The impact of left circumflex coronary artery ostium stenosis on outcomes for patients after percutaneous coronary intervention for unprotected left main disease

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ABSTRACT

Background: The impact of left circumflex coronary artery (LCx) ostium atherosclerosis in left main coronary artery (LM) bifurcation disease is not well-known.

Aim: The study aimed to assess whether the involvement of LCx ostium carries prognostic implications in patients undergoing unprotected LM percutaneous coronary intervention (PCI).

Methods: Consecutive 564 patients with unprotected LM (ULMCA) disease who underwent LM PCI between January 2015 and February 2021, with at least 1 year of available follow-up were included in the study. The first group was composed of 145 patients with ULMCA disease with LCx ostium stenosis, and the second group consisted of 419 patients with ULMCA disease without LCx ostium stenosis.

Results: Patients in the group with ULMCA disease with LCx ostium stenosis were significantly older and had more comorbidities. The two-stent technique was used more often in the group with LCx ostium stenosis (62.8% vs. 14.6%; $P < 0.001$). During 7-year follow-up, all-cause mortality did not differ significantly between groups with and without LCx ostium stenosis ($P = 0.50$). The use of one-stent or two-stent technique also did not impact mortality in patients with LCx ostial lesions ($P = 0.75$). Long-term mortality subanalysis for three groups of patients: (1) patients with LM plus LCx ostium stenosis; (2) LM plus left anterior descending artery (LAD) ostium stenosis; (3) LM plus LCx ostium plus LAD ostium stenosis also did not differ significantly ($P = 0.63$).

Conclusions: LCx ostium involvement in LM disease PCI is not associated with adverse long-term outcomes, which is highly beneficial for the Heart Team's decision-making process.

Key words: left circumflex coronary artery ostium, percutaneous coronary intervention, unprotected left main coronary artery

INTRODUCTION

Percutaneous coronary intervention (PCI) in left main coronary artery (LM) disease is widely used worldwide with documented favorable results in large studies. However, the impact of left circumflex coronary artery (LCx) ostium atherosclerosis in LM bifurcation disease is not well-known. Evidence from computed tomography angiography and fractional flow reserve (FFR) shows that the side branch supplies a smaller portion of the myocardium compared to the main branch and that a stenosis in the side branch is less likely to result in significant ischemia compared to a similar stenosis in the main artery [1]. Nevertheless, side branch occlusion is one of the most significant potential complications after LM stenting and may be a major reason why operators choose the two-stent technique [2]. Significant ostium stenosis of the side branch has also been reported to be a frequent source of side branch occlusion after stent implantation in the main vessel [3]. The European Bifurcation Club advocates use of the "jailing wire" technique which involves leaving a wire in the side branch while a stent

WHAT'S NEW?

The impact of left circumflex coronary artery (LCx) ostium atherosclerosis in left main coronary artery (LM) bifurcation disease is not well-known. This study aimed to evaluate whether the involvement of LCX ostium significantly influences outcomes of patients undergoing unprotected LM percutaneous coronary intervention (PCI). The main finding is that the LCX ostium involvement in LM disease PCI is not associated with long-term mortality, which is highly beneficial for the Heart Team's decision-making process. In patients with LM disease and LCx ostium stenosis, there is no significant difference in long-term mortality between groups operated on using one-stent or two-stent techniques. No significant differences in long-term mortality were observed regardless of the presence of coexisting lesions in the LCX ostium or left anterior descending artery ostium. A subgroup of patients without significant LCX ostium disease who underwent LCX stenting during LM PCI because of the plaque burden shift or carina shift presents favorable long-term outcomes.

is implanted in the main branch [4]. The study based on a small group showed that the patients with higher FFR in the jailed LCX had better long-term results than those with low FFR [5]. In terms of the one-stent technique in LM PCI, two mechanisms of acute luminal loss at the ostium of the left circumflex coronary artery have been suggested, i.e. carina shift and plaque shift [6–8]. Angioplasty in the area of huge atherosclerotic plaque around the bifurcation often results in plaque burden shifting to the coronary branch, sometimes causing subsequent occlusion [9]. However, recent articles demonstrated that the carina shift was the principal mechanism of ostial LCX lumen loss during LM PCI [10]. In the study performed by Kang et al., carina shift was associated with a narrow distal angle between the LAD and the LCX and a wide proximal angle between the LCX and the LM [10].

