCT, optical coherence tomography; SB, side branch; SPECT, single-photon emission computed tomography; TIMI, thrombolysis in myocardial infarction.

than traditional 2-stent techniques; that is why the main determinant of the outcomes is adherence to guideline recommendations. Supporting this, in this study, it was shown that regardless of the technique chosen for CBL, the main effect on clinical outcomes was adherence to the EBC guideline recommendations. As a result of this study, the authors showed that if your compliance with current guideline recommendations and your technical success are low, you may have worse results with the 2-stent technique compared to provisional stenting.

CONCLUSION

Adherence to current guideline recommendations is the main determinant of clinical outcomes in the percutaneous treatment of CBLs rather than the selected techniques.

Limitations

The are several limitations to the current study. The first limitation was a retrospective and non-randomized design of the study. However, it is not possible to conduct a comparative randomized study with a technique that does not comply with current guideline recommendations. Secondly, although the diversity of operators in the study creates difficulties in terms of technical standardization, this multicenter study is valuable in that it reflects real-life data and shows the rate of compliance with the guidelines. Relatively small sample size of each group was the third limitation of the study. However, the lack of a significant difference in demographic and angiographic characteristics between the groups limits the possible impact on the results. Fourth, the lower use of IVUS was the other limitation.

Ethics Committee Approval: This trial was approved by the Istanbul Mehmet Akif Ersoy Training and Research Hospital local ethic committee with the number: 2024.01-03 and date: 10.09.2024.

Informed Consent: Written informed consent was waived due to the retrospective design of the study.

Peer-review: Externally peer reviewed.

Author Contributions: Concept - S.K., M.D., C.Y.K., A.K.K., M.E.; Design - S.K., M.D., C.Y.K., M.A.E., H.A., E.D., E.O., R.Z., A.R.A., A.K.K., M.E., C.Y.; Supervision - S.K., M.D., M.E.; Resources - I.S., C.E., G.D., A.G., Y.E.A., M.A.Y., A.G.E., M.A.S., B.M.U., A.C.C., A.N., B.G., A.O.A., I.Y.; Materilas - I.S., C.E., G.D., A.G., Y.E.A., M.A.Y., A.G.E., M.A.S., B.M.U., A.C.C., A.N., B.G., A.O.A., I.Y.; Data Collection and/or Processing - S.K., I.S., C.E., G.D., A.G., Y.E.A., M.A.Y., A.G.E., M.A.S., B.M.U., A.C.C., A.N., B.G., A.O.A., I.Y.; Analysis and/or Interpretation – S.K., M.E.; Literature Search – S.K., A.K.K., M.E.; Writing - S.K., M.E.; Critical Review - S.K., M.D., C.Y.K., M.A.E., H.A., E.D., E.O., R.Z., A.R.A., A.K.K., M.E., C.Y.Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

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