ORIGINAL ARTICLE

Culprit plaque location within the left circumflex coronary artery predicts clinical outcomes in patients experiencing acute coronary syndromes with percutaneous coronary intervention: Data from the ORPKI registry

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ABSTRACT

Background: The left circumflex (LCx) artery is the most diagnostically challenging of the coronary branches in terms of diagnostics because the clinical presentation and electrocardiography (ECG) do not always suggest critical occlusion despite its presence. Therefore, it is important to determine the factors contributing to the clinical manifestation and outcome, such as the culprit location.

Aims: To determine the relationship between the location of the culprit plaque and clinical outcomes in the LCx artery.

Methods: Data from the Polish Registry of Invasive Cardiology Procedures (ORPKI) from the years 2019–2020 concerning percutaneous coronary intervention (PCI) procedures were extracted and analyzed using appropriate statistical tests.

Results: 97 899 clinical records were analyzed. Patients with proximal occlusion received a worse grade using the Killip classification. Patients with Thrombolysis in Myocardial Infarction (TIMI) score 0 had worse clinical presentation in each of the occlusion locations. The periprocedural cardiac arrest and death rates were the highest among patients with proximal circumflex (Cx) occlusion. The death rate among patients with proximal occlusion and non-ST-segment elevation myocardial infarction (NSTEMI) was greater than among patients with distal occlusion and ST-segment elevation myocardial infarction (STEMI).

Conclusions: Among patients with proximal occlusions of the Cx artery and TIMI 0 grade flow on initial angiogram, a STEMI-like approach should be undertaken apart from initial ECG findings. This is driven by a higher rate of critical and fatal complications such as cardiac arrest and periprocedural death. Fatal complications occur more often in patients with proximal occlusion of Cx than in medial or distal occlusion. Grade IV according to the Killip classification can suggest a proximal culprit location.

Key words: acute coronary syndromes, clinical outcomes, culprit lesion, Killip classification, left circumflex artery

WHAT'S NEW?

Data from the Polish Registry of Invasive Cardiology Procedures (ORPKI) have shown that the location of the culprit plaque has a great impact on the severity of myocardial infarction. Patients with proximal occlusion and non-ST-segment elevation myocardial infarction (NSTEMI) are at a greater risk than patients with distal occlusion and ST-segment elevation myocardial infarction (STEMI). This correlation indicates how important it is to consider other factors alongside the presence of ST-segment elevation, most importantly the Killip score, as a patient with NSTEMI may require more urgent and careful treatment than a patient with STEMI.

INTRODUCTION

Acute coronary syndromes (ACS) encompass ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). When typical symptoms of myocardial infarction (MI) are associated with STEMI changes on baseline electrocardiography (ECG), current guidelines recommend urgent primary percutaneous coronary intervention (PCI) with a maximum reduction of door-to-balloon time [1]. In the NSTEMI subgroup, recommendations are not so strict and depend upon the clinical and hemodynamic condition of the patient [2]. Moreover, among MI patients, those with an occluded or critically stenosed left circumflex (LCx) coronary artery seem to be the most challenging group to identify and immediately qualify for urgent angiography due to non-conclusive ECG changes on admission and confusing clinical presentation [3–11]. Our investigation has gone further, and we focused on assessing whether a different localization of the culprit plaque (proximal vs. medial vs. distal segment) within the circumflex artery responsible for MI has any implications on procedural aspects and clinical outcomes for these patients. The present study aimed to assess the influence of culprit plaque location within the circumflex artery segments (proximal vs. medial vs. distal) on procedural characteristics and clinical outcomes in patients with ACS treated using primary PCI. The impact of the culprit plaque location within the ACS-related artery on the preliminary diagnosis (STEMI, NSTEMI, UA) in different Thrombolysis in Myocardial Infarction (TIMI) flow grade subgroups was also investigated.

METHODS

All data were obtained from the electronic database of the Polish Registry of Invasive Cardiology Procedures (ORPKI) operated by the Jagiellonian University Medical College in Kraków. The ORPKI is a national registry with data compiled from all cardiology percutaneous interventions performed in Poland. Data in the ORPKI registry have been gathered via electronic case report forms at the majority of interventional cardiology centers in Poland since 2004. No personal data is collected in the registry. The presented archive is a single-arm registry of PCIs performed at Polish cath labs within the years 2019–2020 [12–14]. Core lab assessment was not applied. The MI, STEMI, NSTEMI, and UA were defined according to the fourth universal definition of myocardial infarction (2018) [15]. The segmentation visual assessment was performed in accordance with the Coronary Artery Surgery Study (CASS) [16]. The Killip-Kimball classification was used to evaluate the stage of heart failure among patients with acute myocardial infarction [17]. The TIMI score was used to assess coronary artery flow [18].

In the study, the ORPKI patients who were included were admitted to a cath lab with ACS and underwent a primary PCI of a significant circumflex (Cx) artery occlusion. The exclusion criterion was a significant incomplete medical records. Patients were divided according to the culprit location in the Cx artery. Primary endpoints compared between the groups were the intra- and peri-procedural cardiac arrest and death rates.

The study complied with ethical principles for clinical research based on the Declaration of Helsinki and appropriate consent was obtained from the institutional review board.

Statistical analysis

Categorical variables are presented as numbers and percentages. The normality of quantitative variables was assessed *via* the Shapiro-Wilk test. As the distribution of all quantitative data was other than normal, they are expressed as median (interquartile range [IQR]) and were compared using the Kruskal-Wallis ANOVA with the *post hoc* Dunn tests. Categorical variables were compared with the Pearson χ^2 or Fisher exact tests if 20% of cells had an expected count of fewer than 5 (Monte Carlo simulation for tables larger than 2 × 2). The significance level (α) was set at 0.05. Based on the results of univariate analysis, multivariable logistic regression models were constructed to find predictors of periprocedural deaths, cardiac arrests, and all complications in the analyzed group of patients. In the multivariable analysis, we included indices with P <0.1 based on the results of univariate analysis. The best model was obtained using the stepwise regression with minimization of the Bayesian Information Criterion as a target. Statistical analysis was performed using JMP, version 15.2.0 (SAS Institute Inc., Cary, NC, US).