In this study, we aimed to assess whether the involvement of LCX ostium carries prognostic implications in patients undergoing unprotected LM PCI.

METHODS

Our study is part of a larger project concerning LM disease [11–13]. Currently, we analyzed all 564 patients with unprotected LM (ULMCA) disease PCI and with at least 1 year of available follow-up. Patients with significant LM stenosis (≥50% diameter) were prospectively enrolled in the study between January 2015 and February 2021 [14]. An ostial LCX lesion was defined as a lesion with at least 50% diameter stenosis by visual assessment and within 3 mm of the left main stem. Patients were divided into two groups: the first group was composed of 145 patients with unprotected LM disease with LCX ostium stenosis and the second group consisted of 419 patients with unprotected LM disease without LCX ostium stenosis. Established primary outcomes were in-hospital death, in-hospital myocardial infarction (MI), and long-term all-cause death (median [interquartile range (IQR)] follow-up was 1411 (IQR, 908 [max 2553] days). Survival analysis data were gathered by telephone contact or with the use of National Health Fund information. IVUS or OCT imaging were used in 202 (35.8%) patients and were not analyzed in great detail. The antiplatelet regimens were low-dose aspirin (75 mg daily) and clopidogrel (75 mg daily) for a minimum of 6 months after PCI, with the intention of 12 months of dual antiplatelet therapy. In patients without contraindications, a switch to ticagrelor or prasugrel was allowed.

Statistical analysis

All continuous variables were presented as medians (interquartile range [IQR]). Categorical variables were presented as numbers and percentages and were compared using the test for proportions or Fisher's exact test. The normality of the distribution of variables was assessed using the Shapiro-Wilk test. Differences between continuous variables were evaluated with a nonparametric Mann-Whitney test. The survival probability at follow-up was calculated using the Kaplan-Meier method. Log-rank tests were used to compare survival between different groups. *P*-values below 0.05 were considered significant. We used STATISTICA 13.7 (StatSoft, Inc., Tulsa, OK, US).

RESULTS

Patients in the group with ULMCA disease with LCX ostium stenosis were older (median [IQR], 69.0 [65.0–79.0] years vs. 68.0 [62.0–74.0] years; $P = 0.002$) (Table 1). In this group, comorbidities such as chronic kidney disease (44.8% vs. 28.6%; $P < 0.001$), diabetes (46.9% vs. 36.8%; $P = 0.03$), and previous stroke (13.1% vs. 7.9%; $P = 0.06$) were found more often. Naturally, the SYNTAX score was higher in the group with LCX ostium stenosis (28.0 [22.25–34.0] vs. 21 [14.0–28.0]; $P < 0.001$), also LM calcifications were found more often in this group (19.3% vs. 11.5%; $P = 0.02$). The number of implanted stents (2.0 [2.0–3.0] vs. 1.0 [1.0–2.0]; $P < 0.001$), total stent length (46.0 [36.0–64.0] vs. 33.0 [22.0–50.0]; $P < 0.001$), radiation time (19.5 [14.0–26.0] vs. 15.0 [11.0–21.0]; $P < 0.001$), and radiation dose (1436.5 [969–2151] vs. 1120.5 [706.5–1722.5]; $P < 0.001$) were higher in patients with LCX ostium lesions (Table 2). The two-stent technique was used more often in the group with LCX ostium stenosis (62.8% vs. 14.6%; $P < 0.001$). The trend toward more frequent use of crush techniques was observed in the group with LCX ostium involvement. Provisional stenting was performed more often in the group without LCX ostial disease. There were no differences between two study groups in terms of periprocedural complications, periprocedural mortality,

