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Clinical Outcomes of Isolated Non-Left Main Side Branch Ostial Stenosis: Medical Therapy versus Percutaneous Coronary Intervention (the ALP-SBO registry)

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Klíčová slova:
Léze v bifurkacích koronárních tepen
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Postranní větev
Stenóza ostia

SOUHRN

Cíl: Stenóza ostia postranní větve (side branch, SB) je častou bifurkační lézí, přitom o optimální strategii její léčby se stále vede diskuse. Ačkoli je účinnost optimální farmakoterapie dobře známa, i nadále je srovnání farmakoterapie a perkutánní koronární intervence (PCI) předmětem sporu.
Metodika: Celkem bylo retrospektivně hodnoceno 357 po sobě následujících pacientů s izolovanou stenózou ostia SB (klasifikace 0.0.1 podle Mediny). Pacienti byli rozděleni do dvou skupin; pacienti pouze s farmakoterapií (n = 305) a pacienti podstupující PCI (n = 52). Revaskularizace cílové tepny (target vessel revascularization, TVR), infarkt myokardu (IM) a mortalita byly hodnoceny jako závažné nežádoucí kardiovaskulární příhody (major adverse cardiovascular events, MACE).
Výsledky: Průměrný věk pacientů byl 58,2 ± 10,3 roku. Sto dva pacientů (28,6 %) byly ženy. Dvě stě sedmdesát devět pacientů (78,2 %) mělo lézi na diagonální větvi, zatímco 78 (21,8 %) jich mělo lézi na levé marginální větvi. Poměr stenóz SB (70 ± 16; 88 ± 13; $p < 0{,}001$) a délka léze SB (7,5 ± 6,6; 14,7 ± 6,0; $p < 0{,}001$) byly větší ve skupině s PCI. Častou metodou PCI byla implantace stentu do ostia SB (38 pacientů [73,1 %]). Mezi skupinami nebyly nalezeny žádné statisticky významné rozdíly v častosti TVR (1,3 % vs. 1,9 %; $p = 0{,}277$; farmakoterapie vs. PCI), incidenci IM (8,2 % vs. 7,7 %; $p = 0{,}302$; farmakoterapie vs. PCI), v mortalitě (10,2 % vs. 9,6 %; $p = 0{,}095$; farmakoterapie vs. PCI), ani v incidenci MACE (18,0 % vs. 15,4 %; $p = 0{,}113$; farmakoterapie vs. PCI). Navíc Kaplanova–Meierova analýza dlouhodobého přežití nezjistila mezi skupinami žádné rozdíly v častosti TVR (log-rank $p = 0{,}247$), incidenci IM (log-rank $p = 0{,}295$), v mortalitě (log-rank $p = 0{,}086$) ani v incidenci MACE (log-rank $p = 0{,}107$).
Závěry: U pacientů se stenózou ostia postranní větve jiné cévy než hlavního kmene levé věnčité tepny se jako vhodná a optimální léčebná strategie jeví farmakoterapie místo PCI.

ABSTRACT

Aim: Side branch (SB) ostial stenosis is a frequent bifurcation lesion and its optimal treatment strategy is still debated. Although the efficacy of the optimal medical therapy is well known, the comparison of the medical treatment and percutaneous coronary intervention (PCI) is controversial.
Methods: A total of 357 consecutive patients with isolated SB ostial stenosis (Medina 0.0.1 classification) was evaluated retrospectively. Patients were divided into two groups; patients with only medical therapy (n = 305) and patients undergoing PCI (n = 52). Target vessel revascularization (TVR), myocardial infarction (MI), and mortality were evaluated as major adverse cardiovascular outcomes (MACE).
Results: The mean age of the patients was 58.2±10.3 years. 102 patients (28.6%) were female. 279 patients (78.2%) had diagonal lesion while 78 (21.8%) had obtuse marginal lesion. The SB stenosis ratio (70±16; 88±13, $p < 0.001$) and SB lesion length (7.5±6.6; 14.7±6.0, $p < 0.001$) were higher in the PCI group. SB ostial stenting (38 patients [73.1%]) was the common PCI technique. There were no significant differences in terms of TVR (1.3%; 1.9%, $p = 0.277$, medical vs PCI groups, respectively), MI (8.2%; 7.7%, $p = 0.302$, medical vs PCI groups, respectively), mortality (10.2%; 9.6%, $p = 0.095$, medical vs PCI groups, respectively) and MACE (18.0%; 15.4%, $p = 0.113$, medical vs PCI groups, respectively) between groups. Additionally, in Kaplan–Meier long-term survival analysis, there were no differences in TVR (log-rank $p = 0.247$), MI (log-rank $p = 0.295$), mortality (log-rank $p = 0.086$), and MACE (log-rank $p = 0.107$) between groups.
Conclusions: Medical therapy instead of PCI seems to be an appropriate and optimal treatment strategy in patients with non-left main SB ostial stenosis.

