ORIGINAL ARTICLE

Four-year outcomes of unprotected left main lesion treated with one-stent versus two-stent technique

Lucian Predescu[1,2], Marin Postu[1], Lucian Zarma[1], Adrian Bucsa[1], Pavel Platon[1,2], Marian Croitoru[1], Adrian Mereuta[1,2], Leonard Lichiardopol[3], Alexandra Predescu[4], Dan Mihai Dorobantu[1,5], Carmen Ginghina[1,2], Dan Deleanu[1]

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Abstract: **Introduction –** Most reports on left main bifurcation lesions have demonstrated that treatment with a single-stent strategy is superior to a two-stent strategy but have excluded patients with acute coronary syndromes (ACS). **Aims –** The aim of the current study was to compare the four-year outcomes of patients with unprotected left main coronary artery disease (ULMCAD) treated by percutaneous coronary intervention (PCI) with a one-stent or two-stent strategies in a population including those presenting as ACS. **Methods –** A total of 135 patients with ULMCAD treated by PCI were included, of which 75 (55.6%) had a one-stent strategy (Group A) and 60 (44.4%) had a two-stent strategy (Group B). **Results –** Fewer patients in Group A had a TIMI III flow at the end of the procedure (89.4% vs 100%, p=0.03) and complete revascularization (65.3% vs 88.3%, p=0.002). We found a higher early mortality in Group A without reaching statistical significance (13.4% vs 3.3%, p=0.1). Mortality rate at 4-year follow up was higher with Group A after multivariable analysis (adjusted HR 0.36, CI 0.15-0.85, p=0.02). We found no significant differences between the groups in terms of major adverse cardiac event (MACE) (adjusted HR 0.85, CI 0.34-1.48, p=0.7) or target lesion revascularization (TLR) (adjusted HR 1.37, CI 0.42-4.47, p=0.6) at 4-year follow up. **Conclusions –** Among unselected patients with ULMCAD PCI, with or without ACS, the early mortality rate is similar between one and two-stent strategy. Although, 4-year TLR and MACE rates were similar between the two groups, the 4-year all-cause mortality rate was lower in the two-stent strategy group.
Keywords: percutaneous coronary intervention, left main coronary artery disease, one-stent strategy, two-stent strategy.

Rezumat: **Introducere –** Cele mai multe rapoarte privind leziunile principale de bifurcație stângă au demonstrat că tratamentul cu o strategie cu un singur stent este superior unei strategii cu două stenturi, dar au exclus pacienții cu sindroame coronariene acute (ACS). **Scop –** Scopul studiului actual a fost compararea rezultatelor de patru ani ale pacienților cu boală coronariană principală stângă neprotejată (ULMCAD) tratată prin intervenție coronariană percutanată (PCI) cu strategii cu un stent sau cu două stenturi într-o populație, inclusiv cele care prezintă ca ACS. **Metode –** Au fost incluși un număr de 135 de pacienți cu ULMCAD tratat de PCI, dintre care 75 (55,6%) au avut o strategie cu un singur stent (Grup A) și 60 (44,4%) au avut o strategie cu două stenturi (Grupul B). **Rezultate –** Mai puțini pacienți din grupa A au avut un flux TIMI III la sfârșitul procedurii (89,4% față de 100%, p = 0,03) și revascularizare completă (65,3% față de 88,3%, p = 0,002). Am găsit o mortalitate timpurie mai mare în grupul A, fără a atinge o semnificație statistică (13,4% față de 3,3%, p = 0,1). Rata mortalității la urmărirea de 4 ani a fost mai mare cu grupa A după analiza multivariabilă (HR 0,36 ajustat, CI 0,15-0,85, p = 0,02). Nu am găsit diferențe semnificative între grupuri în ceea ce privește evenimentul cardiac advers major (MACE) (HR 0,85 ajustat, CI 0,34-1,48, p = 0,7) sau revascularizarea țintelor (TLR) (HR 1,37, CI 0,42-4,47, p = 0,6) la 4 ani de urmărire. **Concluzii –** Printre pacienții neselectați cu IPC ULMCAD, cu sau fără ACS, rata mortalității precoce este similară între strategia cu unul și două stenturi. Deși, ratele TLR de 4 ani și MACE au fost similare între cele două grupuri, rata de mortalitate cauzală de 4 ani a fost mai mică în grupul de strategie cu două stenturi.
Cuvinte cheie: intervenție coronariană percutanată, boală coronariană principală stângă, strategie cu un singur stent, strategie cu două stenturi.