Table 1. Study population baseline characteristics

Variable	Patients with unprotected LM disease with LCX ostium stenosis (n = 145)	Patients with unprotected LM disease without LCX ostium stenosis (n = 419)	*P*-value
Age, year, median (IQR)	69.0 (65.0–79.0)	68.0 (62.0–74.0)	0.002
Sex, female, n (%)	38 (26.2)	104 (24.8)	0.74
Hypertension, n (%)	123 (84.8)	344 (82.1)	0.45
CKD, n (%)	65 (44.8)	120 (28.6)	<0.001
DM, n (%)	68 (46.9)	154 (36.8)	0.03
Stroke/TIA, n (%)	19 (13.1)	33 (7.9)	0.06
PVD, n (%)	27 (18.6)	61 (14.6)	0.25
AF, n (%)	26 (17.9)	58 (13.8)	0.23
Prior MI, n (%)	68 (46.9)	205 (48.9)	0.67
Stable angina, n (%)	76 (52.4)	239 (57.0)	0.33
Unstable angina, n (%)	35 (24.1)	119 (28.4)	0.32
NSTEMI, n (%)	28 (19.3)	55 (13.1)	0.07
STEMI, n (%)	6 (4.1)	15 (3.6)	0.76
Prior PCI LAD, n (%)	38 (26.2)	98 (23.4)	0.49
Prior PCI LCX, n (%)	27 (18.6)	66 (15.8)	0.42
Prior PCI RCA, n (%)	38 (26.2)	137 (32.7)	0.15
LVEDD, mm, median (IQR)	50.0 (47.0–56.0)	50.0 (46.0–55.0)	0.42
LVEF, %, median (IQR)	50.0 (45.0–60.0)	55.0 (45.0–60.0)	0.18
Coronary artery disease characteristics			
SYNTAX score, median (IQR)	28.0 (22.25–34.0)	21 (14.0–28.0)	<0.001
LM trifurcation, n (%)	23 (15.9)	50 (11.9)	0.22
LM calcification, n (%)	28 (19.3)	48 (11.5)	0.02
RCA recessive (a), n (%)	11 (7.6)	32 (7.6)	0.98
RCA with critical stenosis (b), n (%)	30 (20.7)	56 (13.4)	0.03
RCA total occlusion (c), n (%)	22 (15.2)	66 (15.8)	0.87
Lack of RCA support for LMCAD (a+b+c), n (%)	63 (43.4)	154 (36.8)	0.15

Abbreviations: AF, atrial fibrillation; DM, diabetes mellitus; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; LAD, left anterior descending; LCx, left circumflex; LM, left main; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PVD, peripheral vascular disease; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TIA, transient ischemic attack

Table 2. Left main percutaneous coronary intervention procedure characteristics

Variable	Patients with unprotected LM disease with LCX ostium stenosis (n = 145)	Patients with unprotected LM disease without LCX ostium stenosis (n = 419)	*P*-value
Number of stents, median (IQR)	2.0 (2.0–3.0)	1.0 (1.0–2.0)	< 0.001
Total length of implanted stents, mm, median (IQR)	46.0 (36.0–64.0)	33.0 (22.0–50.0)	< 0.001
Radiation time, min, median (IQR)	19.5 (14.0–26.0)	15.0 (11.0–21.0)	< 0.001
Radiation dose, mGy, median (IQR)	1436.5 (969–2151)	1120.5 (706.5–1722.5)	< 0.001
Contrast volume, ml, median (IQR)	250.0 (200–300)	227.5 (190–300)	0.13
Stenting LM bifurcation, n (%)	145 (100)	363 (86.6)[a]	–
One-stent technique, n (%)	54 (37.2)	310 (85.4)	< 0.001
Two-stents technique, n (%)	91 (62.8)	53 (14.6)	
Two-stents techniques	n = 91	n = 53	
Crush/DK-crush, n (%)	56 (61.5)	24 (45.3)	0.071
Cullote, n (%)	2 (2.2)	0 (0)	
T-stenting, n (%)	17 (18.7)	8 (15.1)	
Provisional stenting, n (%)	16 (17.6)	21 (39.6)	
IVUS/OCT, n (%)	36 (24.8)	166 (39.6)	0.001

