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Original Article

Impact of clinical features on in-hospital outcomes in premature coronary artery disease patients post percutaneous coronary intervention

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ABSTRACT

Background: Premature coronary artery disease (PCAD) is a significant health concern globally, characterized by the onset of coronary atherosclerosis at an early age. The development of PCAD is influenced by a variety of risk factors and leading to substantial morbidity and mortality. Despite advancements in interventions, the clinical and angiographic characteristics influencing in-hospital outcomes for these patients remain underexplored.
Objective: This study aims to investigate the relationship between clinical features and in-hospital outcomes in patients with premature CAD post-percutaneous coronary intervention (PCI) at Dr. Saiful Anwar Hospital.
Method: A retrospective cohort study was conducted on 1279 patients who underwent PCI for premature CAD the period of January 2022–December 2023. Clinical information was gathered from medical records, including risk factors and angiographic results. Statistical analyses were conducted using SPSS 22, employing univariate, bivariate, and multivariate logistic regression analyses to determine correlations.
Result: The study included 1279 patients, with 438 in the premature CAD group and 841 in the non-premature CAD group. Significant differences were observed in age, sex distribution, BMI, lipid profiles, smoking status, and family history between the groups. Premature CAD patients were younger (mean age 50 vs. 64.8, p<0.001) and had higher rates of smoking and dyslipidemia. Angiographic analysis showed significant differences in LAD and LCx involvement and occlusion rates. In-hospital outcomes indicated higher incidences of shock, cardiac complications, and in-hospital mortality in the non-premature CAD group.
Conclusion: Clinical and angiographic characteristics significantly influence in-hospital outcomes for premature CAD patients. Younger age, smoking, and dyslipidemia were prevalent risk factors. Enhanced management strategies focusing on these factors could improve patient outcomes.

1. Introduction

Global Burden of Disease data showed Coronary Artery Disease (CAD) impacts around 154 million individuals with 350.000 deaths over worldwide.[1,2] In 2019, CAD was responsible for one in five deaths among adults under 65 years of age with various studies of age.[3,4,5]

Premature CAD (PCAD) places a considerable burden on healthcare systems, with over 80% of patients with PCAD usually have one or more modifiable risk factors.[6] The prevalence of several risk factors, has risen significantly between 2000 and 2016.[7,8]

Understanding clinical and angiographic characteristics that influence in-hospital outcomes in PCAD patients is crucial. Previous research has focused on CAD populations, with limited attention given to younger individuals and lack of management which are essential for managing PCAD.[9]

Despite the significance, there is limited research on the clinical features impacting in-hospital outcomes for PCAD patients post-percutaneous coronary intervention (PCI). This study aims to address this gap by evaluating how these characteristics affect clinical outcomes at Dr. Saiful Anwar General Hospital

2. Material And Method

Patients and Procedure

This study included patients with PCAD who underwent percutaneous coronary intervention at Dr. Saiful Anwar General Hospital (RSSA). The target population consisted of individuals diagnosed with PCAD. The impact of clinical and angiographic characteristics on in-hospital outcomes for patients with PCAD was assessed using a retrospective cohort study design. Data were extracted from the medical records between January 2022 and December 2023. Participants were selected through consecutive sampling, the inclusion criteria are adults aged 18 years or older with a diagnosis of PCAD, defined as men under 55 years and women under 60 years, as confirmed by coronary angiography. Additionally, participants had to provide consent to be included in the study. Exclusion criteria encompassed patients with comorbid conditions such as tumors, multiple organ failure, autoimmune disorders, stroke, chronic kidney disease, and chronic or acute lung disease. Individuals with heart valve disorders, myocarditis, cardiomyopathy, or pulmonary embolism, patients with systemic infections, recent trauma or surgery, or complications from interventions were also excluded. Patients who refused, could not be followed up, or had incomplete data were also excluded. Data collected included clinical characteristics, angiographic findings, and in-hospital outcomes to comprehensively assess the impact of these variables on patient outcomes.