Table 1. Demographics and characteristics of the analyzed populations

All patients					
Cx narrowing location	**Proximal — A**	**Medial — B**	**Distal — C**	**Total**	***P*-value**
Age, years	68 (61–76)	67 (60–75)	66 (60–75)	67 (60–76)	<0.001
Sex	F: 14029 (32.47) M: 29175 (67.53)	F: 14549 (31.11) M: 30759 (67.89)	F: 2659 (29.51) M: 6352 (70.49)	F: 31237 (32.93) M: 66286 (67.97)	<0.001
Weight, kg	80 (70–90)	80 (70–90)	80 (73–90)	80 (70–90)	<0.001
Diabetes	11209 (25.79)	10584 (23.32)	2356 (25.90)	24149 (24.66)	<0.001
Previous MI	13897 (31.98)	12682 (27.94)	2715 (29.85)	29294 (29.91)	<0.001
Previous PCI	15106 (34.76)	14767 (32.54)	3138 (34.50)	33011 (33.70)	<0.001
Previous CABG	3938 (9.06)	2324 (5.12)	477 (5.24)	6739 (6.88)	<0.001
Previous stroke	1663 (3.83)	1442 (3.18)	348 (3.83)	3453 (3.53)	<0.001
Smoking (overall)	9165 (21.09)	10301 (22.70)	2116 (23.26)	21582 (22.04)	<0.001
Psoriasis	175 (0.40)	208 (0.46)	46 (0.51)	429 (0.44)	0.27
Hypertension	30763 (70.78)	31945 (70.39)	6523 (71.71)	69231 (70.68)	0.03
Kidney disease (GFR <60 ml/min/1.73 m^2 or renal replacement therapy)	3164 (7.28)	2374 (5.23)	538 (5.91)	6076 (6.20)	<0.001
COPD	1102 (2.54)	991 (2.18)	204 (2.24)	2297 (2.35)	0.002
Initial TIMI 0 patients					
Cx narrowing location	**Proximal — A**	**Medial — B**	**Distal — C**	**General**	***P*-value**
Age, years	65 (58–73)	65 (58–72)	65 (57–73)	65 (58–73)	<0.001
Sex	F: 3054 (30.95) M: 6814 (69.05)	F: 2631 (29.34) M: 6337 (70.66)	F: 697 (30.15) M: 1383 (69.85)	F: 6282 (30.18) M: 14534 (69.82)	0.06
Weight, kg	80 (70–90)	80 (70–90)	80 (72–91)	80 (70–90)	<0.001
Diabetes	2107 (21.28)	1780 (19.83)	449 (22.60)	4336 (20.78)	0.005
Previous MI	2005 (20.25)	1671 (18.61)	374 (18.82)	4050 (19.41)	0.01
Previous PCI	1873 (18.92)	1586 (17.67)	363 (18.27)	3822 (18.32)	0.09
Previous CABG	389 (3.93)	227 (2.53)	57 (2.87)	673 (3.23)	<0.001
Previous stroke	360 (3.64)	287 (3.20)	77 (3.88)	724 (3.47)	0.15
Smoking (overall)	2723 (27.50)	2694 (30.01)	571 (28.74)	5988 (28.70)	<0.001
Psoriasis	41 (0.41)	47 (0.52)	17 (0.86)	105 (0.50)	0.04
Hypertension	6305 (63.67)	5798 (64.58)	1349 (67.89)	13452 (64.47)	0.002
Kidney disease (GFR <60 ml/min/1.73 m^2 or renal replacement therapy)	508 (5.13)	367 (4.09)	107 (5.39)	982 (4.71)	0.001
COPD	203 (2.05)	175 (1.95)	43 (2.16)	421 (2.02)	0.79

Data presented as median (interquartile range [IQR]) or n (%)

Abbreviations: CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; Cx, circumflex branch of left coronary artery; F, female; GFR, glomerular filtration rate; M, male; MI, myocardial infarction; PCI, percutaneous coronary intervention

RESULTS

Characteristics

Initially, 97 899 clinical records were analyzed. All patients were divided according to localization of the culprit plaque within the Cx artery: group A — proximal segment (n = 43 444); group B — medial segment (n = 45 363), and group C — distal segment (n = 9092), based on initial angiography. Patient characteristics and data concerning past medical history are presented in Table 1. On admission, patients were assessed according to the Killip-Kimball classification. The patients with proximal occlusion received, on average, the worst score. The results of the assessment on this scale are presented in Table 2.

Clinical status at baseline — whole group (independent of TIMI grade)

On admission, cardiac arrest was observed in 2.31% of patients. The highest rate of cardiac arrest was observed in group A — the proximal segment of Cx, followed by groups B and C (Table 2). This difference was concordant with the Killip classification — the percentage of grade IV in group A was twice as high as in groups B and C. The differences were statistically significant (Table 2).

Hypothermia was used extremely rarely in all groups — most commonly in group A, followed by groups B and C — proportionally to the differences in cardiac arrest in analyzed groups (Table 2). In all groups, direct transport to the Cath lab was relatively rare (8.03%).

