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Clinical Profile and Outcome in Patients with Acute Coronary Syndrome (ACS) with Left Main Disease Presenting at Tertiary Care Hospital Karachi, Pakistan

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Abstract

Background: Left main coronary artery disease (LMCAD) in acute coronary syndrome (ACS) poses significant concerns due to its vital role in myocardial perfusion. A blockage in this artery can precipitate a severe and potentially fatal heart attack. This study aimed to evaluate the clinical profile and outcomes of ACS patients with LMCAD presenting at a tertiary care hospital in Karachi, Pakistan.

Methodology: This cross-sectional study enrolled consecutive ACS patients with LMCAD, defined as 50% or more stenosis in the left main coronary based on coronary angiography. We assessed the clinical characteristics and in-hospital outcomes of these patients.

Results: Among 236 ACS patients with LMCAD, predominantly male (69.1%) with a mean age of 58.8 ± 9.3 years, most presented with three-vessel disease. Common comorbidities included hypertension (65.3%) and diabetes mellitus (47.9%). Complications, such as contrast-induced nephropathy (13.1%) and major bleeding (2.5%), affected 19.5% of patients, with an in-hospital mortality rate of 4.2%.

Conclusion: The in-hospital mortality rate of 4.2% underscores the grave implications of LMCAD in ACS. The predominance of three-vessel disease highlights its severity and complexity. Complications like contrast-induced nephropathy and major bleeding further accentuate the challenges in managing these cases.

Keywords

Acute Coronary Syndrome, Left Main, Coronary Artery Disease, Outcomes

Introduction

Acute Coronary Syndrome (ACS) encompasses a spectrum of conditions arising from inadequate blood flow to the heart muscle, potentially culminating in a heart attack or unstable angina, necessitating urgent medical intervention. Often, ACS is triggered by blockages in one or more coronary arteries, impeding the heart's oxygen supply[1]. Classic symptoms include chest pain, shortness of breath, nausea, and perspiration, underscoring the need for swift detection and treatment to avert further cardiac damage[2].

Among the variants of ACS, Left Main Coronary Artery Disease (LMCAD) poses particular peril due to its pivotal role in supplying a significant portion of the heart. A blockage in this artery can precipitate a severe, even fatal, heart attack. Prognostic risk is heightened given the extensive myocardial territory it serves, ranging from 75% to 100% depending on left coronary circulation dominance[3]. This criticality has historically earned the left main artery the ominous moniker of 'the artery of sudden death'[4]. Swift identification and treatment of LMCAD in ACS are paramount to avert grave complications and preserve life.

During the early era of coronary angiography, clinicians noted a concerning 10% mortality risk associated with LMCA catheterization, emphasizing caution in suspected cases[5]. Studies at the time underscored a staggering over 50% five-year mortality rate among patients receiving solely pharmacological treatment[6]. Timely intervention, often involving procedures like angioplasty or bypass surgery, is pivotal in restoring blood flow, mitigating further myocardial harm, and enhancing recovery prospects[7]. Every moment counts in LMCAD cases, accentuating the imperative for swift action to improve patient outcomes[8].

Current clinical guidelines from esteemed bodies advocate revascularization for all patients with ≥50% stenosis of the left main coronary artery (LM), regardless of symptomatic presentation or associated ischemic burden[9]. Yet, the intricacies of managing LMCAD demand nuanced decision-making, despite the guidance provided by recent clinical practice guidelines[10]. Collaborative efforts have yielded practical approaches to LM CAD treatment, integrating insights from randomized clinical trials, meta-analyses, and guidelines[11].

Traditionally, coronary artery bypass grafting (CABG) has been the gold standard for revascularization in LMCAD cases. However, advancements in stent technology, procedural techniques, and adjunctive medical therapy have substantially enhanced percutaneous coronary intervention (PCI) outcomes over recent decades[12]. Notably, the advent of drug-eluting stents (DES) has rendered PCI increasingly viable, boasting favorable long-term clinical results[13-16]. Comparative trials have even indicated similar survival rates post-PCI and CABG, narrowing the treatment efficacy gap[17]. Reflecting these findings, current guidelines advocate PCI as a suitable alternative to CABG in low-to-intermediate anatomical complexity cases[18,19].