[a]In this group, the percentages do not add up to 100% because not all patients underwent LM bifurcation percutaneous coronary intervention

Abbreviations: IVUS, intravascular ultrasound; LM, left main, DK-crush, double kissing crush technique; OCT, optical coherence tomography

and myocardial infarction type 4a. Median patient (IQR) follow-up was 1411 (908–2553) days. At 7-year follow-up, all-cause mortality between groups with and without LCX ostium stenosis did not differ ($P = 0.50$) (Figure 1). There was no difference in long-term all-cause mortality in patients with LCX ostial lesions who underwent procedures with either one-stent or two-stent technique ($P = 0.75$) (Figure 2). In our cohort, there were some patients without significant LCX ostium disease who underwent LCX stenting during LM PCI (13.4% of patients from the group without LCX ostium involvement) because of the plaque burden shift or carina shift; long-term results of these patients were satisfactory (Figure 3). Subanalysis for three groups of patients: (1) patients with LM plus LCX ostium

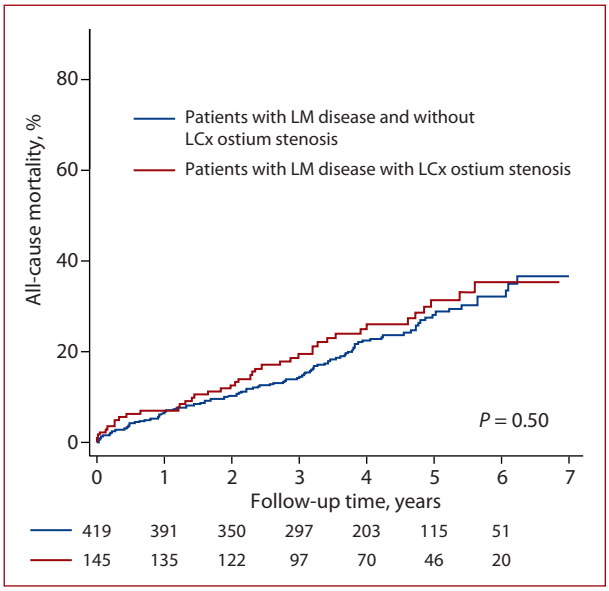

Figure 1. Kaplan-Meier analysis of all-cause mortality: patients with unprotected LM disease with LCx ostium stenosis vs. patients with unprotected LM disease without LCx ostium stenosis

Abbreviations: see Table 1

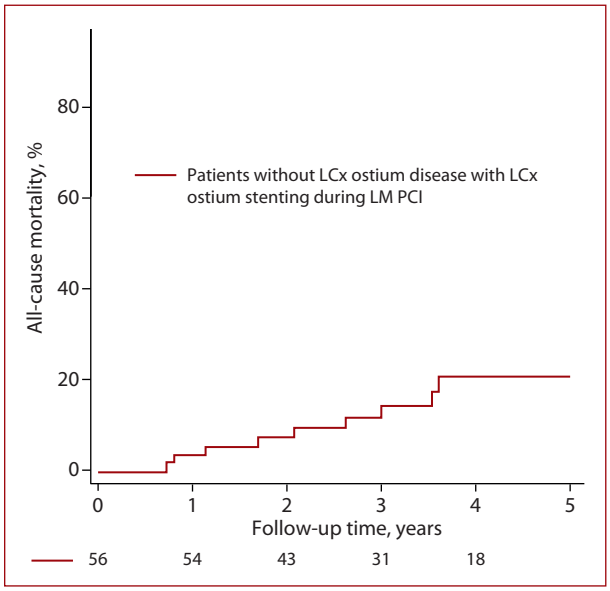

Figure 3. Kaplan-Meier analysis of all-cause mortality: patients without LCx ostium disease with LCx ostium stenting during LM PCI