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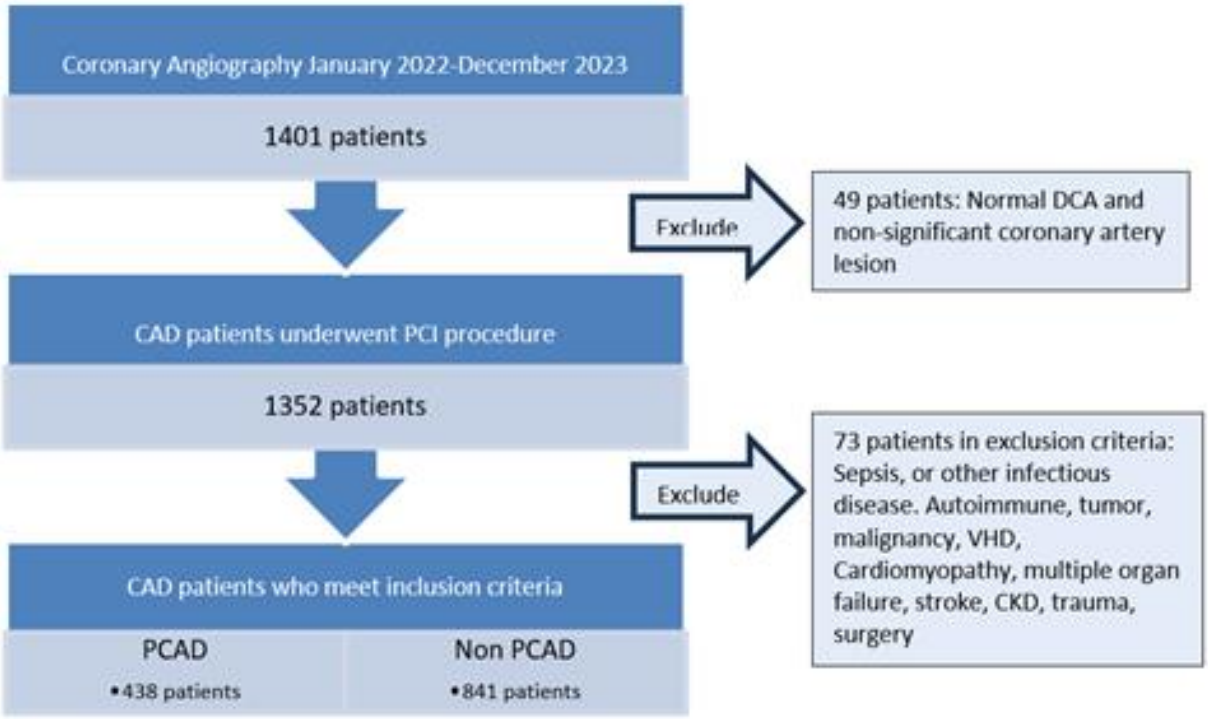

Figure 1. Research Flowchart

Follow-Up and Assessment

Follow-up data were collected through hospital records to assess in-hospital outcomes, including complications and mortality. Clinical outcomes were monitored from the time of PCI until discharge. Data on clinical outcomes were gathered and analyzed to evaluate the association between clinical and angiographic characteristics and in-hospital outcomes.

Statistical analysis

The data were analyzed using SPSS version 22, following a structured approach. Initially, univariate analysis was performed to describe the patient characteristics through descriptive statistics, including mean, standard deviation, and proportions. This provided a basic overview of the sample's demographic and clinical profiles. To compare means between groups, independent t-tests were applied for data that followed a normal distribution. For data not normally distributed, the Mann-Whitney U test was used. To assess differences in categorical variables, Chi-square tests were employed. Statistical significance was determined with a threshold set at $p<0.05$. For a more comprehensive analysis, multivariate analysis was conducted using logistic regression. This method was used to explore the correlation between clinical and angiographic characteristics and the in-hospital outcomes. A confidence level of 95% ($\alpha = 0.05$) was maintained to ensure the reliability of the results.

3. Result

A retrospective cohort observational study was conducted to investigate the association between clinical features and in-hospital clinical outcomes in patients with PCAD who underwent PCI. The study period from January 2022 - December 2023, involving a total of 1279 patients. Data were presented descriptively as mean ± standard deviation (SD). The Kolmogorov-Smirnov test indicated that the data were not normally distributed. As a result, the Mann-Whitney U test was employed to compare means, whereas group comparisons were done using the Chi-square test. One considered a p-value of less than 0.05 to be significant. Additionally, multivariate analysis with logistic regression was conducted to investigate the relationship between angiographic and clinical features and hospitalized clinical outcomes.