Keywords:
Coronary bifurcation lesion
Percutaneous coronary intervention
Ostial stenosis
Side branch

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Introduction

Coronary bifurcation lesion (CBL) is an intriguing disease on account of the uncertainty of the optimal treatment strategy. CBL account for almost 15–20% for all percutaneous coronary intervention (PCI)[1] while isolated side branch (SB) ostial stenosis is the rare form of bifurcation lesions which is encountered in <5% of all CBLs.[2] The treatment of isolated SB ostial disease (Medina 0.0.1 classification) is also debated. It is well known that the optimal medical therapy is indispensable for coronary artery disease. However, the role of the PCI for SB ostial disease is still controversial. On the other hand, the lack of a single proven PCI technique for the lesions of the Medina 0.0.1 classification further complicates the decision for percutaneous intervention.

There is a limited number of studies focused on treatment decision for the isolated non-left main coronary artery (non-LMCA) SB ostial disease.[3,4] The heterogeneous features of the diseased SB as well as the different operator experiences and the advances of the techniques and technology limit the power of these studies to influence our clinical practice. So there is still a gap in the evidence of the optimal treatment decision for the Medina 0,0,1 CBL. In our study, we aimed to evaluate the clinicAL outcomes and Procedural characteristics of isolated non-left main Side Branch Ostial stenosis (the ALP-SBO registry). We also compared the long-term effect of the medical therapy and PCI treatment for the isolated non-LMCA SB ostial stenosis.

Materials and methods

Patient population and Medina classification

This study was conducted in a single tertiary high-volume heart center between 2010 and 2022. Patients were included if they were >18 years old and with isolated non-LMCA SB ostial disease. The Medina classification was used for the definition of the CBL.[5] According to the Medina classification, the coronary tree was divided into three vessel segments; proximal main vessel (PMV), distal main vessel (DMV) and SB. This classification reflects the pattern of the atherosclerotic disease based on the angiographic appearance. Each segment is defined either 0 or 1 to indicate the absence or presence of a significant stenosis (>50%), respectively. The first number refers to PMV while the second and third refers to DMV and SB, respectively. In our study, we included patients with the only side branch (SB) ostial disease as the Medina 0.0.1 classification. Patients with proximal main vessel (PMV) and/or distal main vessel (DMV) disease (>50% stenosis) were excluded from the study. For study inclusion, all patients had Medina 0.0.1 coronary bifurcation lesion (CBL) and the SB reference diameter was >2 mm. Patients with reduced ejection fraction heart failure, moderate to severe valvular heart disease, hematological disorder, end-stage liver or renal failure, active bleeding history, pregnancy and life-expectancy of less than 1 year were excluded from the study. Additionally, patients having ostial circumflex disease (as a left main-SB ostial disease) were also excluded. For the patients with SB ostial lesion, it was required that the distal main vessel diameter was at least as large as or more advanced than the SB branch. It was an important decision marker, especially for the obtuse marginal (OM) side branch. Additionally, for patients with ST segment elevation myocardial infarction (STEMI), if the culprit lesion was the SB osteal lesion, they were also excluded from the study. The baseline clinical, laboratory, angiographic, and demographic parameters were recorded from the hospital database. The patient's follow-up visits were done at hospital admission for suitable patients within last 6 months and telephone follow-up visits were done for others who did not attend a follow-up visit. Peri-procedural and post-procedural clinical evaluation and time of clinical outcomes were recorded from all subjects.

In the present study, all side branches were prognostic relevant coronary arteries. According to the recent guidelines, the prognostic relevant SB is defined at least one criterion as follows;[6] (A) the SB length is >73 mm, (B) SNUH score is ≥2 (referans vessel diameter >2.5 mm [1 point], ≤2 side branches [1 point], no SB below the target SB [1 point]), (C) if SB is a diagonal branch: size 2.5 mm, and single diagonal branch or dominant diagonal branch if >1, and nondominant circumflex artery (= high likelihood of diagonal branch myocardial territory >10%), (D) myocardial segmentation software: fractional myocardial mass >10%, (E) moderate-severe ischemia in the SB myocardial territory; echocardiography ≥ 3 segments stress-induced moderate or severe hypokinesia or akinesia or – myocardial perfusion SPECT ≥10% left ventricle ischemia or ≥2 contiguous reduced perfusion segments on cardiac magnetic resonance perfusion imaging. If the SB was not a prognostic relevant artery according to the mentioned criterion above, the patient was excluded from the study.

The definition of clinical outcomes

Firstly, all patients included in the study were symptomatic patients and also received optimal medical therapy. The patients with at least Class 2 angina pectoris that had documented ischemia and prognostic relevant side branch were included in the study. Then the patients were divided into two groups; only medical therapy group (group 1) and patients undergoing percutaneous coronary intervention (PCI) besides medical treatment (group 2). The selection of treatment strategy was made at the operator's discretion. Additionally, both transradial (TR) and transfemoral (TF) approaches were used. In the recent guidelines TR approach is recommended for coronary interventions. However, this study includes all patients since 2010. Thus, TF approach was used more frequently as a result of traditional habits due to the retrospective nature of the study.