[1] Department of Cardiology, „Prof. C.C. Iliescu" Institute for Cardiovascular Diseases, Bucharest, Romania
[2] „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[3] Department of Cardiology, Tulcea County Hospital, Romania
[4] Colentina Clinical Hospital, Bucharest, Romania
[5] Faculty of Health Sciences, University of Bristol, United Kingdom

Contact address:
Lucian M. Predescu, MD
„Prof. Dr. C.C. Iliescu" Emergency Institute for Cardiovascular Diseases 258 Fundeni Street, Bucharest, Romania.
E-mail: lucianpredescu@gmail.com

INTRODUCTION

With the new developments in device technology, stent platforms and intracoronary imaging, percutaneous coronary intervention (PCI) of unprotected left main coronary artery disease (ULMCAD) has become a safer and more efficient treatment method. Although, coronary artery bypass grafting (CABG) was the standard treatment for complex left main lesions, an increasing number of patients with ULMCAD are treated by PCI[1]. The increasing experience with complex left main PCI had led to more ULMCAD patients with severe comorbidities and high surgical risk to be treated by PCI[2,3]. Comparative studies of PCI and CABG for ULMCAD have showed similarities between the two revascularization methods concerning major adverse cardiac event (MACE)[4,5]. Most studies on left main bifurcation lesions found that treatment with a single stent strategy is superior to a two-stent strategy[6-12]. The need for planned two-stent strategy varies between studies from 30% to 70%[6,13]. Some studies have shown that some two-stent techniques, like Double Kissing Crush technique, was associated with better outcomes than one-stent technique[11]. All those reports though have excluded patients with acute coronary syndrome (ACS). As such there is a significant gap in knowledge when it comes to the treatment of patients presenting in an acute setting with a ULMCAD.

AIM

The aim of current study was to compare the 4-year outcomes of unselected patients with ULMCAD treated by PCI with a one-stent or two-stent strategy including those presenting with ACS.

MATERIAL AND METHODS

Study Population

All patients with ULMCAD treated by PCI between January 2014 and December 2018 were selected from the electronic hospital records at the „Prof. Dr. C.C. Iliescu" Institute for Cardiovascular Diseases, Bucharest, Romania. Patients with a history of CABG and occluded grafts and patients presenting with ACS were included, also. Two young patients were excluded due to uncommon etiologies of left main (LM) stenosis: a case of coronary lesion secondary to tertiary syphilis and a case of spontaneous coronary dissection involving the LM. Only patients with complete data were included in the study. We included only patients with distal left main stenosis. Patients with ostial and mid-shaft left main stenosis were excluded. This resulted in a total of 135 patients for which demographic, clinical, angiographic, procedural, post-procedural and outcome data were extracted from the hospital electronic records. Life status was verified using the National Insurance Agency Platform in June 2019 to identify possible out of hospital deaths. Data analysis was performed with the approval of the institutional ethics committees of the hospital involved.

Study outcomes

MACEs were defined as the occurrence of death, myocardial infarction (MI) or target lesion revascularizations (TLRs). ACS was defined as either unstable angina, non-ST segment elevation MI (NSTEMI) or ST segment elevation MI (STEMI). TLR was defined as repeated PCI for restenosis of the entire segment involving the implanted stent and the 5-mm distal and proximal borders adjacent to the stent. Stent thrombosis was defined on the basis of Academic Research Consortium definitions according to timing of presentation as early (0–30 days), late (31–360 days), or very late (>360 days)[14]. Angiographic success was defined as residual stenosis of <30% by visual estimation in the presence of Thrombosis in Myocardial Infarction (TIMI) flow grade 3. Complete revascularization was defined as any attempt to revascularize all diseased segments (≥2.5 mm in diameter). The diagnosis of periprocedural MI was made if after PCI there was an increase in CK-MB or troponin levels that was 5 times the upper normal level.

Statistical analysis

Frequencies are given as numbers and percentages, continuous values as median (inter-quartile range or minimum-maximum values). Population characteristics were compared using the Mann-Whitney U test, Kruskall Wallis test and Fisher's exact test. Patients were divided into two main groups based on the PCI technique used: one group used a one stent technique (Group A), while the other used a two/three stent technique (Group B).

Early outcomes (mortality, stent thrombosis, need for intra-aortic balloon pump (IABP), access site complications) are based on known status at 30 days and presented as percentage. Late outcomes are estimated using the Kaplan Meier method. Late outcomes of interest are mortality, TLR and MACE.

Predictors of early outcomes were identified using univariable linear regression adjusted by acute coronary syndrome at the time of procedure. Multivariable

analysis was not possible due to only 12 early events. Predictors of late outcomes (death, TLR) were identified using a combination of backward and forward stepwise multivariable Cox regression, including all variables with a univariable regression p value of less than 0.1 and less than <10% missing values. The statistically significant variables left in the final model were considered independent predictors. The Group A vs Group B variable was always kept in the model, as a variable of interest. Statistical analyses were done with STATA/SE 12.0 (StataCorp LP, College Station, TX).

RESULTS

A total of 135 patients undergoing left main PCI were included, age ranging from 33 to 86 years (median of 63 years). Group A consisted of n=75 (55.6%), Group B of the remaining n=60 (44.4%). Detailed demographic and baseline clinical characteristics by group are presented in Table 1. We found few significant differences among the two groups, namely more hypertensive patients in Group B (93.3% Group B vs 76% Group A, p=0.009).