Despite global research, data regarding the clinical profiles and outcomes of ACS with LMCA in Pakistan remain scant. While a few studies have been conducted in the subcontinent, the anticipated variability within our population, stemming from socioeconomic and cultural diversity, underscores the need for localized research. Hence, this study endeavors to evaluate the clinical profiles and outcomes of ACS patients with left main disease at a tertiary care hospital in Karachi, Pakistan.

Methodology

This cross-sectional study aimed to evaluate the clinical profile and outcomes of left main disease

in patients presenting with acute coronary syndrome (ACS). Conducted from January to June 2023 at the National Institute of Cardiovascular Diseases, Karachi, Pakistan, the study included patients aged 40 to 80 years of both genders presenting to the emergency department with diagnosed ACS and left main disease identified via coronary catheterization.

Patients were excluded if they declined consent, had a history of cardiac surgeries (CABG or PCI), heart failure, required angioplasty of multiple major coronary arteries, needed bypass surgery within 30 days due to extensive CAD, or had concomitant valvular heart disease or cardiomyopathy.

The primary variable of interest was left main coronary artery disease (LMCAD), defined as ≥50% stenosis on coronary angiography, while the dependent variable was in-hospital mortality. Additional variables included demographics (age, gender, weight, height, BMI), comorbidities (diabetes, hypertension, dyslipidemia, smoking), and clinical and angiographic parameters.

Data collection involved informed written consent from patients or guardians, with demographic and clinical details recorded at hospital admission. Comorbidities were defined using standardized criteria, and patients were managed per clinical guidelines. To mitigate bias, non-probability consecutive sampling and stringent exclusion criteria were used.

Ethical approval was obtained from the Institutional Ethical Committee. The sample size of 236 participants was determined using the WHO calculator, targeting an in-hospital mortality rate of 7.9%, with a 95% confidence level and a 3.5% margin of error. Quantitative variables such as age, BMI, and hospital stay were summarized as mean ± standard deviation or median with interquartile range. Statistical analyses were performed using SPSS version 21.0, with normality assessed via the Shapiro-Wilk test and categorical variables compared using Chi-square tests, considering $p \leq 0.05$ as significant.

Results

A cohort of 236 patients diagnosed with ACS and LMCAD participated in the study, comprising predominantly males (69.1%) with a mean age of 58.8 ± 9.3 years. Upon presentation, 3 (1.3%) patients were classified as Killip class IV, and 11 (4.7%) as Killip class III. Among the diagnoses, 94 (39.8%) were STEMI, while 95 (40.3%) were NSTEMI. Hypertension emerged as the most prevalent comorbidity, affecting 154 (65.3%) patients, followed by diabetes mellitus in 113 (47.9%) individuals.

The majority exhibited extensive coronary involvement, with 176 (74.6%) presenting with three-vessel disease, followed by 40 (16.9%) with two-vessel disease, and 20 (8.5%) with single-vessel disease. Complications arose in 46 (19.5%) patients, including contrast-induced nephropathy in 31 (13.1%) and major bleeding in 6 (2.5%) cases. The in-hospital mortality rate stood at 4.2%, resulting in 10 fatalities. For detailed findings, refer to Table 1.

Table 1: Clinical characteristics of the ACS patients with LM coronary artery disease

Variables		Summary
Total (N)		**236**
Gender	Male	163 (69.1%)
	Female	73 (30.9%)
Mean age (years)		58.8 ± 9.3
40 to 60		139 (58.9%)
61 to 80		97 (41.1%)
Mean body mass index (kg/m^2)		25.2 ± 3.7
	ST elevation myocardial infarction	94 (39.8%)

Acute coronary syndrome	Non-ST elevation myocardial infarction	95 (40.3%)
	Unstable angina	47 (19.9%)
Killip Class	I	209 (88.6%)
	II	13 (5.5%)
	III	11 (4.7%)
	IV	3 (1.3%)
Median chest pain to ER (h)		16 [5.3-48]
Median ER to catheterization laboratory (h)		4 [0.6-12]
Co-morbid conditions	Diabetes mellitus	113 (47.9%)
	Hypertension	154 (65.3%)
	Dyslipidemia	43 (18.2%)
	Smoking	55 (23.3%)
	Obesity	32 (13.6%)
	Family history of IHD	32 (13.6%)
Access	Radial	207 (87.7%)
	Femoral	29 (12.3%)
Number of vessels involved	Single vessel disease	20 (8.5%)
	Two vessel disease	40 (16.9%)
	Three vessel disease	176 (74.6%)
Complication		46 (19.5%)
Contrast induced nephropathy		31 (13.1%)
Cerebrovascular accident		2 (0.8%)
Arrhythmia		3 (1.3%)
Cardiogenic shock		3 (1.3%)
Major bleeding		6 (2.5%)
Thrombus		1 (0.4%)
Cardiac arrest		2 (0.8%)
Emergency CABG		1 (0.4%)
Length of stay (days)		2 [2-3]
Mortality (within 48 hours)		10 (4.2%)