The primary endpoint of the study was a major adverse cardiovascular event (MACE) defined as the composite outcome of target vessel revascularization (TVR), myocardial infarction (MI), and all-cause death. MI as defined as the 5-fold increase in the high-sensitive troponin level and patients with elevated pre-procedural troponin level, in whom they were stable or falling, meet the criteria for a 5-fold increase or at least >20% change from the baseline. And at least one of the following: (a) new onset ischemic electrocardiographic changes, (b) new pathological Q wave, (c) imaging evidence of loss of a viable myocardium, (d) angiographic findings of a procedural flow-limiting complication. If they were present within 48 hours after the procedure, it was defined as the procedure-related MI. TVR was also defined as angina or ischemia referable to the coronary bifurcation lesion (CBL) requiring repeat PCI or coronary artery bypass grafting surgery (CABG). Additionally, the stroke rates were evaluated as the secondary endpoint. The death was defined as the composite outcome of both cardiac and non-cardiac death. The study was approved by the local Ethics Committee. Our study was conducted in accordance with Helsinki Declaration.

Statistical analysis

Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York, USA). Fisher's exact test and Pearson chi-square analyses were used for categorical variables. Fitness to normal distribution was analyzed with the Kolmogorov–Smirnov test. Data were expressed as "mean ± standard deviation (SD)" for normal distribution, "median (25th–75th percentiles)" for variables without normal distribution and "n (%)" for categorical variables. Mann–Whitney U test was used for comparing quantitative variables without normal distribution while Student t-test was used for comparing the means between two groups with normal distribution. Cox regression analysis was also used to compare the differences in both primary and secondary endpoints, with outputs of hazard ratio (HR) and 95% confidence interval (CI). The long-term survival curve was analyzed using the Kaplan–Meier method, and statistical assessment was performed with the log-rank test. A *p*-value <0.05 was considered statistically significant.

Results

A total of 357 consecutive coronary bifurcation lesion (CBL) patients with the Medina 0.0.1 classification were included in this study. The mean age was 58.2±10.3 years while 102 patients (28.6%) were female. The mean fo-

Table 1 – Baseline clinical and demographic parameters of the study population

	All patients (n = 357)	Medical group (n = 305)	PCI group (n = 52)	*p*
Age (years)	58.2±10.3	58.4±10.4	57.1±9.7	0.386
Gender (female), n (%)	102 (28.6)	95 (31.1)	7 (13.5)	0.009
Diabetes mellitus, n (%)	103 (28.9)	85 (27.9)	18 (34.6)	0.321
Hypertension, n (%)	142 (39.8)	124 (40.7)	18 (34.6)	0.411
Chronic obstructive lung disease, n (%)	35 (9.8)	31 (10.2)	4 (7.7)	0.580
Previous CVA, n (%)	8 (2.2)	6 (2.0)	2 (3.8)	0.329
PAD, n (%)	8 (2.2)	8 (2.6)	0 (0)	0.280
Smoking, n (%)	67 (18.8)	51 (16.7)	16 (30.8)	0.016
Previous PCI, n (%)	40 (11.2)	30 (9.8)	10 (19.2)	0.047
Previous MI, n (%)	29 (8.1)	21 (6.9)	8 (15.4)	0.043
Atrial fibrillation, n (%)	15 (4.2)	14 (4.6)	1 (1.9)	0.330
Baseline symptom, n (%)				
CCS 2 angina	158 (44.3)	154 (50.5)	4 (7.7)	<0.001
CCS 3–4 angina	199 (55.7)	151 (49.5)	48 (92.3)	
Post-management symptom, n (%)				
CCS 1 angina	185 (51.8)	157 (51.5)	28 (53.8)	0.435
CCS 2–3 angina	172 (48.2)	148 (48.5)	24 (46.2)	
Syncope, n (%)	6 (1.7)	6 (2.0)	0 (0)	0.386
Acetylsalicylic acid, n (%)	258 (72.3)	209 (68.5)	49 (94.2)	<0.001
Clopidogrel, n (%)	108 (30.3)	82 (26.9)	26 (50.0)	0.001
Prasugrel, n (%)	2 (0.6)	1 (0.3)	1 (1.9)	0.270
Ticagrelor, n (%)	48 (13.4)	23 (7.5)	25 (48.1)	<0.001
Beta-blocker, n (%)	235 (65.8)	195 (63.9)	40 (76.9)	0.068
ACEI/ARB, n (%)	173 (48.5)	138 (45.2)	35 (67.3)	0.003
Statin, n (%)	231 (64.7)	189 (62.0)	42 (80.8)	0.009
Calcium channel blocker, n (%)	45 (12.6)	41 (13.4)	4 (7.7)	0.248
Oral anti-diabetic, n (%)	69 (19.3)	56 (18.4)	13 (25.0)	0.262
Insulin, n (%)	19 (5.3)	17 (5.6)	2 (3.8)	0.458

ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker; CCS – Canadian Cardiovascular Society; CVA – cerebrovascular accident; MI – myocardial infarction; PAD – peripheral arterial disease; PCI – percutaneous coronary intervention.

llow-up time was 59±39 months. The history of previous percutaneous coronary intervention (PCI) was 11.2% (40 patients). 305 patients (85.4%) were treated only with medical therapy and they were categorized as group 1 while 52 patients (14.6%) undergone PCI in addition to medical therapy were categorized as group 2. 279 patients (78.2%) had diagonal lesion while 78 (21.8%) had obtuse marginal (OM) lesion. For the patients treated with PCI, the major procedural technique was the side branch (SB) ostial stenting technique performed in 38 patients (73.1%). The inverted provisional/cross-over stenting was performed in 13 patients (25%).

The baseline, clinical, and demographic variables of the study population were demonstrated in Table 1. The incidence of female gender was higher in group 1 (95 [31.1%]; 7 [13.5%], p = 0.009) while the incidence of smoking (51 [16.7%]; 16 [30.8%], p = 0.016) and previous MI (21 [6.9%]; 8 [15.4%], p = 0.043) were higher in group 2. The incidence of acetylsalicylic acid (209 [68.5%]; 49 [94.2%], p <0.001), clopidogrel (82 [26.9%]; 26 [50.0%], p = 0.001), ticagrelor (23 [7.5%]; 25 [48.1%], p <0.001), angiotensin converting enzyme inhibitor/angiotensin receptor blocker (138 [45.2%]; 35 [67.3%], p = 0.003), and statin (189 [62.0%]; 42 [80.8%], p = 0.009) usage was higher in group 2 patients.

The laboratory and echocardiographic evaluations were demonstrated in Table 2. There were no differences in terms of laboratory parameters between groups. The ejection fraction was similar in both groups (60 [50–60]; 60 [50–60], p = 0.063). Additionally, baseline angina severity was higher in the PCI group (class 3 angina 151 [49.5%]; 48 [92.3%], p <0.001). Post-management angina severity was the same for both groups.

The clinical and angiographic variables were demonstrated in Table 3. 279 patients (78.2%) had a diagonal disease while 78 patients (21.8%) had an obtuse marginal (OM) disease. In patients undergoing percutaneous coronary intervention (PCI), the incidence of a diagonal lesion (29 patients [55.8%]) was higher than OM lesion (23 patients [44.2%]). Similarly, in patients treated with medical therapy, the incidence of diagonal lesion (250 patients [82.0%]) was higher compared to OM lesion (55 patients [18.0%]). However, the incidence of PCI procedure was higher in patients with OM lesion (23 to 78 patients [29.4%]) compared to patients with a diagonal lesion (29 to 279 patients [10.3%]). The side branch (SB) stenosis ratio (70±16; 88±13, p <0.001), SB lesion length (7.5±6.6; 14.7±6.0, p <0.001), and SB reference vessel diameter (2.33±0.29; 2.52±0.33, p <0.001) were higher in patients undergoing PCI. The incidence of multivessel disease, bifurcation angle and Syntax score were similar in both groups.

The procedural characteristics of patients treated with PCI were demonstrated in Table 4. The femoral artery was the common access site in 49 patients (94.2%). No SB occlusion occurred. The SB ostial stenting technique was performed in 38 patients (73.1%) while the inverted provisional/cross-over stenting was performed in 13 patients (25%). Only 1 patient (1.9%) treated with planned 2-stent strategy. The final kissing balloon dilatation ratio was 13.5% (7 patients). The complication ratio was 1.9% (1 patient, contrast nephropathy). No peri-procedural MI or mortality occurred. The mean SB stent size was 2.56±0.28 mm and length was 21.6±5.8 mm. The mean main vessel (MV) stent size was 3.0±0 mm and length was 19.0±0 mm.

The primary endpoint of the study was the composite endpoint of TVR, MI and all-cause death (Table 5). There was no difference in MACE between groups. The incidence of MACE was 18.0% (55 patients) in patients treated with medical therapy alone (group 1) while it was 15.4% (8 patients) in patients who had undergone PCI (group 2) (HR: 1.852, 95% CI: 0.865–3.964, p = 0.113). The incidence of TVR was 1.3% in group 1 and 1.9% in group 2 (HR: 3.544, 95% CI: 0.363–34.630, p = 0.277). The incidence of MI was 8.2% and 7.7% (HR: 1.765, 95% CI: 0.600–5.186, p = 0.302)