Abbreviations: see Table 1

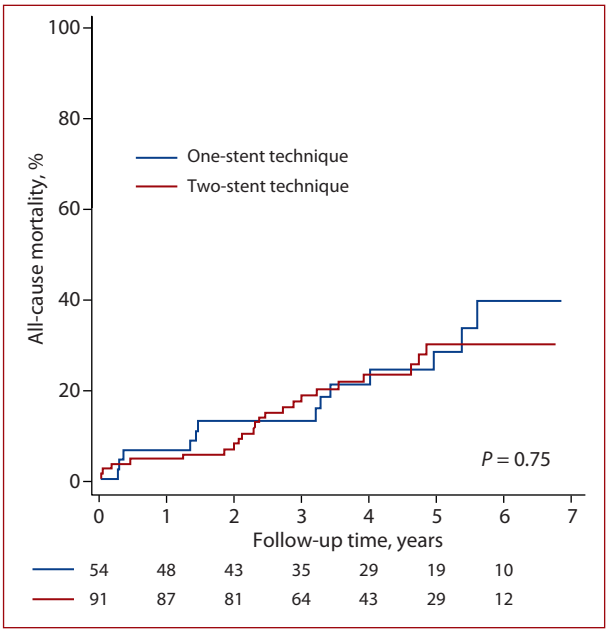

Figure 2. Kaplan-Meier analysis of all-cause mortality: one-stent vs. two-stent technique in patients with unprotected LM disease with LCx ostium stenosis

Abbreviations: see Table 1

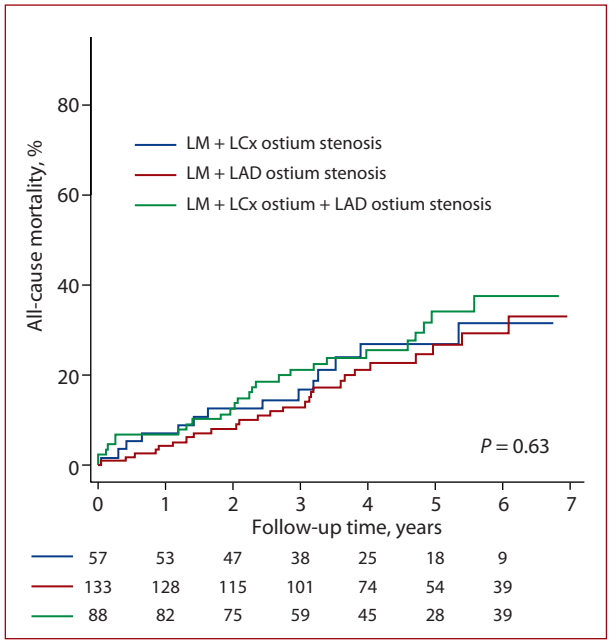

Figure 4. Kaplan-Meier analysis of all-cause mortality: LM + LCx ostium stenosis vs. LM + LAD ostium stenosis vs. LM + LCx ostium + LAD ostium stenosis

Abbreviations: see Table 1

stenosis, (2) LM plus LAD ostium stenosis, (3) LM plus LCX ostium plus LAD ostium stenosis was performed. Long-term mortality rates also did not differ in these groups ($P = 0.63$) (Figure 4).

DISCUSSION

The choice of stenting strategy in LM PCI is generally determined by the stenosis at the LCX ostium, atherosclerotic lesion length, and/or difficult coronary artery side branch access. These situations generally require initial use of two-stent strategies. Bailout stenting of a diseased coronary side branch can often be more demanding than opting for an up-front two-stent strategy. In other LM bifurcation cases, a provisional stenting strategy is usually chosen [15]. In the study performed by Park et al. [16], a group of patients with true bifurcation lesions had a significantly higher risk of major adverse cardiovascular events than those with non-true bifurcations (HR, 1.39; 95% CI, 1.08–1.80; $P = 0.01$); however, this study was not performed only on the LM disease population. Moreover, patients with Medina 1-0-1 had a lower