Table 1 describes the clinical features categorized into two groups: those with PCAD (n=438) and mature PCAD (Non-PCAD, n=841). Several clinical parameters compared include age, gender, blood pressure, body mass index (BMI), laboratory results, risk factors, and clinical indications for PCI. The PCAD group's average age was 50 years, while the non-PCAD group's average age was 64.8 years. There was a notable distinction as well (p=0.003) in the groups' gender distribution. In PCAD, 73.1% were male showed predominant in both groups. BMI distribution between the two groups showed a significant difference (p=0.003). In the PCAD group 31.1% were overweight, and 9.1% were obese. This indicates that the PCAD group had a higher BMI level.

In the PCAD group, found significantly the average total cholesterol level was 165.77 mg/dL (p=0.000), triglyceride was 155.55mg/dL (p=0.000), LDL was 110.29 mg/dL (p=0.001) and the HDL was 36.85 mg/dL (p=0.001). The average HbA1c in the PCAD group was 7.110. The average left ventricular ejection fraction (LVEF) in the PCAD group was 47.79%. Smoking was prevalent in 68% of PCAD patients significantly (p=0.042). Dyslipidemia was present in 10.3% of PCAD patients (p=0.011). Additionally, 22.8% of PCAD patients had a family history (p= 0.002). Most patients in both groups underwent PCI for stable CAD, with 65.8% in the PCAD. Other indications ACS and others, showing no significant difference (p=0.200).

Table 2 describes angiographic characteristics in two groups. Most patients in both groups had three-vessel disease. Non-PCAD group showed a greater proportion (10.5%) and higher proportion of patients in the >70% stenosis category (47.1%). However, in terms of target vessels, there were significant differences, with the PCAD group having a higher proportion in LAD (92%) and LCx (82.2%) (p=0.000). For total occlusions, there was a significant difference, with the PCAD group having a higher proportion (17.9%) (p=0.023) and evident in acute total occlusions (p=0.028).

Table 1. Clinical Characteristics

Clinical Characteristics	PCAD (n=438)		Non PCAD (n=841)		*p-value*
	N (%)	Mean±SD	N (%)	Mean±SD	
Age (years)	-	50 ± 5,609	-	64,8 ± 6,496	0,000[a]
Gender					
Male	320 (73,1)	-	676 (80,4)	-	0,003[b]
Female	118 (26,9)		165 (19,6)		
Blood Pressure					
Systolic	-	128,54 ± 19,986	-	130,05 ± 21,843	0,383[b]
Diastolic		77,86 ± 10,977		76,91 ± 13,328	0,061[b]
BMI					
Underweight	4 (0,9)		15 (1,8)		
Normal	258 (58,9)	-	567 (67,4)	-	**0,003**[b]
Overweight	136 (31,1)		213 (25,3)		
Obese	40 (9,1)		46 (5,5)		
Laboratory					
Total Cholesterol (mg/dL)		165,77 ± 45,268		157,01 ± 42,308	0,000
Triglycerides (mg/dL)		155,55 ± 79,267		133,96 ± 73,74	0,000
LDL (mg/dL)	-	110,29 ± 39,706	-	103,19 ± 38,543	0,001
HDL (mg/dL)		36,85 ± 8,684		39,32 ± 10,675	0,000
HBA1C (%)		7,110 ± 3,740		6,982 ± 1,905	0,634
LVEF (%)	-	47,79 ± 13,454	-	48,94 ± 14,199	0,155
Risk Factors					
Smoking	298 (68)		524 (62,3)		0,042[b]
Hypertension	176 (40,2)		359 (42,7)		0,389[b]
Dyslipidemia	45 (10,3)	-	53 (6,3)	-	0,011[b]
Diabetes Mellitus	138 (31,5)		302 (35,9)		0,116[b]
Family History	100 (22,8)		132 (56,9)		**0,002**[b]
Clinical Indication PCI					
Stable CAD	288 (65,8)		540 (64,2)		
UA/NSTEMI	33 (7,5)	-	94 (11,2)	-	0,200[b]
STEMI	115 (26,3)		202 (24)		
Others	2 (0,5)		5 (0,6)		