Clinical status at baseline — patients with TIMI 0 on initial angiogram

On admission, cardiac arrest was observed in 4.89% of patients in the TIMI 0 subgroup, which was over 2 times higher than in the general comparison (Table 2). In the TIMI 0 subgroup, the highest rate of cardiac arrest was also observed in group A — the proximal segment of Cx, followed by groups B and C (Table 2). This difference was

Table 2. Clinical characteristics of the groups

Initial diagnosis based on ECG and troponin level					
	Proximal — A	Medial — B	Distal — C	General	*P*-value
STEMI	11039 (25.41)	11214 (24.72)	2425 (26.67)	24678 (25.21)	<0.001
NSTEMI	15575 (35.85)	14802 (32.63)	2979 (32.76)	33356 (34.07)	
UA	16830 (38.74)	19347 (42.65)	3689 (40.57)	39866 (40.72)	
TIMI 0 without ST-segment elevation	4637 (51.67)	4084 (50.03)	893 (46.22)	9614 (50.59)	0.02
Cardiac arrest on admission	1234 (2.84)	903 (1.99)	132 (1.45)	2269 (2.32)	<0.001
Cardiac arrest on admission (TIMI 0)	575 (5.81)	390 (4.35)	55 (2.79)	1020 (4.89)	<0.001
Therapeutic hypothermia	52 (0.12)	32 (0.07)	1 (0.01)	85 (0.09)	0.001
Therapeutic hypothermia (TIMI 0)	28 (0.28)	11 (0.12)	1 (0.05)	40 (0.19)	0.01
Killip classification					
All patients					
Killip class	**Proximal — A**	**Medial — B**	**Distal — C**	**General**	***P*-value**
I	36814 (84.74)	40654 (89.62)	8145 (89.58)	85613 (87.45)	<0.001
II	3893 (8.96)	3248 (7.16)	706 (7.77)	7847 (8.02)	
III	1208 (2.78)	785 (1.73)	120 (1.32)	2113 (2.16)	
IV	1529 (3.52)	680 (1.50)	121 (1.33)	2330 (2.38)	
Initial TIMI 0					
Killip class	**Proximal — A**	**Medial — B**	**Distal — C**	**General**	***P*-value**
I	7711 (77.88)	7675 (85.52)	1729 (87.04)	17115 (82.04)	<0.001
II	1117 (11.28)	745 (8.30)	173 (8.70)	2035 (9.74)	
III	402 (4.06)	237 (2.64)	35 (1.76)	674 (3.22)	
IV	671 (6.78)	319 (3.55)	49 (2.49)	1039 (4.97)	

Data presented as n (%)

Abbreviations: ECG, electrocardiography; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; UA, unstable angina

concordant with the Killip classification — the percentage of grade IV was the highest in group A, followed by groups B and C. The differences were statistically significant (Table 2).

Hypothermia was used extremely rarely in all groups – most commonly in group A, followed by groups B and C — proportionally to differences regarding cardiac arrest in analyzed groups (Table 2). In the TIMI 0 subgroup, direct transport to the cath lab was observed more frequently than in the whole cohort (16.11%).

Initial diagnosis based on ECG and troponin level (STEMI vs. NSTEMI vs. UA)

The most common reason for the procedure in all of the groups was UA. STEMI was most common in group C, followed by groups A and B.

Based on initial diagnosis, the cardiac arrest rate was significantly higher in patients with STEMI on the initial ECG, and considering segment division, more frequent in the proximal segments: 1.51% in group A; 0.75% in group B and 0.74% in group C (P <0.001). In NSTEMI patients, this totaled 0.56% vs. 0.24 % vs. 0.30%, respectively (P = 0.007), while in UA patients, this was 0.17% vs. 0.08% vs. 0.03% (P = 0.015).

Vascular access

The most frequently used access during the procedures in all of the groups was the right radial approach. More specific data concerning vascular access are presented in Supplementary material, *Table S1*.

Angiographic characteristics

Multivessel coronary artery disease (CAD) without left main coronary artery (LMCA) involvement was present in more than half of the performed procedures. Single-vessel CAD was the second most common finding. Specific data concerning the results of the angiograms are given in Table 3.

Advanced morphology and functional assessment

Additional assessments, such as intracoronary ultrasound (ICUS), plaque assessment with optical coherence tomography (OCT), or functional assessment with fractional coronary flow reserve measurement (FFR) were rarely performed in all groups. Further data are presented in Supplementary material, *Table S2*.

Procedural characteristics — the amount of contrast and radiation dose

In the whole group, the median contrast volume used during the procedure was 160 (120–210) ml. The smallest amount of contrast was used in group B (medial segment) followed by the C and A groups. In the TIMI 0 subgroup, the median general contrast usage was greater compared to the whole group: 170 (135–220) ml; with the same pro-

Table 3. Angiographic characteristics of the groups — results of angiography

Result of angiography	Proximal — A	Medial — B	Distal — C	General	*P*-value
All patients					
No significant stenosis	4 (0.01)	14 (0.03)	1 (0.01)	19 (0.02)	<0.001
No atherosclerotic changes	9 (0.02)	14 (0.03)	5 (0.05)	28 (0.03)	
Single-vessel CAD	12768 (29.39)	17624 (38.85)	3312 (36.43)	33704 (34.43)	
Multi-vessel CAD without LMCA involvement	24802 (57.09)	25576 (56.38)	5378 (59.15)	55756 (56.95)	
Multi-vessel CAD with LMCA involvement	5787 (13.32)	2096 (4.62)	387 (4.26)	8270 (8.45)	
Only LMCA disease	70 (0.16)	41 (0.09)	9 (0.10)	120 (0.12)	
Initial TIMI 0					
Result of angiography	**Proximal — A**	**Medial — B**	**Distal — C**	**General**	***P*-value**
No significant stenosis	0 (0.00)	5 (0.06)	0 (0.00)	5 (0.03)	<0.001
No atherosclerotic changes	2 (0.02)	4 (0.05)	2 (0.10)	8 (0.04)	
Single-vessel CAD	3139 (31.70)	3277 (36.51)	767 (38.61)	7183 (34.44)	
Multi-vessel CAD without LMCA involvement	5802 (58.60)	5241 (58.39)	1128 (56.78)	12171 (58.33)	
Multi-vessel CAD with LMCA involvement	946 (9.55)	441 (4.91)	87 (4.40)	1474 (7.06)	
Only LMCA disease	13 (0.13)	7 (0.08)	2 (0.10)	22 (0.11)	

Data presented as n (%)

Abbreviations: CAD, coronary artery disease; LMCA, left main coronary artery; other — see Table 2

portion between segments. It was significantly higher in group B (medial segment) in comparison to groups A and C. A detailed comparison is provided in Table 4.