Table 1. Demographic and baseline clinical characteristics according to the stent strategy in patients with unprotected left main coronary artery disease treated by PCI (Group A – one stent strategy: Group B – two stent strategy)

	Group A	Group B	Total	p value
Age, y (median, IQR)	62 (55-69)	65 (55-71)	63 (55-71)	0.2
Male	55 (73.3)	43 (71.7)	98 (72.6)	0.8
Cardiovascular Risk factors				
Hypertension	57 (76)	56 (93.3)	113 (83.7)	0.009
Dyslipidemia	64 (86.5)	51 (85)	115 (85.8)	0.8
Diabetes	17 (23)	19 (31.7)	36 (26.9)	0.3
Obesity	15 (20)	20 (33.3)	35 (25.9)	0.1
Smoking status				
Active smoker	27 (36)	12 (20)	39 (28.9)	0.06
Former smoker	10 (13.3)	15 (25)	25 (18.5)	
Patient history				
ACS	29 (39.2)	24 (40)	53 (39.6)	0.5
Unstable angina	1 (3.4)	4 (16.7)	5 (9.4)	
NSTEMI	6 (20.7)	7 (29.2)	13 (24.5)	
STEMI	22 (75.9)	13 (54.1)	35 (66.1)	0.2
PCI	15 (20)	17 (28.3)	32 (23.7)	0.2
Atrial Fibrillation	8 (10.8)	10 (16.7)	18 (13.4)	0.4
Stroke/TIA	8 (10.7)	6 (10)	14 (10.4)	0.6
Bleeding	1 (1.4)	4 (6.7)	5 (3.7)	0.2
COPD	2 (2.7)	0 (0)	2 (1.5)	0.5
PAD	13 (17.6)	8 (13.3)	21 (15.7)	0.6
Neoplasm	5 (6.8)	3 (5)	8 (6)	0.7
Clinical presentation				
Stable angina	34 (45.3)	31 (51.6)	65 (48.2)	
Unstable angina	13 (17.3)	14 (23.3)	27 (20)	
NSTEMI	6 (8)	7 (11.7)	13 (9.6)	
STEMI	14 (18.7)	4 (6.7)	18 (13.3)	
ACS with cardiogenic shock	8 (10.6)	4 (6.7)	12 (8.9)	0.2
Atrial Fibrillation	6 (8.2)	6 (10)	12 (8.9)	0.8
LVEF, % (median, IQR)	45 (35-55)	50 (35-60)	45 (35-55)	0.1
LV systolic disfunction				
None (>=50%)	35 (46.7)	31 (53.4)	66 (49.6)	
Mild (40-49%)	16 (21.3)	12 (20.7)	28 (21.1)	
Moderate (30-39%)	13 (17.3)	11 (19)	24 (18)	
Severe (<30%)	11 (14.7)	4 (6.9)	15 (11.3)	0.6
Blood samples pre-PCI				
HB, g/dl (median, IQR)	13.7 (12.7-15)	14.4 (12.3-14.7)	13.7 (12.3-14.8)	13.7 (12.7-15)
Troponin, ng/ml (median, IQR)	0.2 (0.03-1.3)	0.6 (0.03-3.1)	0.2 (0.03-2.2)	0.2 (0.03-1.3)
Creatinine clearance, ml/min/1.73m^2 (median, IQR)	86 (64-97)	77 (64-93)	81 (64-96)	86 (64-97)

(ACS – acute coronary syndrome; NSTEMI – nonST segment elevation myocardial infarction; STEMI – ST segment elevation myocardial infarction; PCI – percutaneous coronary intervention; TIA – transient ischemic attack; COPD - chronic obstructive pulmonary disease; PAD – peripheral artery disease; LVEF – left ventricular ejection fraction; HB – hemoglobin)

SYNTAX, SYNTAX II (PCI and CABG, with respective predicted mortality) and EuroSCORE II scores did not differ between the two groups. Mean SYNTAX and SYNTAX II score were 21 and 31.9, respectively, in Group A and 23.5 and 32.1, respectively, in Group B.

Angiographic characteristics

Table 2 shows the main angiographic findings by used technique. As expected, true bifurcation lesions (Medina 1/1/1 and 0/1/1) were more frequent in Group B, as are those involving the LCX (1/0/1 and 0/0/1). Medina 0/1/0 or those involving the LAD (1/0/0, 1/1/0) were more frequent in Group A.

Table 2. Angiographic findings of patients with unprotected left main coronary artery disease treated by PCI (Group A – one stent strategy; Group B – two stent strategy)