* ER = "emergency room", IHD = "ischemic heart disease", CABG = "coronary artery bypass grafting"

A notable association emerged between in-hospital mortality and Killip class, revealing a significant increase in mortality rate with higher Killip class (p=0.006). Specifically, mortality rates were starkly elevated at Killip IV (33.3%) compared to Killip class III (18.2%). Additionally, mortality was notably higher among diabetic patients compared to non-diabetic counterparts, with mortality rates of 7.1% versus 1.6%, respectively (p=0.038). For further details, please refer to Table 2.

Table 2: In-hospital mortality rate by clinical characteristics of the ACS patients with LM coronary artery disease

Variables		**Total (N)**	**In-hospital Outcome**		**P-value**
			Survived	**Died**	
		236	**226**	**10**	**-**
Gender	Male	163	156 (95.7%)	7 (4.3%)	0.948
	Female	73	70 (95.9%)	3 (4.1%)	
Age (years)	40 to 60	139	134 (96.4%)	5 (3.6%)	0.559
	61 to 80	97	92 (94.8%)	5 (5.2%)	

Acute coronary syndrome	ST elevation myocardial infarction	94	88 (93.6%)	6 (6.4%)	0.137
	Non-ST elevation myocardial infarction	95	94 (98.9%)	1 (1.1%)	
	Unstable angina	47	44 (93.6%)	3 (6.4%)	
Killip Class	I	209	202 (96.7%)	7 (3.3%)	0.006
	II	13	13 (100%)	0 (0%)	
	III	11	9 (81.8%)	2 (18.2%)	
	IV	3	2 (66.7%)	1 (33.3%)	
Diabetes mellitus	No	123	121 (98.4%)	2 (1.6%)	0.038
	Yes	113	105 (92.9%)	8 (7.1%)	
Hypertension	No	82	80 (97.6%)	2 (2.4%)	0.317
	Yes	154	146 (94.8%)	8 (5.2%)	
Dyslipidemia	No	193	186 (96.4%)	7 (3.6%)	0.324
	Yes	43	40 (93%)	3 (7%)	
Smoking	No	181	172 (95%)	9 (5%)	0.309
	Yes	55	54 (98.2%)	1 (1.8%)	
Obesity	No	204	194 (95.1%)	10 (4.9%)	0.201
	Yes	32	32 (100%)	0 (0%)	
Family history of ischemic heart disease	No	204	196 (96.1%)	8 (3.9%)	0.543
	Yes	32	30 (93.8%)	2 (6.3%)	
Access	Radial	207	200 (96.6%)	7 (3.4%)	0.081
	Femoral	29	26 (89.7%)	3 (10.3%)	
Number of vessels involved	Single vessel disease	20	19 (95%)	1 (5%)	0.832
	Two vessel disease	40	39 (97.5%)	1 (2.5%)	
	Three vessel disease	176	168 (95.5%)	8 (4.5%)	

Discussion

The findings of this study underscore the critical nature of LMCAD in the context of ACS. The high mortality rate of 4.2% among ACS patients with LMCAD highlights the grave implications of this condition. The predominance of three-vessel disease in the study population further emphasizes the complexity and severity of LMCAD, which necessitates comprehensive management strategies.

One notable aspect is the significant prevalence of comorbidities among patients with LMCAD, particularly hypertension and diabetes mellitus. These comorbid conditions likely contribute to the increased risk and severity of ACS in this population. The association between comorbidities and adverse outcomes in ACS patients with LMCAD warrants further investigation and highlights the importance of aggressive risk factor modification and secondary prevention measures.

The occurrence of complications, such as contrast-induced nephropathy and major bleeding, in nearly one-fifth of patients underscores the multifaceted challenges in managing ACS patients with LMCAD. These complications not only increase morbidity but also pose significant barriers to optimal treatment and recovery. Strategies to mitigate these complications should be incorporated into the management protocols for ACS patients with LMCAD.