risk of cardiac death and MI than other patients with true bifurcation lesions [16]. Nevertheless, the LCX is not always last in the order of numbers in the Medina classification. In subanalysis from the EXCEL trial in 524 patients, both LM major side branches i.e. the LAD and LCX had ostial diameter stenosis ≥50% in 34.7% of cases [17]. In patients who underwent provisional stenting, a bailout stent was implanted in 28.6% of those with and 12.1% without both side branches ostium stenoses (P = 0.0005) [17]. Bailout stenting was performed in 1 in 6 cases in EXCEL, although it was needed more often when the major coronary side branch, usually the LCX, had ostium stenosis. In EXCEL, all-cause mortality rates were insignificantly lower in the group with LM bifurcation without involvement of both side branches ostia treated with the provisional approach vs. planned two-stent technique (6.1% vs. 13.0%; hazard ratio [HR], 0.46; 95% CI, 0.21–1.01). However, one- and two-stent techniques in LM disease, where both ostial coronary side branches were affected, resulted in comparable mortality rates [17]. In the EBC MAIN study, patients with true bifurcation of left main stem lesions who underwent PCI using the stepwise layered provisional method had fewer major cardiac incidents compared to planned dual stenting, although the difference was not statistically significant [18]. Therefore, the stepwise provisional approach should continue to be the preferred option for intervention in bifurcation of the distal left main stem [18].

Study limitations

One limitation of our study was the absence of a surgical group for comparison. Nevertheless, examining such a group alongside the coronary artery bypass grafting (CABG) group was not within the study's intended scope. Additionally, while the study was based on a prospective registry, not all clinical data were accessible. Thirdly, the follow-up did not include analysis of the antiplatelet regimen or duration of dual antiplatelet therapy (DAPT) after discharge. Lastly, intravascular imaging (IVUS or OCT) were not analyzed in great detail.

CONCLUSIONS

In this study, we evaluated whether the involvement of LCX ostium significantly influences the results in real-world patients undergoing unprotected LM PCI. As far as we know, this is the first study to assess this issue broadly. The main finding of the study is that the LCX ostium involvement in LM disease PCI is not associated with increased long-term mortality, which is highly beneficial for the Heart Team's decision-making process. Moreover, in patients with LM disease and LCX ostium stenosis, there was no significant difference in long-term mortality between groups operated on using one-stent or two-stent techniques. Also, there were no significant differences in long-term mortality regardless of coexisting LCX ostium or LAD ostium lesions. An interesting subgroup of patients without significant LCX ostium disease who underwent LCX stenting during LM PCI, because of the plaque burden shift or carina shift, also presented good long-term outcomes.