	Group A	Group B	Total	p value
Arterial access site				
Radial	14 (18.7)	17 (28.3)	31 (23)	0.2
Femoral	61 (81.3)	43 (71.7)	104 (77)	0.2
Left main lesion localization				
Distal	65 (86.7)	47 (78.4)	112 (83)	
Ostial and distal	2 (2.7)	2 (3.3)	4 (3)	
Whole length	8 (10.7)	11 (18.3)	19 (14)	0.4
Bifurcation	56 (74.7)	49 (81.7)	105 (77.8)	0.3
Trifurcation	19 (25.4)	11 (18.3)	30 (22.2)	0.4
Other lesions				
None	28 (37.3)	18 (30)	46 (34.1)	
One vessel	20 (26.7)	20 (33.3)	40 (29.6)	
Two vessels	19 (25.3)	18 (30)	37 (27.4)	
Three vessels	8 (10.7)	4 (6.7)	12 (8.9)	0.6
Chronic total obstruction	20 (26.6)	11 (18.3)	31 (22.9)	0.3
LAD ostium affected	51 (68)	44 (73.3)	95 (70.4)	0.6
CX ostium affected	15 (20)	45 (75)	60 (44.4)	<0.001
LAD non-ostial	35 (46.7)	26 (43.3)	61 (45.2)	0.7
CX non-ostial	15 (20)	20 (33.3)	35 (25.9)	0.1
RCA lesion	24 (32)	19 (31.7)	43 (31.8)	0.6
Left main lesion characteristics				
Diffuse lesion	35 (46.7)	37 (61.7)	72 (53.3)	0.1
Eccentric lesion	57 (76)	44 (73.3)	101 (74.8)	0.8
Calcified lesion	18 (24)	23 (38.3)	41 (30.4)	0.09
Ulcerated lesion	25 (33.3)	11 (18.3)	36 (26.7)	0.05
Carina implicated	7 (9.3)	2 (3.3)	9 (6.7)	0.3
Medina classification				
1/1/1	9 (12)	25 (42.4)	34 (25.2)	
1/0/0	19 (25.3)	4 (6.7)	23 (17)	
1/1/0	12 (16)	4 (6.7)	16 (11.8)	
1/0/1	2 (2.7)	7 (11.7)	9 (6.7)	
0/1/0	30 (40)	7 (11.7)	37 (27.4)	
0/1/1	2 (2.7)	8 (13.3)	10 (7.4)	
0/0/1	1 (1.3)	5 (8.3)	6 (4.4)	<0.001
True bifurcation (1/1/1, 0/1/1)*	11 (14.7)	33 (55.7)	44 (32.6)	<0.001
LM take-off angle <70 degrees	26 (41.9)	14 (25.9)	40 (34.5)	0.08
Bifurcation angle				
>90 degrees	9 (15.5)	3 (5.6)	12 (10.7)	
70-90	25 (43.1)	20 (37)	45 (40.2)	
45-69	7 (12.1)	12 (22.2)	19 (17)	
<45	17 (29.3)	19 (35.2)	36 (32.1)	0.2
LM stenosis, % (median, IQR)	55 (12-80)	50 (22-76)	50 (20-77)	0.9
LAD stenosis, % (median, IQR)	86 (67-95)	83 (58-92)	85 (66-93)	0.2
CX stenosis, % (median, IQR)	25 (15-82)	75 (50-88)	70 (32-86)	0.03

(LM – left main; LAD – left anterior descending artery; LCX – left circumflex artery; RCA – right coronary artery; PCI – percutaneous coronary intervention)

Procedural characteristics

In 59 cases (40.4%) the PCI procedure was performed during the same session as the diagnostic coronary angiogram. In the remaining cases the median time between the two procedures was 11 days. Six patients (4.1%) were on mechanical support system with IABP prior to the PCI procedure. Femoral access was the preferred approach, in 88.9% of cases. Either a 6F (50.4%) or a 7F (48.2%) guiding catheter was used in most procedures.

More details on the procedural steps, use of proximal optimization technique (POT) and kissing balloon post dilatation (KBPD) are shown in Table 3. Pre-dilatation of main vessel was done at nominal pressure in more cases among Group B patients. POT was used in similar proportions in both groups (60% in Group A

Table 3. Procedural characteristics according to the stent strategy in patients with unprotected left main coronary artery disease treated by PCI (Group A – one stent strategy: Group B – two stent strategy)

	Group A	Group B	Total	p value
Arterial access site				
Femoral	67 (89.3)	53 (88.3)	120 (88.9)	0.7
Radial	8 (10.7)	7 (11.7)	15 (11.1)	0.5
Pre-PCI IABP	3 (4)	3 (5)	6 (4.4)	0.5
Guide catheter				
6F	45 (60)	23 (38.3)	68 (50.4)	
7F	28 (37.3)	37 (61.7)	65 (48.2)	
8F	2 (2.7)	0 (0)	2 (1.5)	0.008
Rotablation	2 (2.7)	1 (1.7)	3 (2.2)	0.6
MV predilatation	59 (79.7)	47 (78.3)	106 (79.1)	0.5
SB predilatation	8 (11)	40 (66.7)	48 (36.1)	<0.001
Predilatation at nominal	19 (32.2)	21 (44.7)	40 (37.7)	0.2
Dissection after predilatation	11 (17.2)	15 (31.9)	26 (23.4)	0.6
POT	45 (60)	42 (70)	87 (64.4)	0.3
POT after stent	35 (46.7)	33 (55)	68 (50.4)	0.4
POT after KBPD	11 (14.7)	27 (45)	38 (28.1)	<0.001
POT balloon diameter, mm (median, IQR)	4 (4-4.5)	4 (4-4.5)	4 (4-4.5)	
KBPD	14 (18.7)	48 (80)	62 (45.9)	<0.001
TKBPD	1 (1.3)	4 (6.7)	5 (3.7)	0.1
Stent underexpansion of >30%	8 (10.7)	6 (10)	14 (10.4)	0.6
IFR used pre-PCI	4 (5.3)	2 (3.3)	6 (4.4)	0.7
IFR used post-PCI	2 (2.7)	2 (3.3)	4 (3)	0.6
IVUS used pre-PCI	2 (2.7)	0 (0)	2 (1.5)	0.5
IVUS used post-PCI	10 (13.3)	16 (26.7)	26 (19.3)	0.08
SB residual stenosis				
None	36 (49.3)	47 (78.3)	83 (62.4)	
<50%	26 (35.6)	12 (20)	38 (28.6)	
>50%	11 (15.1)	1 (1.7)	12 (9.1)	0.001
Procedural success	68 (90.7)	59 (98.3)	127 (94.1)	0.08
Complete revascularisation	49 (65.3)	53 (88.3)	102 (75.6)	0.002
TIMI				
1	4 (5.3)	0 (0)	4 (3)	
2	4 (5.3)	0 (0)	4 (3)	
3	67 (89.4)	60 (100)	127 (94)	0.03
Peri-procedural complications				
Hematoma	4 (5.3)	2 (3.3)	6 (4.4)	0.7
Stroke/TIA	0 (0)	1 (1.7)	1 (0.7)	0.4
Myocardial infarction	1 (1.3)	3 (5)	4 (3)	0.3
Atrial fibrillation	1 (1.3)	1 (1.7)	2 (1.5)	0.4
Need for external electric shock	2 (2.7)	2 (3.3)	4 (3)	0.6
Bradi-arrhytmia	7 (9.3)	3 (5)	10 (7.4)	0.5
Death during PCI	3 (4)	0 (0)	3 (2.2)	0.2
CIN*	6 (13)	5 (12.8)	11 (12.9)	0.6