Furthermore, the distribution of Killip classes among the study population provides insights into the clinical presentation and severity of ACS in patients with LMCAD. The presence of patients in

Killip class IV and III at presentation highlights the acute and potentially life-threatening nature of LMCAD-related ACS.

Current treatment guidelines for ACS with LMCAD recommend immediate revascularization with either coronary artery bypass grafting or percutaneous coronary intervention to restore blood flow to the affected area of the heart. These interventions can help alleviate symptoms, reduce the risk of further complications, and improve overall outcomes for patients with this serious condition. It is essential for healthcare providers to be vigilant in recognizing the signs and symptoms of ACS with left main disease and to act quickly to provide life-saving treatment. By following evidence-based guidelines and protocols, healthcare teams can effectively manage this critical condition and improve the chances of a positive outcome for their patients. However, there's a debate on the superiority between PCI and CABG for LMCA disease. A study indicates no statistically significant difference in 5-year all-cause death between PCI and CABG, although Bayesian analysis suggests a probable slight advantage for CABG[21]. However, another study suggests that at 5 years, PCI is associated with inferior outcomes compared to CABG, with higher rates of non-procedural myocardial infarction and repeat revascularization[22]. The choice between PCI and CABG depends on factors such as anatomical complexity, patient comorbidities, and left ventricular dysfunction. Most LMCA PCI cases don't require support, but in some cases, IABP support may be necessary. Rates of IABP use during LMCA PCI vary, with more complex lesions and patient factors like severe left ventricular dysfunction increasing the likelihood of needing support[23,24].

Previous research on outcomes in patients with ACS and LMCAD has shown that prompt intervention and adherence to treatment protocols are crucial in improving survival rates and reducing the risk of adverse events. Additionally, ongoing monitoring and adjustments to treatment plans based on individual patient needs can further enhance outcomes in this high-risk population. By staying informed on the latest research and advancements in the field, healthcare providers can continue to improve their ability to effectively manage ACS with left main disease and provide the best possible care for their patients. Long-term follow-up suggests comparable risks of composite outcomes (all-cause death, myocardial infarction, or stroke) between PCI and CABG for LMCA stenosis[25]. However, patients treated with PCI have a higher risk of repeat revascularization compared to those who undergo CABG[25]. Studies using large registries or nationwide databases report an increasing age and higher risk of comorbidities among patients undergoing coronary revascularization over time[26,27]. The reasons behind these trends include aging populations, changes in disease epidemiology, and improved cardiovascular preventive measures leading to delayed symptomatic onset requiring revascularization[28].

Limitations of the study and areas for future research include the lack of long-term follow-up data and the need for larger, multicenter studies to validate the findings. Additionally, exploring the role of emerging technologies and precision medicine, in guiding treatment decisions for this patient population could be a promising avenue for future research. Overall, addressing these limitations and advancing research in these areas will be crucial in improving the care and outcomes of patients with ACS and left main disease.

Conclusion

In conclusion, our study underscores the critical nature of LMCAD in the context of ACS. The findings reveal a concerning clinical profile with a high prevalence of comorbidities such as hypertension and diabetes mellitus further emphasizes the importance of comprehensive management strategies addressing not only the acute cardiac event but also the underlying health conditions.

The distribution of vessel involvement, with a majority exhibiting three vessel disease, underscores the complexity and severity of LMCAD in this patient population. Additionally, the occurrence of complications, including contrast-

induced nephropathy and major bleeding, highlights the multifaceted challenges in managing these cases.

Of particular concern is the in-hospital mortality rate of 4.2%, underscoring the grave implications of LMCAD in ACS. This emphasizes the urgent need for early detection, aggressive intervention, and meticulous monitoring to optimize patient outcomes.

Moving forward, further research and clinical efforts are warranted to refine risk stratification, enhance treatment modalities, and improve prognostic outcomes for patients with ACS and LMCAD. Multidisciplinary approaches integrating advanced diagnostic techniques, innovative therapeutics, and comprehensive care pathways are essential to mitigate the morbidity and mortality associated with this high-risk cardiovascular condition.