Table 2 – Laboratory parameters of the patients

	All patients (n = 357)	Medical group (n = 305)	PCI group (n = 52)	p
Hemoglobin (g/dL)	14.5 (13.1–15.5)	14.3 (13.0–15.4)	14.9 (13.6–16.0)	0.082
Platelet (10^9/L)	248 (210–294)	248 (212–294)	242.5 (207.5–288.5)	0.689
Leukocyte (10^9/L)	8.8 (7.35–10.8)	8.7 (7.25–10.72)	9.59 (7.68–11.46)	0.183
Creatinine (mg/dL)	0.82 (0.70–0.97)	0.81 (0.70–0.97)	0.83 (0.74–0.97)	0.649
Total cholesterol (mg/dL)	195 (166–221)	195 (165–222)	189 (172–218)	0.968
LDL cholesterol (mg/dL)	116 (94–140)	116 (94–139.5)	116 (99–141)	0.998
HDL cholesterol (mg/dL)	41 (34–48)	42 (35–48)	39 (32–44)	0.052
Triglyceride (mg/dL)	156 (106–224.25)	155 (106–219)	185 (113–262)	0.417
C-reactive protein (mg/L)	3.88 (1.81–7.93)	3.54 (1.73–7.93)	4.06 (2.12–7.95)	0.365
Glucose (mg/dL)	119 (101.5–150.5)	117 (101–146)	128.5 (106–216)	0.055
Ejection fraction (%)	60 (50–60)	60 (50–60)	60 (50–60)	0.063
LVEDD (mm)	48 (45–50)	48 (45–50)	47 (45–51)	0.955
LVESD (mm)	30 (27–33)	30 (27–33)	31.1 (26–35)	0.841
LA diameter (mm)	36 (34–39)	36 (34–39)	36 (34–39)	0.792

HDL – high-density lipoprotein; LA – left atrium; LDL – low-density lipoprotein; LVEDD – left ventricle end-diastolic diameter; LVESD – left ventricle end-systolic diameter; PCI – percutaneous coronary intervention.

Table 3 – Angiographic evaluation of the patients

	All patients (n = 357)	Medical group (n = 305)	PCI group (n = 52)	*p*
Group, n (%)				
Diagonal	279 (78.2)	250 (82.0)	29 (55.8)	<0.001
OM	78 (21.8)	55 (18.0)	23 (44.2)	
Clinical presentation, n (%)				
Stable	143 (40.1)	133 (43.6)	10 (19.2)[a]	
USAP	21 (5.9)	17 (5.6)	4 (7.7)	<0.001
NONSTEMI	112 (31.4)	85 (27.9)	27 (51.9)[b]	
STEMI	39 (10.9)	30 (9.8)	9 (17.3)	
Silent ischemia	42 (11.8)	40 (13.1)	2 (3.8)	
SB stenosis ratio (%)	72.6±16.6	70±16	88±13	<0.001
MV proximal diameter (mm)	3.2±0.58	3.18±0.59	3.32±0.56	0.128
MV distal diameter (mm)	2.85±1.37	2.90±1.52	2.71±0.45	0.370
SB diameter (mm)	2.37±0.30	2.33±0.29	2.52±0.33	<0.001
SB lesion length (mm)	8.9±7.0	7.5±6.6	14.7±6.0	<0.001
Bifurcation angle (°)	58.9±11.5	58.4±11.5	61.3±11.4	0.257
SB ostial thrombosis, n (%)	5 (1.4)	4 (1.3)	1 (1.9)	0.547
Multivessel disease, n (%)				
Only SB	216 (60.5)	188 (61.6)	28 (53.8)	
1-vessel	129 (36.1)	109 (35.7)	20 (38.5)	0.215
2-vessel	10 (2.8)	7 (2.3)	3 (5.8)	
3-vessel	2 (0.6)	1 (0.3)	1 (1.9)	
Syntax score	7.0±3.9	6.9±3.9	7.7±4.0	0.201

MV – main vessel; NONSTEMI – non-ST segment elevation myocardial infarction; OM – obtuse marginal; PCI – percutaneous coronary intervention; SB – side branch; STEMI – ST segment elevation myocardial infarction; USAP – unstable angina pectoris.
[a] Significantly lower compared to medical group; [b] significantly higher compared to medical group.