(PCI – percutaneous coronary intervention; IABP – intra-aortic balloon pump; LAD – left anterior descending artery; LCX – left circumflex artery; POT – proximal optimization technique; KBPD – kissing balloon post dilatation; TKBPD – triple kissing balloon post dilatation; MV – main vessel; SB – side branch; iFR - instantaneous wave-free ratio; IVUS – intravascular ultrasound; CIN – contrast induced nephropathy)

vs 70% in Group B, p=0.3), but was done after KBPD more frequently in Group B (14.7% in Group A vs 45% in Group B, p<0.001), owning in part to the higher use of KBPD in this group (18.7% in Group A vs 80% in Group B, p<0.001).

Procedural success with TIMI 3 flow was achieved in 94.1% cases, with complete revascularization in 75.6% patients. Instantaneous wave-free ratio (iFR) was performed before the PCI in 6 cases (4.4%) and after in 4 cases (3%). In 2 cases (1.5%) intravascular ultrasound (IVUS) was used before the procedure, while in 26 (19.3%) it was used after the procedure.

Technical outcomes and post-procedural complications by strategy group are summarized in Table 3. Single stent technique (Group A) resulted in more side branch residual stenosis, fewer cases of complete revascularization and fewer cases of TIMI 3 flow at the end of the procedure. There were fewer successful procedures in Group A, but only approaching statistical significance (90.7% vs 98.3%, p=0.08). There were no differences between the two groups in term of peri-procedural complications.

Early outcomes

There was an 8.8% early mortality (30 days mortality) (n=12), with a 2.2% peri-procedural mortality (n=3). We found a higher early mortality in Group A compared to Group B, without reaching statistical significance (13.4% vs 3.3%, p=0.1).

Most deaths occurred in patients presenting with ACS (n=11) and mostly in patients complicated with cardiogenic shock (n=8). As such, early mortality in non-ACS patients was 1.48% with no peri-procedural deaths.

Predictors of early mortality are summarized in Table 4. All values are from bivariable regression adjusted by presence of ACS since most deaths occurred in these patients. ACS itself is a strong predictor of early mortality. We found no significant differences in early mortality between Groups A and B. Patients with ACS had a 11.93 times higher risk of early mortality when compared to non-ACS patients (p=0.02), 59.49 times higher if also in cardiogenic shock (p<0.001).

Table 4. Thirty-day mortality according to the stent strategy in patients with unprotected left main coronary artery disease treated by PCI (Group A – one stent strategy; Group B – two stent strategy)