When we evaluated the contrast volume between assessed segments and stratified it by differential diagnoses, we found that patients with STEMI were related to the greatest contrast volume use during the procedures and this concerned proximal and distal occlusion; while in NSTEMI — the greatest contrast volume was used in proximal and distal occlusion; and in UA — the greatest contrast volume was used in proximal occlusion (Table 4).

The radiation dose received during the procedure was higher in the TIMI 0 subgroup than in the main comparison. In this subgroup, the radiation exposure was the greatest in group C, followed by groups A and B, whereas in the general comparison, it was greatest in group A, followed by groups C and B (Table 4).

Comparing the radiation dose according to initial diagnosis; in patients with STEMI, the highest dose of radiation was used during the procedures which concerned distal occlusion; in NSTEMI — distal occlusion; in UA — distal occlusion (Table 4).

COMPLICATIONS

Lesions in the proximal segment of the Cx artery resulted in significantly greater rates of intra-procedural cardiac arrests and death compared to other locations, both in the TIMI 0 subgroup and in the main comparison. There was no difference in terms of puncture-site bleeding (Table 4).

On division into subgroups according to the initial diagnosis, the results were concordant with the whole group comparison — the cardiac arrest and death rates were the highest in the A group (proximal occlusion), followed by the B and C groups. This relationship occurred in every subgroup (STEMI, NSTEMI, UA). The death rate in NSTEMI patients with proximal occlusion was comparable to that in STEMI patients with medial occlusion and was twice as high as the death rate in STEMI patients with distal occlusion (Table 4).

Procedural characteristics: time delays

Time from first contact to inflation or angiogram was the shortest in groups C and A, followed by group B, considering the whole group. In the TIMI 0 subgroup, the time from first contact to inflation or angiogram was the shortest in the C group (distal), followed by the A and B groups. The results were statistically significant (Table 5).

Regarding the initial diagnosis: in each occlusion location group, patients with STEMI had undergone an angiography much faster than patients with NSTEMI, and even faster than patients with UA. NSTEMI patients had undergone an angiography slightly faster than UA patients (Table 5).

Stenting

Stenting comparison was performed in the TIMI 0 subgroup. In each group, the most commonly used stent type was drug eluting stent. Bioresorbable vascular stent was used extremely rarely — in fewer than 0.5% of cases. Stents were implanted most commonly in the medial location. A substantial percentage of patients did not receive any implant (Supplementary material, *Table S3*).

Risk factors for periprocedural death and complications

Among risk factors influencing periprocedural death, there is the culprit location (the worst survival in the proximal location), the type of ACS (the worst survival in STEMI, followed by NSTEMI and UA), TIMI flow after the intervention (worse survival in cases of smaller flow) and the Killip class

Table 4. Contrast, radiation and complications

All patients					
	Proximal — A	**Medial — B**	**Distal — C**	**General**	***P*-value**
Contrast volume, ml	170 (130–220)	150 (120–200)	170 (130–220)	160 (120–210)	<0.001
Post hoc test	A vs. C: *P* = 0.02	B vs. A: *P* <0.001	C vs. B: *P* <0.001		
Radiation dose, mGy	956 (527–1630.50)	826 (459–1407)	908 (524–1557.50)	889 (493–1518)	<0.001
Post hoc test	A vs. C: *P* <0.001	B vs. A: *P* <0.001	C vs. B: *P* <0.001		
Bleeding at the puncture site, %	70 (0.16)	68 (0.15)	18 (0.20)	156 (0.16)	0.45
Cardiac arrest during procedure, %	569 (1.31)	236 (0.52)	50 (0.55)	855 (0.87)	<0.001
Death during procedure, %	478 (1.10)	172 (0.38)	21 (0.23)	671 (0.69)	<0.001
Initial TIMI 0					
	Proximal — A	**Medial — B**	**Distal — C**	**General**	***P*-value**
Contrast volume, ml	180 (140–220)	170 (130–220)	180 (140–220)	170 (135–220)	<0.001
Post hoc test	A vs. C: *P* = 0.81	B vs. A: *P* <0.001	C vs. B: *P* <0.01		
Radiation dose, mGy	973 (543–1668)	920 (526–1547)	1000 (581.75–1675.50)	952 (540–1619)	<0.001
Post hoc test	A vs. C: *P* =0.85	B vs. A: *P* <0.001	C vs. B: *P* <0.01		
Bleeding at the puncture site, %	18 (0.18)	19 (0.21)	4 (0.20)	41 (0.20)	0.90
Cardiac arrest during procedure, %	308 (3.11)	123 (1.37)	20 (1.01)	451 (2.16)	<0.001
Death during procedure, %	264 (2.67)	90 (1.00)	8 (0.40)	362 (1.73)	<0.001
Exposition compared according to initial diagnosis and location of narrowing					
Diagnosis		**Proximal — A**	**Medial — B**	**Distal — C**	***P*-value**
STEMI	Contrast volume, ml	170 (130–220)	150 (120–200)	170 (130–220)	<0.001
	Radiation dose, mGy	957 (530–1656)	825 (459–1404.50)	922 (529–1597.50)	<0.001
NSTEMI	Contrast volume, ml	175 (130–220)	160 (120–200)	175 (130–220)	<0.001
	Radiation dose, mGy	974 (544–1665.75)	850 (484–1439.25)	949 (553–1600)	<0.001
UA	Contrast volume, ml	170 (120–220)	150 (120–200)	160 (130–210)	<0.001
	Radiation dose, mGy	937.00 (505.75–1593.00)	806.00 (442.00–1391.00)	871.50 (498.00–1484.50)	<0.001
Complications compared according to initial diagnosis and location of narrowing					
Diagnosis		**Proximal — A** **Medial — B**	**Distal — C**	**General**	***P*-value**
STEMI	Bleeding at puncture site	26 (0.24) 17 (0.15)	6 (0.25)	49 (0.19)	0.27
	Cardiac arrest during procedure	317 (2.87) 132 (1.18)	25 (1.03)	476 (1.93)	<0.001
	Death during procedure	281 (2.54) 110 (0.98)	14 (0.58)	405 (1.65)	<0.001
NSTEMI	Bleeding at puncture site	25 (0.16) 27 (0.18)	3 (0.10)	55 (0.16)	0.61
	Cardiac arrest during procedure	187 (1.20) 75 (0.51)	18 (0.60)	280 (0.83)	<0.001
	Death during procedure	161 (1.03) 44 (0.30)	5 (0.17)	210 (0.62)	<0.001
UA	Bleeding at puncture site	18 (0.11) 22 (0.11)	11 (0.30)	51 (0.13)	0.01
	Cardiac arrest during procedure	66 (0.39) 27 (0.14)	7 (0.19)	100 (0.25)	<0.001
	Death during procedure	36 (0.21) 17 (0.09)	2 (0.05)	55 (0.14)	<0.001