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REFERENCES

1. Kim HY, Doh JH, Lim HS, et al. Identification of coronary artery side branch supplying myocardial mass that may benefit from revascularization. JACC Cardiovasc Interv. 2017; 10(6): 571–581, doi: 10.1016/j.jcin.2016.11.033, indexed in Pubmed: 28259665.
2. Gwon HC, Song YB, Pan M. The story of plaque shift and carina shift. EuroIntervention. 2015; 11 Suppl V: V75–V77, doi: 10.4244/EIJV11SVA16, indexed in Pubmed: 25983177.
3. Fischman DL, Savage MP, Leon MB, et al. Fate of lesion-related side branches after coronary artery stenting. J Am Coll Cardiol. 1993; 22(6): 1641–1646, doi: 10.1016/0735-1097(93)90589-s, indexed in Pubmed: 8227832.
4. Banning AP, Lassen JF, Burzotta F, et al. Percutaneous coronary intervention for obstructive bifurcation lesions: the 14th consensus document from the European Bifurcation Club. EuroIntervention. 2019; 15(1): 90–98, doi: 10.4244/EIJ-D-19-00144, indexed in Pubmed: 31105066.
5. Lee CH, Choi SW, Hwang J, et al. 5-year outcomes according to FFR of left circumflex coronary artery after left main crossover stenting. JACC Cardiovasc Interv. 2019; 12(9): 847–855, doi: 10.1016/j.jcin.2019.02.037, indexed in Pubmed: 31072505.
6. Gil RJ, Vassilev D, Formuszewicz R, et al. The carina angle-new geometrical parameter associated with periprocedural side branch compromise and the long-term results in coronary bifurcation lesions with main vessel stenting only. J Interv Cardiol. 2009; 22(6): E1–E10, doi: 10.1111/j.1540-8183.2009.00492.x, indexed in Pubmed: 19702678.
7. Shimada Y, Courtney BK, Nakamura M, et al. Intravascular ultrasonic analysis of atherosclerotic vessel remodeling and plaque distribution of stenotic left anterior descending coronary arterial bifurcation lesions upstream and downstream of the side branch. Am J Cardiol. 2006; 98(2): 193–196, doi: 10.1016/j.amjcard.2006.01.073, indexed in Pubmed: 16828591.
8. Vassilev D, Gil R. Clinical verification of a theory for predicting side branch stenosis after main vessel stenting in coronary bifurcation lesions. J Interv Cardiol. 2008; 21(6): 493–503, doi: 10.1111/j.1540-8183.2008.00400.x, indexed in Pubmed: 18973506.
9. Nakamura S, Hall P, Maiello L, et al. Techniques for Palmaz-Schatz stent deployment in lesions with a large side branch. Cathet Cardiovasc Diagn. 1995; 34(4): 353–361, doi: 10.1002/ccd.1810340217, indexed in Pubmed: 7621549.
10. Kang SJ, Mintz G, Kim WJ, et al. Changes in left main bifurcation geometry after a single-stent crossover technique. Circ Cardiovasc Interv. 2011; 4(4): 355–361, doi: 10.1161/circinterventions.110.961045, indexed in Pubmed: 21712525.
11. Skorupski WJ, Grygier M, Araszkiewicz A, et al. The impact of right coronary artery support on outcomes of patients with unprotected left main disease undergoing percutaneous coronary intervention. Kardiol Pol. 2021; 79(6): 631–637, doi: 10.33963/KP.15972, indexed in Pubmed: 33909388.
12. Kałużna-Oleksy M, Skorupski WJ, Grygier M, et al. A personalized approach to percutaneous coronary interventions in the left main coronary artery-is the female gender associated with worse outcomes? J Pers Med. 2021; 11(6), doi: 10.3390/jpm11060581, indexed in Pubmed: 34203081.
13. Skorupski WJ, Kałużna-Oleksy M, Lesiak M, et al. Short- and long-term outcomes of left main coronary artery stenting in patients disqualified

from coronary artery bypass graft surgery. J Pers Med. 2022; 12(3), doi: 10.3390/jpm12030348, indexed in Pubmed: 35330348.
14. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. Considerations for the choice between coronary artery bypass grafting and percutaneous coronary intervention as revascularization strategies in major categories of patients with stable multivessel coronary artery disease: an accompanying article of the task force of the 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J. 2019; 40(2): 204–212, doi: 10.1093/eurheartj/ehy532, indexed in Pubmed: 30165435.
15. Collet C, Capodanno D, Onuma Y, et al. Left main coronary artery disease: pathophysiology, diagnosis, and treatment. Nat Rev Cardiol. 2018; 15(6): 321–331, doi: 10.1038/s41569-018-0001-4, indexed in Pubmed: 29599504.
16. Park TK, Park YH, Song YB, et al. Long-term clinical outcomes of true and non-true bifurcation lesions according to medina classification- results from the COBIS (Coronary Bifurcation Stent) II registry. Circ J. 2015; 79(9): 1954–1962, doi: 10.1253/circj.CJ-15-0264, indexed in Pubmed: 26134457.
17. Kandzari DE, Gershlick AH, Serruys PW, et al. Outcomes among patients undergoing distal left main percutaneous coronary intervention. Circ Cardiovasc Interv. 2018; 11(10): e007007, doi: 10.1161/CIRCINTERVENTIONS.118.007007, indexed in Pubmed: 30354633.
18. Hildick-Smith D, Egred M, Banning A, et al. The European bifurcation club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). Eur Heart J. 2021; 42(37): 3829–3839, doi: 10.1093/eurheartj/ehab283, indexed in Pubmed: 34002215.