30 days mortality	Univariable analysis			ACS adjusted		
	OR	CI	p value	OR	CI	p value
Group B vs Group A	0.22	0.05;1.06	0.06	0.23	0.05;1.13	0.07
ACS at presentation	11.93	1.49;95.26	0.02			N/A
History of atrial fibrillation	4.44	1.15;17.13	0.03	4.66	1.11;19.53	0.02
ACS with cardiogenic shock	59.49	12.5;283.11	<0.001	36.66	6.89;194;89	<0.001
IAPB pre-PCI	13.33	2.34;75.79	0.003	7	1.2;40.82	0.03
Atrial fibrillation at presentation	7.06	174;28.58	0.006	6.29	1.4;28.19	0.02
LVEF at PCI	0.89/%	0.84;0.94	<0.001	0.9	0.85;0.96	0.001
LVEF <50%	5.61	1.18;26.7	0.03			0.07
LVEF <30%	19.77	5.1;76.52	<0.001	12	2.93;49.09	0.001
Severe mitral regurgitation	6.1	1.32;28.22	0.02	5.09	1.01;25.55	0.05
Hb pre-PCI value	0.63/g/dl	0.43;0.94	0.02	0.64	0.44;0.95	0.03
CK-MB pre-PCI value	1.28/100U	1.02;1566	0.04			0.1
Creatinine clearance pre-PCI	0.97/ml/min/1.73m^2	0.94;0.99	0.015			0.06
CIN*	8.87	1.52;51.55	0.02	10.63	1.68;67.26	0.01
LM stenosis degree	1.02/%	1;1.04	0.03			0.06
Predilatation at nominal	5.46	1.05;28.36	0.04	6.9	1.26;37.58	0.03
POT	0.24	0.06;0.84	0.03	0.26	0.07;0.96	0.04
KBPD	0.22	0.46;1.08	0.06			0.08
Post-PCI LM diameter	0.22/mm	0.05;1.05	0.06	0.2	0.04;0.98	0.05
Post-PCI LAD diameter	0.007/mm	0.0006;0.09	<0.001	0.01	0.0009;0.13	<0.001
Post-PCI CX diameter	0.37	0.19;0.69	0.002	0.34	0.17;0.69	0.003
Stent underexpansion of >30%	3.39	0.79;14.41	0.1			0.2
SB residual stenosis <50%	2.03	0.97;4.25	0.06			0.2
Complete revascularization	0.08	0.02;0.32	0.001	0.08	0.02;0.32	<0.001
TIMI flow	0.04/level	0.006;0.22	<0.001	0.06	0.01;0.33	0.001

ACS – acute coronary syndrome; IABP – intra-aortic balloon pump; PCI – percutaneous coronary intervention; LVEF – left ventricular ejection fraction; Hb – hemoglobin; CIN – contrast induced nephropathy; LM – left main; POT – proximal optimization technique; KBPD – kissing balloon post dilatation; LAD – left anterior descending artery; LCX – left circumflex artery; SB – side branch; TIMI - Thrombolysis In Myocardial Infarction

Late outcomes

Mortality, TLR and MACE at 4 years were 21.9%, 14% and 32.5% overall, 9.6%, 15% and 24.1% in non-ACS patients and 33.3%, 12.8% and 40.1% respectively in ACS-patients, respectively. Unadjusted comparisons of mortality, TLR and MACE at 4 years between Group A and Group B are shown in Figure 1. Mortality rate at 4-year follow up was higher in Group A compared to Group B after multivariable analysis (HR 0.36, CI 0.15-0.85, p=0.02).

Predictors of late mortality and coronary reintervention are summarized in Table 5. In multivariable analysis, two/three stent technique (Group B) is associated with a threefold reduction in 4-year mortality compared to one stent technique (Group A). Current risk and complexity scores were not independent predictors of mortality at 4 years in this group, but cardiogenic shock, severe left ventricular disfunction hemoglobin level below 12 g/dl and diffusely infiltrated left main were.

Diabetes, a non-ostial circumflex artery lesion at diagnostic and the use of a Stentys stent were independent predictors of TLR at 4 years. We found no significant differences between Group A and Group B in terms of MACE at 4 years when adjusting for predictors of death and TLR (adjusted HR 0.85, adjusted p value 0.7).

DISCUSSIONS

Our study included an unselected population with ULMCAD PCI without considering the clinical presentation. Patients presenting with ACS that had ULMCAD were not excluded. The aim of this study was to show the result of real-life practice of ULMCAD PCI in a high-volume working center with experience in treating elective and urgent patients with com-