Data presented as median (interquartile range [IQR]) or n (%)

Abbreviations: see Table 2

(worse survival in higher class) and others. The presence of multi-vessel disease also increased the risk of death. All risk factors found are presented in Figure 1.

When it comes to periprocedural cardiac death, similar risk factors have been determined. The risk factors include, among others: unsuccessful PCI (TIMI 0 vs. TIMI 3 after PCI), Killip class (worse survival in higher score), and initial diagnosis (STEMI worse than NSTEMI, followed by UA). Surprisingly, intervention on vessel bifurcation were found to be a protective factor. All risk factors determined in this study were presented in Figure 2.

In terms of overall complications, the risk factors include, among others: unsuccessful PCI, Killip class (greater odds of complications in higher score), initial diagnosis, and application of non-standard vascular access (mostly brachial) instead of radial access. The access site was not

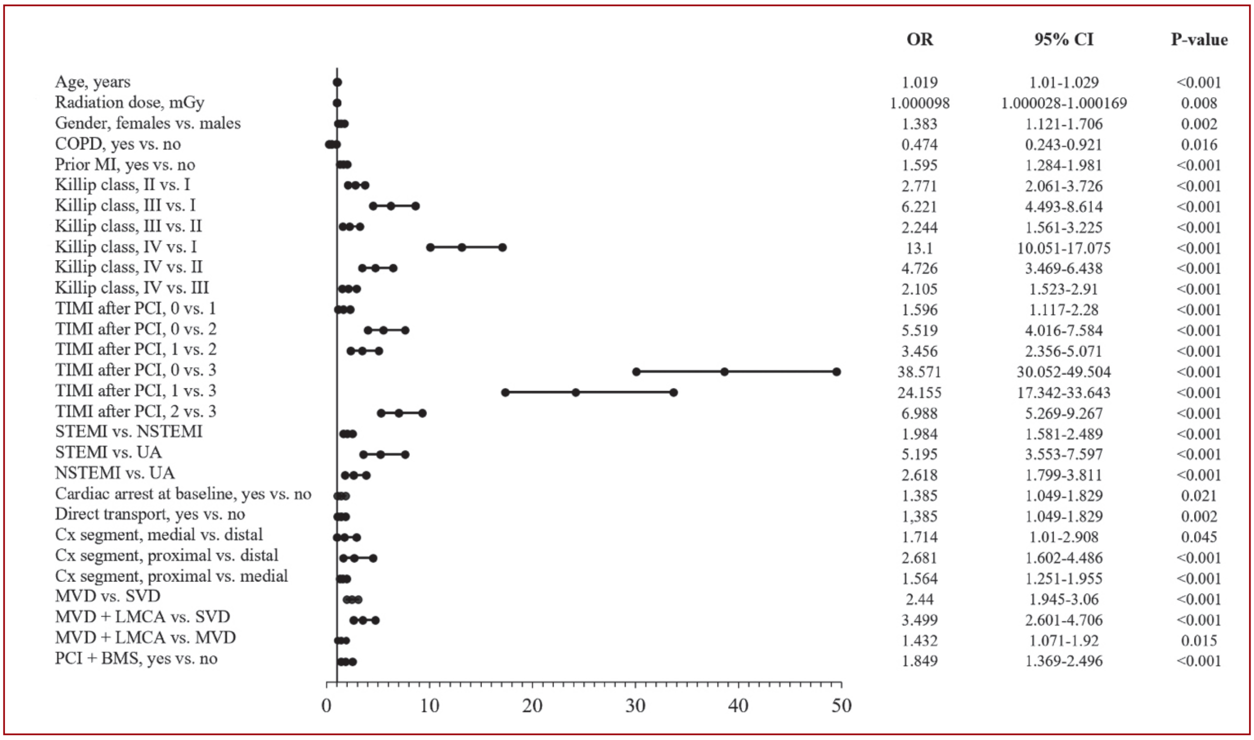

Figure 1. Risk factors for periprocedural death

Abbreviations: BMS, bare metal stent; CI, confidence interval; MVD, multivessel disease; OR, odds ratio; SVD, single-vessel disease; other — see Tables 1–3