[a]Mann-Whitney test, [b]Chi-square test

Table 2. Angiographic Characteristics

Variable	**Total**	**PCAD (n=438) N (%)**	**Non-PCAD (n=841) N (%)**	***p-value***[b]
Number of vessels				
1	106	38 (8,7)	68 (8,1)	0,372
2	154	62 (14,2)	92 (10,9)	
3	954	316 (72,1)	638 (75,9)	
4	65	22 (5)	43 (5,1)	
Single vessel disease	125	39 (8,9)	86 (10,2)	0,450
Multi vessel disease	1154	399 (91,1)	755 (89,8)	
Calcification lesion	455	101 (5,8)	354 (10,5)	0,000
Stenosis Diameter				
Undetected	2049	715 (40,8)	1334 (39,7)	0,058
< 50%	444	174 (9,9)	270 (8)	
50 – 70%	255	81 (4,6)	174 (5,2)	
> 70%	2368	782 (44,6)	1586 (47,1)	
Diffuse Lesion	476	156 (8,9)	320 (9,5)	0,477
Target vessel				
LM	118	69 (15,8)	119 (14,1)	0,442
LAD	1022	403 (92)	619 (73,6)	0,000
LCx	830	360 (82,2)	470 (55,9)	0,000
RCA	798	286 (65,3)	512 (60,9)	0,122
Total occlusion lesion	831	313 (17,9)	518 (15,4)	0,023
Acute total occlusion	224	92 (5,3)	132 (3,9)	0,028
Chronic total occlusion	644	237 (13,5)	407 (12,1)	0,144

[b]*Chi-square test*

Table 3. Clinical Outcomes

Clinical Outcomes	Total	PCAD (n=438) N (%)	Non-PCAD (n=841) N (%)	*p-value*[b]
Complications				
Mechanical Complications	2	1 (0,2)	1 (0,1)	0,638
Shock Cardiogenic	94	21 (4,8)	73 (8,7)	0,012
Heart Failure	159	40 (9,1)	119 (14,1)	0,010
Pneumonia	27	13 (3)	14 (1,7)	0,124
Bleeding	1	0 (0)	1 (0,1)	0,470
Acute Thrombosis	1	1 (0,2)	0 (0)	0,166
ALI	2	2 (0,5)	0 (0)	0,050
Ischemic Stroke	0	0 (0)	0 (0)	-
Hemorrhagic Stroke	0	0 (0)	0 (0)	-
Kidney Failure	7	2 (0,5)	5 (0,6)	0,751
Respiratory Failure	4	2 (0,5)	2 (0,2)	0,506
Cardiac arrest	47	9 (2,1)	38 (4,5)	0,026
Arrhythmia	12	5 (1,1)	7 (0,8)	0,586
Length of Stay				0,133
≤ 7 days	1157	401 (91,6)	756 (89,9)	
> 7 days	122	37 (8,4)	85 (10,1)	
Mortality in Hospital				0,033
Yes	46	9 (2,1)	37 (4,4)	
No	1233	429 (97,9)	804 (95,6)	

[b]*Chi-square test*

Table 4. Multivariate Logistic Regression Analysis

Characteristic	Multivariate Analysis	
	P Value	OR (95% CI)
Age	**0,000**	2,775 [2,335 – 3,299]
Gender	**0,000**	0,008 [0,002 – 0,026]
BMI	**0,040**	0,994 [0,627 – 1,574]
Total Cholesterol	0,721	0,997 [0,978 – 1,016]
Triglycerides	0,357	1,003 [0,997 – 1,009]
LDL	0,682	1,004 [0,986 – 1,022]
HDL	0,891	1,002 [0,969 – 1,037]
Smoking	**0,020**	0,599 [0,274 – 1,309]
Dyslipidemia	**0,039**	0,401 [0,140 – 1,148]
Family History	**0,029**	1,056 [0,259 – 4,296]
Calcification Lesion	0,786	3,546 [0,000 – 33432,093]
LAD	**0,006**	0,499 [0,188 – 1,327]
LCx	**0,000**	0,249 [0,116 – 0,532]
Total Occlusion Lesion	1,000	410,755 [0,000 – -]
Acute Total Occlusion	1,000	0,001 [0,000 – -]
Shock Cardiogenic	0,512	0,563 [0,101 – 3,138]
Heart Failure	0,276	2,044 [0,565 – 7,397]
Cardiac Arrest	1,000	58347,84 [0,000 – -]
In-Hospital Mortality	1,000	0,000 [0,000 – -]

Table 3 presents clinical outcomes in both groups after PCI. The data reveal several significant differences in clinical outcomes between the two groups. In terms shock cardiogenic condition, the incidence was greater in non-PCAD patients (p=0.012). Worsening heart failure were also more common in Non-PCAD patients (p=0.010). For cardiac arrest, the Non-PCAD group had a higher proportion compared to the PCAD group (p=0.026). The incidence of arrhythmias was relatively low in both groups without a significant difference (p=0.586). Most patients in both groups were treated for ≤ 7 days, but in-hospital mortality showed a significant difference, with the Non-PCAD group having a higher mortality rate (4.4%) (p=0.033).