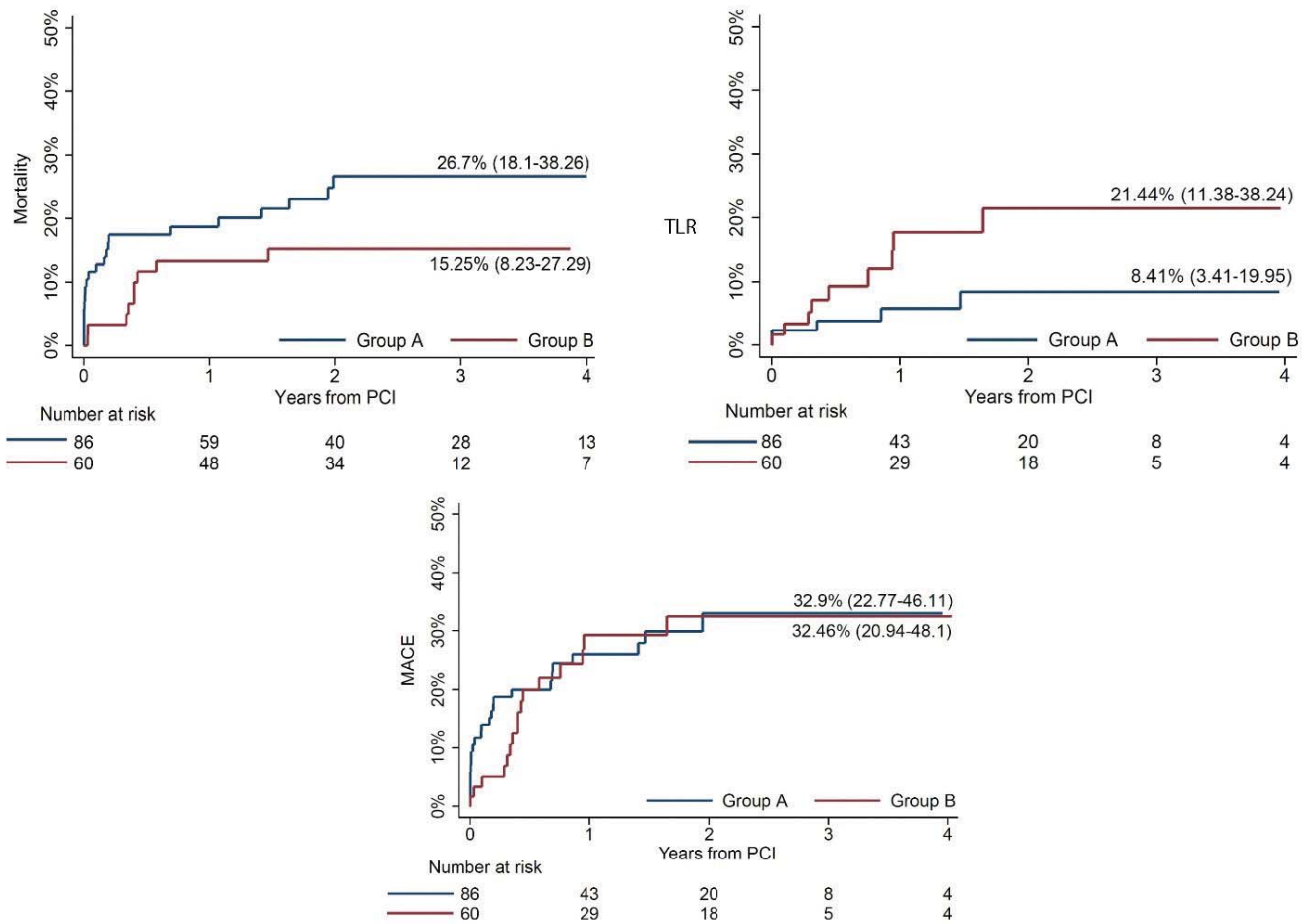

Figure 1. Unadjusted comparisons of mortality, target lesion revascularization (TLR) and major adverse cardiac events (MACE) at 4 years according to the stent strategy in patients with unprotected left main coronary artery disease treated by percutaneous coronary intervention (Group A – one stent strategy; Group B – two stent strategy). Curves represent Kaplan-Meier failure function.

Table 5. Predictors of late mortality and target lesion revascularization according to the stent strategy in patients with unprotected left main coronary artery disease treated by PCI (Group A – one stent strategy; Group B – two stent strategy)

Long term mortality	Univariable analysis			Multivariable analysis		
	HR	CI	p value	HR	CI	p value
Group B vs Group A	0.5	0.23;1.09	0.08	0.36	0.15;0.85	0.02
Age	1.03/y	0.99-1.06	0.14			
Male gender	1.89	0.72;4.96	0.19			
Hypertension	0.48	0.21;1.09	0.08			
Former smoker	0.3	0.07;1.32	0.11			
History of stroke	2.33	0.95;5.74	0.06			
SYNTAX	1.05/unit	1.02-1.1	0.002			
SYNTAX-2 PCI	1.07/unit	1.04-1.1	<0.001			
SYNTAX-2 CABG	1.04/unit	1.02-1.08	0.003			
EUROSCORE II	1.16/unit	1.11-1.22	<0.001			
ACS	4.37	1.77;10.75	0.001			
ACS with cardiogenic shock	13.74	6.15;30.68	<0.001	6.09	2.08;17.75	0.001
Atrial Fibrillation at presentation	2.67	1.01;7.04	0.05			
LVEF (%)	0.93/%	0.9-0.96	<0.001			
LVEF <30%	12.52	5.93;26.43	<0.001	5.77	2.26;14.75	<0.001
Severe mitral regurgitation	3.42	1.3;9.02	0.01			
Pulmonary hypertension*	1.83	0.68;4.94	0.23			
Hb at PCI	0.64/g/dl	0.52-0.80	<0.001			
Hb <12 g/dl	5.13	2.45;10.72	<0.001	3.52	1.61;7.67	0.002
CK-MB at PCI*	1.001	1-1.003	0.06			
Creatinine clearance at PCI	0.97	0.96-0.98	<0.001			
CIN*	5.33	1.95;14.52	0.001			
Associated two/three vessel disease	1.62	1.02;2.58	0.04			
Diffuse LM plaques	2.19	0.99;4.82	0.05	2.57	1.1;6.01	0.03
Ulcerated LM lesion	3.07	1.48;6.38	0.003			
LM stenosis (%)	1.01/%	1.005-1.03	0.004			
Post PCI CX diameter (mm)	0.53/mm	0.37;0.75	<0.001			
Pre-PCI IABP	8.65	3.21;23.31	<0.001			
Post-PCI IABP	4.15	1.57;10.94	0.004			
Predilation at nominal diameter	2.98	1.3;6.81	0.01			
POT used	0.48	0.23;1.007	0.05			
Residual SB stenosis >50%	1.8	1.15;2.83	0.01			
Procedural succes	0.17	0.06-0.45	<0.001			
Complete revascularisation	0.26	0.13-0.55	<0.001			
	Univariable analysis			Multivariable analysis		
TLR	HR	CI	p value	HR	CI	p value
Group B vs Group A	2.22	0.74;6.63	0.15	1.37	0.42;4.47	0.6
Diabetes	4.85	1.67;14.09	0.004	3.88	1.24;12.12	0.02
History of Atrial Fibrillation	3.23	1.01;10.34	0.05			
Associated two/three vessel disease	3.49	0.94;12.93	0.06			
Non ostial LCX lesion	5.23	1.75;15.63	0.003	5.52	1.78;17.15	0.003
Calcified LM lesion	2.77	0.97;7.93	0.06			
LAD stenosis (%)	1.01/%	0.99-1.04	0.1			
Stentys stent used	3.07	0.96;9.8	0.06	3.61	1.11;11.74	0.03
MV stent diameter (mm)	0.27	0.04;1.98	0.2			
Stent underexpansion of >30%	2.75	0.76;9.89	0.12			
*>10% missing value, not used in multivariable analysis						