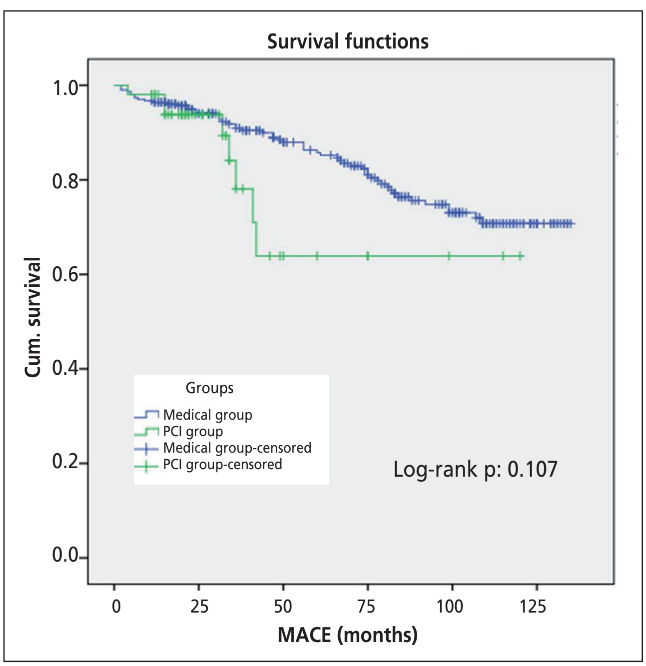

Fig. 1 – Kaplan–Meier survival curve for MACE. MACE – major adverse cardiovascular event.

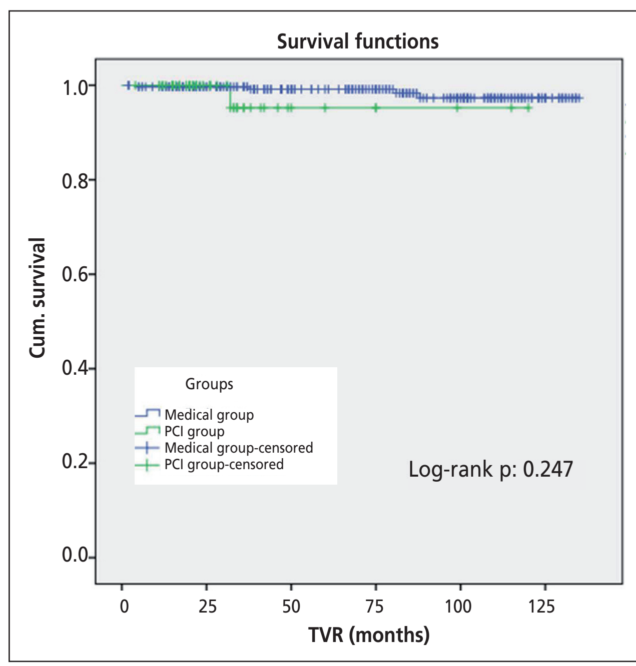

Fig. 2 – Kaplan–Meier survival curve for TVR. TVR – target vessel revascularization.

and the incidence of mortality was 10.2% and 9.6% (HR: 2.298, 95% CI: 0.864–6.110, $p = 0.095$) in group 1 and 2, respectively. The stroke rate as a secondary endpoint was 1.3% (4 patients) in group 1 while it was 0% in group 2 (HR: 0.042, 95% CI: 0–540, $p = 0.740$).

A Kaplan–Meier survival analysis also revealed that a long-term major adverse cardiovascular event MACE (log-rank $p = 0.107$) (Fig. 1), TVR (log-rank $p = 0.247$) (Fig. 2), MI (log-rank $p = 0.295$) (Fig. 3), and mortality (log-rank $p = 0.086$) (Fig. 4) were found to be similar in both groups.

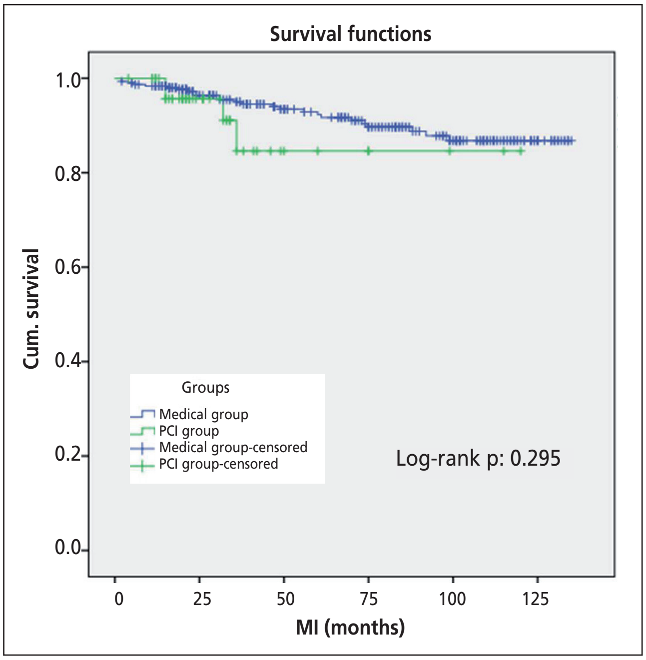

Fig. 3 – Kaplan–Meier survival curve for MI. MI – myocardial infarction.