Table 4 presents the results of a multivariate logistic regression analysis to determine the factors influencing clinical outcomes in patients with PCAD and Non-PCAD. This analysis uses odds ratios (OR) and 95% confidence intervals (CI) to assess the strength and direction of the relationship between various characteristics and clinical outcomes. Based on Table 4, the results of the multivariate analysis using logistic regression indicate a relationship between clinical characteristics (age, sex, BMI, smoking, dyslipidemia, family history) and angiographic variables (LAD and LCx) with in-hospital clinical outcomes in patients with PCAD following percutaneous coronary intervention, as evidenced by a p-value < 0.05.

4. Discussion

PCAD is defined as an atherosclerotic coronary artery disease which involved men under 55 and women under 60 based on ESC Guidelines 2021 significantly impacting public health.[8,10]

In this study at Dr. Saiful Anwar General Hospital, in-hospital outcomes for PCAD patients undergoing PCI were compared to their

clinical characteristics. The average age of PCAD patients was 50, with men being the majority (73.1%), consistent with the literature indicating that men are at higher risk for PCAD. There was a significant difference in body mass index (BMI), with PCAD patients more often being overweight and obese.

Reports indicate that 4%-10% of acute myocardial infarction (AMI) cases occur before the age of 45.[10] A large survey in Germany reported a PCAD prevalence of 37% in men <55 years and women <65 years.[8] Zeitouni et al. reported that 6.5 percent of the 101,061 between 1995 and 2013—72.5% of whom were men—presented before the age of 35. [11] Vikulova et al. discovered that men continue to have a greater incidence of CAD (46–53 versus 18–23 per 100,000).[7] However, a study by Sharma et al. found that women more frequently experienced PCAD (31.9%) and had higher risks for high cholesterol, high LDL, and smoking [12] Collet et al.'s study involving 880 PCAD patients found an average age of 40.1 ± 5.7 years, with the majority being men, smokers, and having a family history of CAD or hypercholesterolemia. [13] This study found a relatively high proportion of women with PCAD, though not statistically significant compared to non-PCAD, likely due to differences in risk profiles and genetic and hormonal variability. However, other studies showed a higher percentage of PCAD among females, possibly due to a younger age cutoff and higher obesity and risk factor accumulation in women.

A part of the pathophysiology of CAD is the creation and release of tissue plasminogen activator inhibitors, which can be stimulated by elevated serum TG. Furthermore, increased LDL concentrations which are essential for the development of atherosclerotic plaque as a result of raised plasma TG. Patients with PCAD tend to have a worse lipid profile which is a major risk factor in the development of PCAD. [13,14]

Smoking is more common in PCAD patients as a major risk factor for cardiovascular disease, aligns with the literature. Additionally, a family history of CAD are more prevalent in PCAD patients, indicating that hereditary factors have a significant role in the development of this condition.[12,14]

The prevalence of PCAD in individuals under 65 with more than one of modifiable risk factor has increased from 2000 to 2016.[8] Vikulova et al. reported that traditional multiple risk factors of cardiovascular were present in 67% of patients.[7] Toth et al. found that 94.3% had at least one significant cardiovascular risk factors.[15]

Zeitouni et al.'s research showed that ACS was the primary presentation in PCAD, with 14.4% experiencing recurrent myocardial infarction. Both PCAD and non-PCAD groups had a high incidence of multivessel disease, likely due to similar atherosclerotic processes and aggressive risk factors. This suggests that coronary involvement may be more linked to risk profiles than age alone. Although there was no significant difference in stenosis or diffuse lesions, PCAD patients were more prone to LAD and LCx artery involvement and acute total occlusion, indicating a higher risk of acute events. This contrasts with Zeitouni et al.'s finding of mostly single-vessel disease in PCAD (59.6%).[11]

The study by Chen et al. (1995), also indicated that younger patients more often had single-vessel disease compared to older patients, who more frequently had multi-vessel disease. The left anterior descending artery was the most frequently involved vessel. [16]

The CARDIA (Coronary Artery Risk Development in Young Adults) study examines coronary artery calcification in young versus older adults, showing that while calcification is less common in younger patients, those affected face a higher risk of premature cardiovascular events, with lesions more prone to rupture and linked to worse outcomes. [17]

Clinical results show that PCAD are more likely to experience myocardial infarction, worsening heart failure in late presentation, and in-hospital death. Although PCAD patients are younger, they face a greater risk of serious cardiovascular events during hospitalization compared to non-PCAD patients. These findings should be interpreted with caution due to certain study limitations, such as a limited sample size and lack of long-term follow-up data.