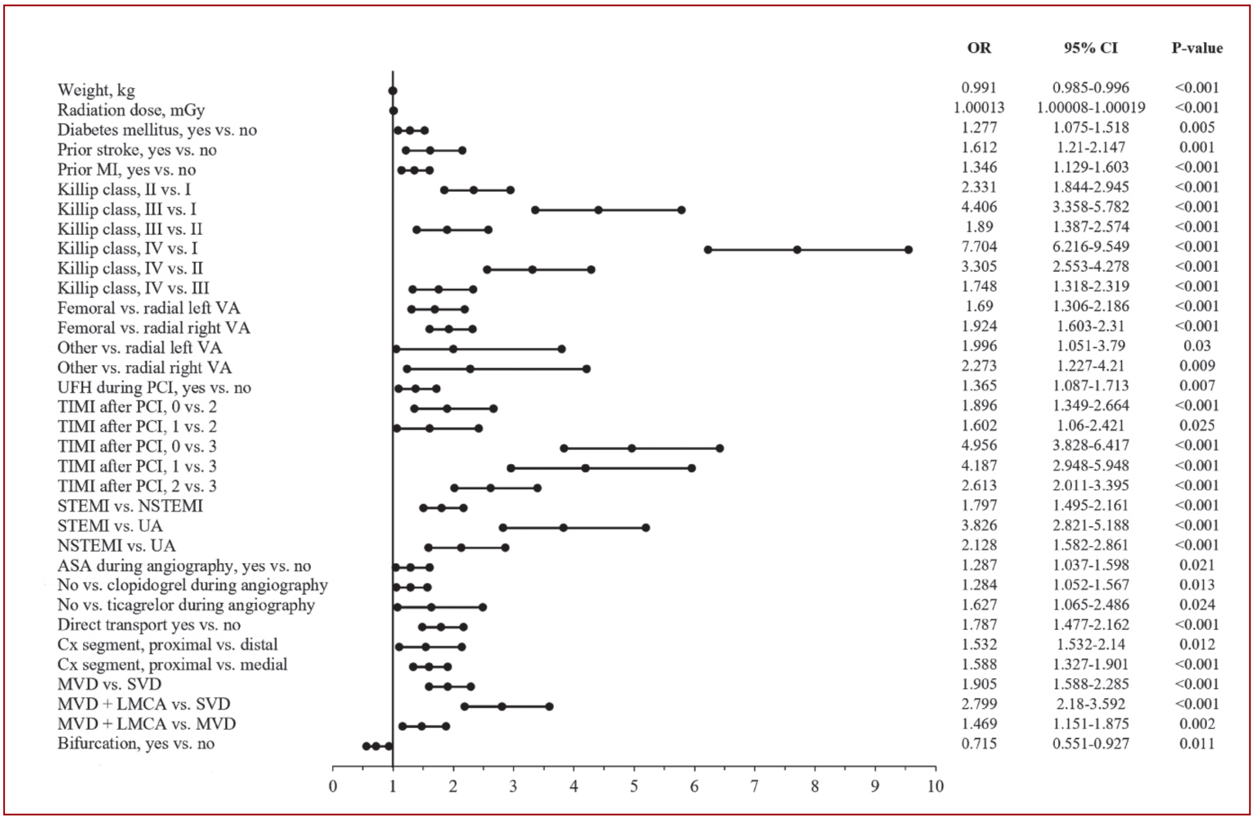

Figure 2. Risk factors for periprocedural cardiac death

Abbreviations: ASA, acetylsalicylic acid; UFH, unfractionated heparin; VA, vascular access; other — see Figure 1 and Tables 1–3