ACS – acute coronary syndrome; IABP – intra-aortic balloon pump; PCI – percutaneous coronary intervention; LVEF – left ventricular ejection fraction; Hb – hemoglobin; CIN – contrast induced nephropathy; LM – left main; POT – proximal optimization technique; KBPD – kissing balloon post dilatation; LAD – left anterior descending artery; LCX – left circumflex artery; TLR – target lesion revascularization; SB - side branch.

plex LM lesions. The study included 135 patients with ULMCAD PCI of which 51.8% presented with ACS. The study population was divided in two groups to compare different stent strategy for the left main PCI (one-stent strategy versus two-stent strategy). There are few reports of such comparison that included the patient presented with ACS.

Although, our study has included the patients presented with ACS, the early mortality was similar to the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial (8.8% in our study vs 8.1% in EXCEL trial)[12,15]. The 4-year mortality rate was significantly higher than in the NOBLE (Nordic-Baltic-British left main revascularisation) trial at 5 year follow up (mortality rate in our study was 21.9% versus 12% in NOBLE trial)[16]. When we excluded the patient presented with ACS, the long-term mortality and TLR rates were comparable in the two studies (mortality and TLR rate in our study were 9.6% and 15%, respectively versus 12% and 16% in NOBLE trial)[16].

As we expected, the two-stent strategy was used in more complex patients, with diffuse left main plaques, calcified left main lesions and with Medina 1/1/1 or 0/1/1 lesion. POT use was similar among the two groups, but KBPD was used more frequently in the two-stent strategy group (18.7% in Group A vs 80% in Group B, p<0.001). In univariable analysis POT, but not KBPD, was a predictor for early mortality. Neither POT nor KBPD were a predictor for long-term outcomes in the multivariable analysis.

Although we found a higher early mortality in patients with ULMCAD treated with one-stent strategy compared to two-stent strategy, it didn't reach the statistical significance (13.4% vs 3.3%, p=0.1), possibly in the context of low number of events. This can be since the group treated with a one-stent strategy included a bigger number of patients with ACS complicated with cardiogenic shock, which was a strong predictor and confounder of 30 days mortality. The results are consistent with other studies[6,10,11,17].

In contrast to other studies, the 4-year mortality rate was significantly lower in the two-stent strategy group compared to the one-stent strategy group. No significant differences between the two group in terms of MACE at 4 years was found when adjusting for predictors of death and TLR (adjusted HR 0.85, adjusted p value 0.7). This findings can partially be explained by the lower number of patients in the Group A with TIMI III flow at the end of the procedure (89.4% vs 100%, p=0.03), with complete revascularization (65.3% vs 88.3%, p=0.002) and with no residual side branch stenosis (49.3% vs 78.3%, p=0.001). Considering this data, we can emphasize that the one-stent strategy group was a higher risk group with patients in a more severe clinical status although the anatomical complexity of LM lesion was lower in the one-stent strategy group. This finding can show that in a high-volume center with a big experience in performing LM PCI the long-term outcomes can be driven more by the clinical condition of the patient and other patient related features, than maybe technical aspects. Nevertheless, the influence of an acute setting in left main PCI needs to be further investigated, as it might also contribute, by unknown mechanisms, to different outcomes than expected from studies looking at stable angina.

One important study limitation is the nonrandomized study design. Although it might have offered more data on restenosis, routine angiographic reevaluation is no longer recommended and was not performed.

CONCLUSIONS

Among patients with ULMCAD PCI with or without ACS, the early mortality rate is similar between one and two-stent strategy. Although, 4-year TLR and MACE rates were similar between the two groups, the 4-year mortality rate was lower in the two-stent strategy group. The optimal strategy in UPMLCA PCI outside stable angina requires further research.

Conflict of interest: none declared.

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