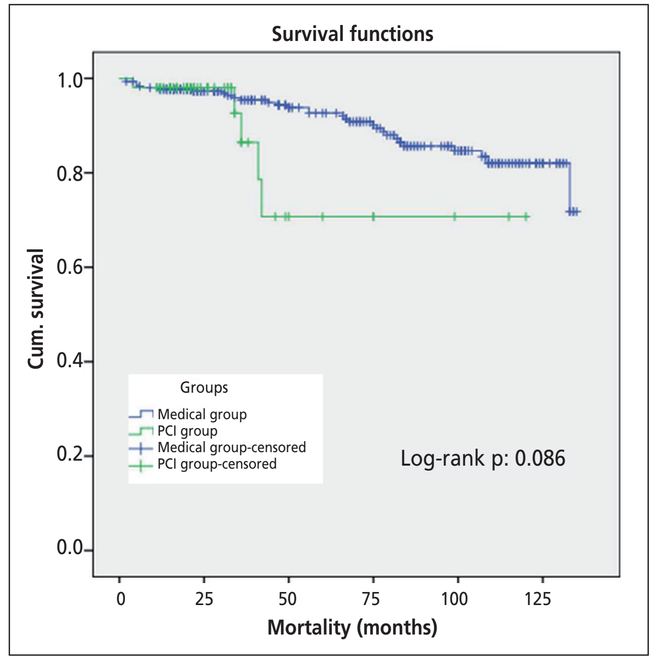

Fig. 4 – Kaplan–Meier survival curve for mortality.

Table 4 – Procedural characteristics of the patients undergoing percutaneous intervention

PCI group (n = 52)	n (%)	PCI group (n = 52)	Mean±std
Guiding catheter size, n (%) 6 7	 22 (42.3) 30 (57.7)	MV stent size (mm)	3.0±0
Access site, n (%) Femoral Radial	 49 (94.2) 3 (5.8)	MV stent length (mm)	19.0±0
IABP usage, n (%)	0 (0)	SB stent size (mm)	2.56±0.28
Acute SB occlusion, n (%)	0 (0)	SB stent length (mm)	21.6±5.8
Acute CABG, n (%)	0 (0)	MV predilatation balloon diameter (mm)	2.0±0
Gp IIb/IIIa receptor inhibitor, n (%)	1 (1.9)	MV predilatation balloon length (mm)	10.0±0
Stenting technique, n (%) • SB ostial stenting • Inverted provisional/cross-over stenting • Bail-out 2-stent • Planned 2-stent	 38 (73.1) 13 (25.0) 0 (0) 1 (1.9)	SB predilatation balloon diameter (mm)	2.0±0.33
MV predilatation, n (%)	1 (1.9)	SB predilatation balloon length (mm)	15.0±3.41
SB predilatation, n (%)	28 (53.8)	MV FKBD diameter (mm)	3.1±0.28
Final kissing balloon dilatation, n (%)	7 (13.5)	MV FKBD length (mm)	13.4±3.86
Pre-procedural MV TIMI blood flow, n (%) 3	52 (100)	SB FKBD diameter (mm)	2.75±0.14
Post-procedural MV TIMI blood flow, n (%) 3	52 (100)	SB FKBD length (mm)	12.7±4.38
Pre-procedural SB TIMI blood flow, n (%) 0 1 2 3	 15 (28.8) 1 (1.9) 5 (9.6) 31 (59.6)	Procedural time (min)	24.95±13.99
Post-procedural SB TIMI blood flow, n (%) 3	52 (100)	Radiation time (min)	10.2±5.3
Complication, n (%)	1 (1.9)	Contrast volume (ml)	184.6±67.8

CABG – coronary artery bypass grafting; FKBD – final kissing balloon dilatation; Gp – glycoprotein; IABP – intra-aortic balloon pump; MV – main vessel; PCI – percutaneous coronary intervention; SB – side branch; TIMI – Thrombolysis in Myocardial Infarction.

Table 5 – Clinical outcomes of the patients

	Medical group (n = 305)	PCI group (n = 52)	Hazard ratio (95% CI)	*p*
Primary composite endpoint (MACE), n (%)	55 (18.0)	8 (15.4)	1.852 (0.865–3.964)	0.113
TVR, n (%)	4 (1.3)	1 (1.9)	3.544 (0.363–34.630)	0.277
MI, n (%)	25 (8.2)	4 (7.7)	1.765 (0.600–5.186)	0.302
All-cause mortality, n (%)	31 (10.2)	5 (9.6)	2.298 (0.864–6.110)	0.095
Secondary endpoint, n (%) Stroke	4 (1.3)	0 (0)	0.042 (0.0–0.540)	0.740

CI – confidence interval; MACE – major adverse cardiovascular outcome; MI – myocardial infarction; PCI – percutaneous coronary intervention; TVR – target vessel revascularization.

Discussion

In our study, it was revealed that in patients with isolated non-left main coronary artery (LMCA) side branch (SB) ostial disease (Medina 0.0.1 classification), there was no difference in terms of MACE; TVR, MI, and mortality between patients treated with medical therapy alone and patients having undergone PCI in addition to medical therapy. On the other hand, PCI had a high procedural success and low complication rates in patients with coronary bifurcation lesion (CBL) with Medina 0.0.1 classification.