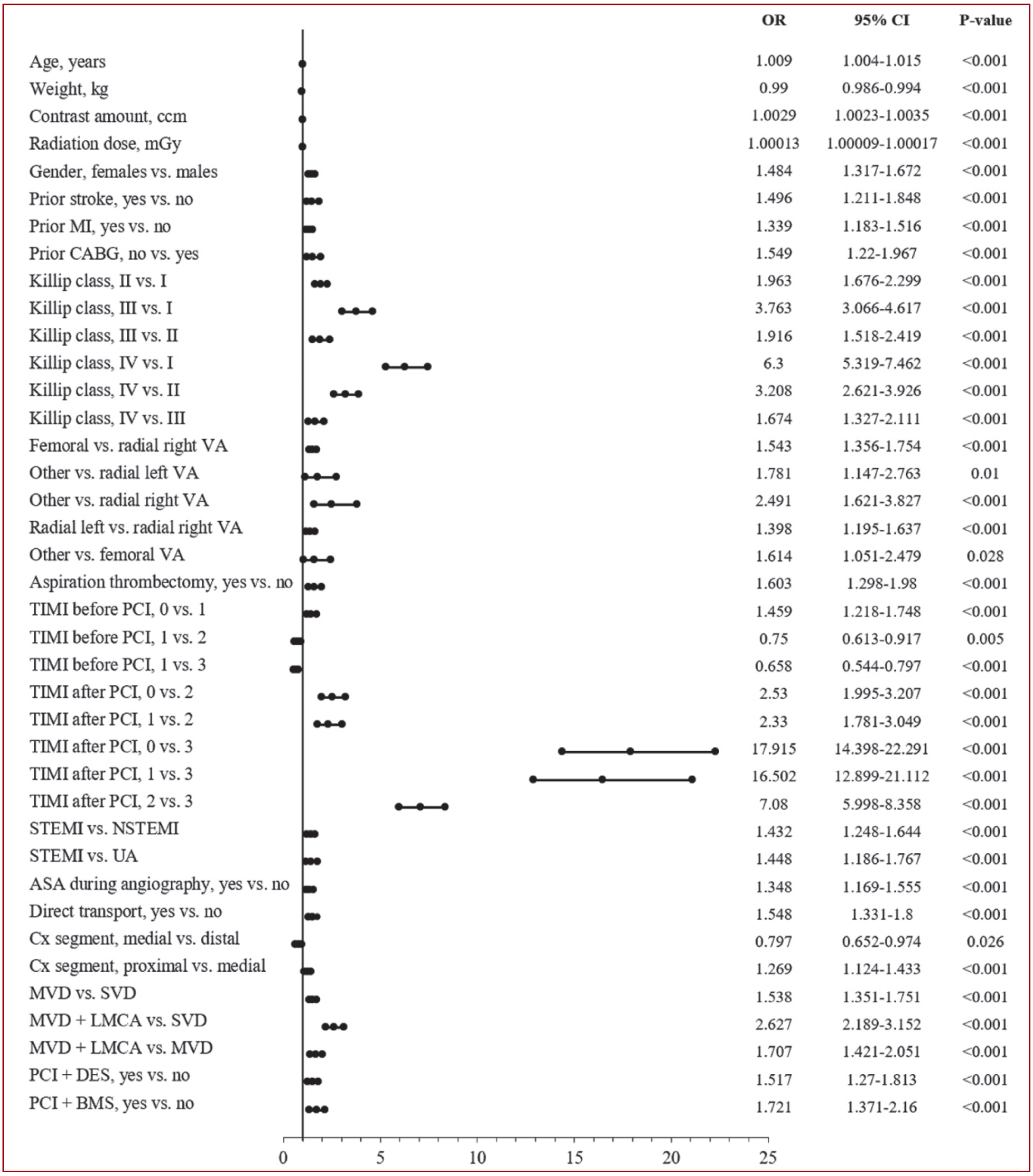

Figure 3. Risk factors for the overall periprocedural complications occurrence

Abbreviations: DES, drug-eluting stent; other — see Figures 1–2 and Tables 1–3

a risk factor for previously mentioned outcomes (fatal complications). All risk factors determined in this study were presented in Figure 3.

DISCUSSION

The study has shown that the culprit location in the Cx artery greatly impacts the clinical manifestation in patients with ACS. Patients with the proximal location of the culprit lesion are generally in a worse condition — considering the Killip class upon admission — and suffer from higher periprocedural mortality. Further multifactorial investigation confirmed these findings, determining the culprit location and Killip classification upon admission as independent risk factors for periprocedural death. Other risk factors worth mentioning are the unsuccessful PCI and initial diagnosis (STEMI/NSTEMI/UA).

In comparison to other coronary arteries, the culprit location in the Cx artery remains the most difficult and

Table 5. Time from first healthcare contact to inflation or angiogram in minutes, excluding cases over 24 hours

Compared according to the location of narrowing					
	Proximal — A	**Medial — B**	**Distal — C**	**General**	***P*-value**
All patients	140.00 (70.00–345.00)	150.00 (75.00–355.00)	140.00 (70.00–346.75)	145.00 (72.00–350.00)	<0.001
Post hoc test	A vs. C: $P = 0.72$	B vs. A: $P < 0.01$	C vs. B: $P = 0.59$		
Initial TIMI 0	113.00 (60.00–240.00)	117.00 (63.00–240.00)	110.00 (60.00–229.50)	115.00 (60.00–240.00)	0.04
Post hoc test	A vs. C: $P = 0.60$	B vs. A: $P = 0.16$	C vs. B: $P = 0.10$		
Compared according to initial diagnosis and location of narrowing					
	Proximal — A	**Medial — B**	**Distal — C**	***P*-value**	
STEMI	85.00 (59.00–140.00)	90.00 (60.00–145.00)	89.00 (58.00–144.00)	0.002	
NSTEMI	240.00 (115.00–512.50)	260.00 (120.00–540.00)	270.00 (120.00–565.00)	<0.001	
UA	253.50 (148.50–825.00)	330.00 (72.00–426.00)	629.00 (37.00–1222.50)	0.79	

Data presented as median (interquartile range [IQR])

Abbreviations: see Table 2

challenging to properly diagnose in patients with acute myocardial infarction (AMI) [19]. This may be associated with the location on the lateral and posterior wall of the left ventricle and limited effectiveness of ECG to detect ischemia/infarction in this area [20, 21]. Time delays or failure in the case of the Cx artery occlusion diagnosis have serious clinical consequences because it supplies a significant area of the left ventricle myocardium [22]. This is extremely important when the left coronary artery is the dominant one [23]. Delayed treatment of the culprit artery located within Cx results in the worst clinical outcomes [3, 24].

The most serious periprocedural complications during primary PCI are cardiac arrest and death. Despite frequent lack of ischemic changes on ECG and less pronounced clinical symptoms, cardiac arrest and death are also observed in patients with AMI of the Cx artery, as in the case of AMI of the right coronary artery, left anterior descending artery, or bypass grafts. Our study revealed that when the culprit plaque is located in the proximal segment of the Cx artery, fatal complications occur more frequently — both on admission and during the procedure. The location of the culprit plaque within the proximal segment also results in a higher rate of left ventricular dysfunction, which could predispose these patients to further fatal complications. All these findings could be explained by the significantly larger mass of the left ventricle muscle affected by an infarct in the case of proximal segment occlusion compared to medial and distal ones.