In a study by Collet et al., over a 20-year follow-up period, one-third of patients experienced 399 ischemic events, with 36% having at least one recurrent event. Myocardial infarction was the most common first recurrent event.[13] The study by Zeitouni et al. reported that 9.5% of patients had renal impairment and stroke was 3.5% of patients. [11] The mortality rate for PCAD was significantly higher in women under 45 years compared to men.[7] Research by Al-Khlaiwi et al. reported a mortality rate of around 4% among PCAD patients.[17] Collet et al. also found that overall mortality was 6.3% with a median time to death of 8.4 years.[13]

The study by Shi et al. investigated adverse cardiovascular events in patients with acute coronary syndrome (ACS) of premature and late onset following PCI during hospitalization and a follow-up period of 23.5±5.3 months. There were no significant differences in the incidence of heart failure, non-fatal myocardial infarction, recurrent angina, stroke, bleeding, in-stent restenosis, and thrombosis between the two groups.[14]

In PCAD, there was a significant decline in cardiovascular mortality from 1979 to 1989 but no further improvement over the next 20 years, despite the medications. This study found that one in five patients PCAD died within 10 years, and many experienced recurrent events. [15] Patients with PCAD had worse outcomes compared to those over 50 years of age, including higher rates of ischemic recurrence and mortality in women compared to men. Factors such as suboptimal secondary prevention, lack of awareness, and differences in race and ethnicity contribute to these uneven outcomes.[11]

This study's multivariate analysis reveals that individuals with PCAD are more likely to have poor clinical outcomes when their age, gender, body mass index (BMI), and LDL cholesterol levels are higher. These findings provide important insights into the clinical profile, angiographic characteristics, and clinical outcomes of PCAD patients. Identifying these independent risk factors can aid in developing more effective management strategies for PCAD patients.

A study by Smith et al. found that the majority of PCAD patients are men, with a history of active smoking, family history of CAD, and hypercholesterolemia. Interestingly 18.2% experiencing recurrent ischemic events.[18] Patients with PCAD were more likely to be men, obese, have a family history of PCAD, dyslipidemia or hypercholesterolemia, and were more likely to smoke. [19] This study also confirms that patients with PCAD more frequently have a family history of CAD, higher rates of active smoking, and higher BMI.

A study by Pinxterhuis et al. also showed patients with PCAD were more likely to smoke, have a higher BMI, and more frequently had a family history of CAD.[20] These findings emphasize the importance of preventive interventions and management of risk factors in this population, particularly concerning lipid control and lifestyle management.

This study has several limitations, such as selection biases and small sample size, which may impact the generalizability and statistical power of the findings. Furthermore, the absence of long-term follow-up data limits the assessment of the sustained effects of PCAD management.Variability in clinical data collection and a lack of standardization in the definition of PCAD may also impact the consistency of the results and the ability to compare findings with other studies.

5. Conclusion

This study identified several significant clinical and angiographic characteristics and their association with clinical outcomes in patients with PCAD undergoing PCI at RSSA. The findings suggest that younger age, male gender, higher BMI, and higher LDL levels are important factors to consider in managing patients with PCAD to improve clinical outcomes. Future studies are recommended to further explore these associations and develop targeted interventions to enhance patient care.

6. Declaration

6.1 Ethics Approval and Consent to participate
The subjects in this study are humans, so ethical rules must be followed. This research has passed the ethical due diligence, approved based on the Certificate of Ethical Eligibility No. No. 400/159/K.3/102.7/2024 issued by the Health Research Ethics Committee at Dr. Saiful Anwar Malang.

6.2. Consent for publication
Not applicable.

6.3 Availibility of data and materials
Data used in our study were presented in the main text.

6.4 Competing interests
Not applicable.

6.5 Funding Source
Not applicable.

6.6 Authors contributions
Idea/concept: NN. Design: NN. Control/supervision: MSR, AFR. Data collection/processing: NN. Analysis/interpretation: NN, MSR, AFR. Literature review: NN, MSR, AFR. Writing the article: NN. Critical review: MSR, AFR. All authors have critically reviewed and approved the final draft and are possible for the content and similarity index of the manuscript.

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