CBL is one of the most challenging diseases among invasive cardiologists. The optimal treatment strategy of CBL is still debated due to the improvement of medical therapy options and the advances in the PCI procedures and novel interventional strategies. Isolated SB ostial disease is the rare form of CBL. The incidence of CBL is approximately 15–20% in all PCI[1] while the incidence of SB ostial disease (Medina 0.0.1 classification) is less than 5% in all CBLs.[2] As it is a rare disease and is often excluded from the bifurcation trials, there is an uncertainty about the treatment strategy and stenting method of patients who had isolated SB ostial lesion.

The comparison of medical therapy and invasive strategy for coronary artery disease (CAD) was investigated in previous studies. In the COURAGE trial, 2287 patients with stable CAD were randomized to medical therapy and PCI group. There was no difference in 4.6-year cumulative primary-event rates between the PCI group (19.0%) and medical group (18.5%).[7] However, the randomization was done after angiography in this trial and bare metal stent was also used in the PCI group. In the ISCHEMIA trial, 5179 patients with stable CAD and moderate to severe ischemia were evaluated over a median of 3.2 years.[8] The primary study endpoint was a composite of cardiovascular death, MI, hospitalization for unstable angina pectoris, and resuscitated cardiac arrest. The cumulative event rate was 16.4% in the PCI group while it was 18.2% in the medical group without statistical significance. On the other hand, there was evidence of symptomatic benefit with PCI. Similarly, in our study there was no difference in terms of MACE, target vessel revascularization, MI, and mortality between medical therapy alone and PCI in addition to medical therapy. Additionally, in our study, it was demonstrated that the ratio of TVR was relatively lower while the MI rates was higher. This showed us that the MI experienced by these patients in the long term was not related to the culprit SB. In a study by Brueck et al., medical therapy was compared to PCI in patients with isolated ostial lesions of diagonal branch.[3] 233 patients treated with medical therapy and 69 with PCI. The risk of 12-month rehospitalization (22% and 55% in medical group and PCI group respectively, *p* <0.001) and repeat PCI (8% and 23% in the medical group and the PCI group, respectively) were higher in the PCI group.

Percutaneous intervention for the culprit vessel is the recommended treatment strategy for patients with acute coronary syndrome.[9] However, there is no randomized clinical trial for patients with side branch (SB) ostial disease in this population. There is a gap in the evidence for SB ostial disease for some reasons. The PCI of the SB ostium has a potential risk of compromise or injury to the MV.[6] This may cause a larger amount of myocardial ischemia. It should also be recognized that an ostial lesion seems to be a fibrotic and calcific. This may cause an underexpansion or malapposition of stent strats and may result in restenosis. On the other a carina or plaque shift may also affect main vessel (MV) and make the disease more complex formation.[6] Thus, there is a trend among interventional cardiologists to treat patients for isolated ostial lesions medically. In our study, supporting to this, PCI had no MACE benefit in patients with Medina 0.0.1 CBL. However, it should be noted that we excluded patients who presented with STEMI and the culprit lesion was the SB ostium. An uncertainty as an optimal stenting strategy is also effective on these conflicting results regarding PCI. Although inverted provisional strategy is the recommended strategy for Medina 0.0.1 coronary bifurcation lesion (CBL) in recent years,[10,11] intervention of non-diseased main vessel and the risk of distal main vessel (DMV) compromise bring discussion on this strategy. In conclusion, medical therapy appears to be the primary treatment strategy for SB ostial disease.

In conclusion, medical therapy should be the first line therapy in non-left main side branch osteal stenosis. However, patients who are still symptomatic despite optimal medical therapy may be treated with PCI. On the other hand, these lesions should be treated as a culprit lesion in patients presented with acute coronary syndrome.

Conclusion

Medical therapy instead of PCI seems to be an appropriate and optimal treatment strategy in patients with non-left main side branch (SB) ostial stenosis. However, PCI seems to be a safe and successful treatment strategy in patients who are still symptomatic despite optimal medical therapy.

Limitations

The main limitation of the study was the relatively small sample size. Moreover, this was a retrospective and non-randomized trail. We did not have the exact reason of death. So we could not have the results of PCI procedure on cardiac death. Additionally, the inverted provisional stenting is the recommended PCI strategy for the Medina 0.0.1 classification in recent years, was performed on a small number of patients. This technique may change the results in future trials for these patients. This may be supported by the future large-scaled studies.

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Conflict of interest
Authors declared that there is no conflict of interest.

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Ethical statement
The study was approved by the local Ethics Committee of Mehmet Akif Ersoy Training and Research Hospital local Ethics Committee (number: 2023.04-54 and date: 16. 5. 2023). Our study was conducted in accordance with Helsinki Declaration.

Informed consent
Informed consent was not obtained from the patients due to the retrospective nature of the study.

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