Surprisingly, ST-segment elevation was present more frequently in patients with a distal plaque location. It is hard to explain this phenomenon, however, we suspect that this difference might be due to artery thrombosis or embolization, which occurs more likely in smaller vessel diameters, thus in the distal location [25]. This reduces the myocardial perfusion completely, contrary to proximal occlusions where total thrombosis is less likely, and additionally, the affected myocardium can be partially supplied by collateral circulation. However, the difference in the occurrence of STEMI between the groups was small, and we believe that significant result of the statistical test could be caused by the disproportion in the occurence of NSTEMI and UA in different culprit plaque locations, which was much greater than the disproportion in the occurence of STEMI. Moreover, as previously mentioned, the Cx artery supplies an area where ischemia is exceptionally difficult to detect on an ECG [20], which additionally impacts the results. Another consequence of these anatomical conditions was observed in this study, where total occlusion (TIMI 0) did not cause ST-segment elevation in a substantial percentage of patients, further proving that ST-segment elevation depends on many factors and its absence can be misleading in regard to the Cx area.

Considering the initial diagnosis (STEMI vs. NSTEMI vs. UA), the fatal complications were more frequently observed in patients with STEMI, which may be explained by higher intensification of ongoing ischemia in these subgroups. Regarding both serious complications: cardiac arrest and death — they were more frequently observed in patients with an initially occluded artery on index angiogram — TIMI 0 flow. This is probably justified by the earlier appearance of large-area total necrosis followed by serious rhythm disturbances in this case, compared to arteries with critical stenosis but still preserved flow in the coronary artery.

The median contrast volume in the whole group was high probably due to difficulties with the visualization caused by the spatial conditioning of the Cx artery. The larger contrast volume in the proximal segments could be explained by the larger diameter of the vessel and greater area of the distal vascular bed, as well as a more difficult procedure, often resulting in complications that prolong the procedure. In turn, almost the same median volume of contrast used during procedures within the distal segments is most likely due to the difficulties with the infero-basal area visualization despite smaller vessel diameters.

Regarding initial diagnosis in all comparable segments, the greatest volume of contrast was used in patients with NSTEMI. It was previously shown that total procedural time in NSTEMI is longer than in STEMI [26]. In this subgroup, a further difficulty is observed in identifying the culprit plaque in patients with multi-vessel coronary artery disease. Additional tools such as ICUS or OCT, were, unfortunately, applied too rarely during procedures in this registry.

Regarding radiation dose, a smaller dose was used during interventions on the medial segments of the Cx artery. Again, this is probably due to spatial conditioning as proximal and distal segments are more difficult to visualize in the Cx artery.

Regarding time delays, we observed greater delays in the whole group in comparison to the TIMI 0 subgroup when time delays were shorter. This could be explained by more significant clinical symptoms associated with the occluded infarct-related artery in the TIMI 0 group. This condition could influence medical staff to make quicker decisions when directing the patient to urgent angiography. Estimating time delays in different diagnoses, we observed smaller delays in STEMI patients in all analyzed segments similarly due to more pronounced ischemia and clinical symptoms in this situation.

In comparison to other coronary vessels (RCA and LAD), the percentage of patients who underwent PCI more than 24 hours from pain onset is higher in the case of the Cx artery: 30% vs. 20% vs. 17%, respectively, which was explained by the lower sensitivity of ST-segment elevation in the detection of acute Cx occlusion [3, 20]. This hypothesis is also consistent with an underrepresentation of the Cx artery as the culprit artery among patients with STEMI [8, 27].

Risk factors determined in this study indicate that vascular access do not have an impact on serious complications, and thus on clinical outcomes in patients with ACS. However, they do influence overall complications, probably due to the most common, mild complication — puncture-site hematoma, which occurs more often in brachial access [28].

Regarding therapeutic hypothermia, it was most commonly applied in patients with proximal lesions and TIMI 0. This can be again explained by greater ischemia, which was associated with a worse Killip score, and, therefore, a worse clinical condition of the patient. This may be an indication for therapeutic hypothermia due to its cardioprotective effect during transport to a cath lab [29, 30]. However, these cases were rare in our study, which can be explained by the fact that the network of cath labs in Poland is dense and highly developed, and the time of patient transport to a cath lab is relatively short [31].

The results show that patients with NSTEMI and proximal occlusion are at a greater risk than patients with STEMI and distal occlusion. However, according to the results of our study, which are concordant with the current guidelines, NSTEMI patients are treated less urgently than patients with STEMI [1, 2], as the initial ECG diagnosis greatly impacts time delay. Unfortunately, the location of the culprit plaque cannot be considered in initial diagnosis, as it is known only after performing a coronary angiogram. Therefore, apart from the initial ECG diagnosis, it is crucial to make decisions according to the whole clinical presentation, with special emphasis on the Killip score, as there is a group of patients with NSTEMI who require as urgent intervention as patients with STEMI.

Limitations

Considering major limitations, the leading one is the retrospective nature of the present study. Another one is due to the variability in the area that is supplied with blood by the Cx artery, which affects patients' characteristics and clinical outcomes. However, this random bias should be excluded thanks to the large number of patients that we assessed.

CONCLUSIONS

Among patients with culprit lesions located in the proximal segment of the Cx artery and TIMI 0 grade flow on the initial angiogram, a STEMI-like approach should be undertaken apart from initial ECG findings. This is caused by a higher rate of critical and fatal complications such as cardiac arrest and periprocedural death. Fatal complications occur more often in patients with proximal occlusion of Cx than in medial or distal occlusion. The location of the occlusion should be considered, alongside an ECG diagnosis, as a risk factor for periprocedural cardiac arrest and death. The Killip classification can be used to predict the suspected culprit location, as patients with proximal occlusion more often receive grade IV.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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