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References

1) Fuster V, Kovacic JC. Acute coronary syndromes: pathology, diagnosis, genetics, prevention, and treatment. Circulation research. 2014 Jun 6;114(12):1847-51.
2) DeVon HA, Zerwic JJ. Symptoms of acute coronary syndromes: are there gender differences? A review of the literature. Heart & Lung. 2002 Jul 1;31(4):235-45.
3) Ramadan R, Boden WE, Kinlay S. Management of left main coronary artery disease. Journal of the American Heart Association. 2018 Mar 31;7(7):e008151.
4) Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. Circulation. 2009 Mar 3;119(8):1085-92.
5) Ragosta M. Left main coronary artery disease: importance, diagnosis, assessment, and management. Current Problems in Cardiology. 2015 Mar 1;40(3):93-126.
6) Yusuf S, Zucker D, Passamani E, Peduzzi P, Takaro T, Fisher LD, Kennedy JW, Davis K, Killip T, Norris R, Morris C. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. The Lancet. 1994 Aug 27;344(8922):563-70.
7) Gaba P, Christiansen EH, Nielsen PH, Murphy SA, O'Gara PT, Smith PK, Serruys PW, Kappetein AP, Park SJ, Park DW, Stone GW. Percutaneous coronary intervention vs coronary artery bypass graft surgery for left main disease in patients with and without acute coronary syndromes: a pooled analysis of 4 randomized clinical trials. JAMA cardiology. 2023 Jul 1;8(7):631-9.
8) Dąbrowski EJ, Kożuch M, Dobrzycki S. Left Main Coronary Artery Disease—Current Management and Future Perspectives. Journal of Clinical Medicine. 2022 Oct;11(19).
9) Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation. 2011 Dec 6;124(23):2574-609.
10) Armstrong PW, Bates ER, Gaudino M. Left main coronary disease: evolving management concepts. European Heart Journal. 2022 Nov 21;43(44):4635-43.
11) Davidson LJ, Cleveland JC, Welt FG, Anwaruddin S, Bonow RO, Firstenberg MS, Gaudino MF, Gersh BJ, Grubb KJ, Kirtane AJ, Tamis-Holland JE. A practical approach to left main coronary artery disease: JACC State-of-the-Art review. Journal of the American College of Cardiology. 2022 Nov 29;80(22):2119-34.
12) Lee J, Park DW, Park SJ. Past, Present, and Future of Left Main Coronary Artery PCI. Journal of Cardiovascular Intervention. 2023 Feb 9;2.
13) Buszman PE, Kiesz SR, Bochenek A, Peszek-Przybyla E, Szkrobka I, Debinski M, et al. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. J Am Coll Cardiol 2008;51(5):538–545.
14) Morice MC, Serruys PW, Kappetein AP, Feldman TE, Ståhle E, Colombo A, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using

paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. Circulation 2010;121(24):2645–2653.

15) Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. J Am Coll Cardiol 2011;57(5):538–545.
16) Park SJ, Kim YH, Park DW, Yun SC, Ahn JM, Song HG, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med 2011;364(18):1718–1727.
17) Lee PH, Ahn JM, Chang M, Baek S, Yoon SH, Kang SJ, et al. Left main coronary artery disease: secular trends in patient characteristics, treatments, and outcomes. J Am Coll Cardiol 2016;68(11):1233–1246.
18) Neumann F-J , Sousa-Uva M , Ahlsson A , Alfonso F , Banning AP , Benedetto U , Byrne RA , Collet J-P , Falk V , Head SJ , Jüni P , Kastrati A , Koller A , Kristensen SD , Niebauer J , Richter DJ , Seferović PM , Sibbing D , Stefanini GG , Windecker S , Yadav R , Zembala MO ; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.
19) Patel MR , Dehmer GJ , Hirshfeld JW , Smith PK , Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 Appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2012;59:857–881.
20) Sharma R, Bhairappa S, Prasad S, Manjunath CN. Clinical characteristics, angiographic profile and in hospital mortality in acute coronary syndrome patients in south Indian population. Heart India. 2014;2(3):65.
21) Sabatine MS, Bergmark BA, Murphy SA, T O'Gara P, Smith PK, Serruys PW, Kappetein AP, Park SJ, Park DW, Christiansen EH, Holm NR. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis. The Lancet. 2021 Dec 18;398(10318):2247-57.
22) Holm NR, Mäkikallio T, Lindsay MM, Spence MS, Erglis A, Menown IB, Trovik T, Kellerth T, Kalinauskas G, Mogensen LJ, Nielsen PH. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. The Lancet. 2020 Jan 18;395(10219):191-9.
23) Brennan JM, Dai D, Patel MR, Rao SV, Armstrong EJ, Messenger JC, Curtis JP, Shunk KA, Anstrom KJ, Eisenstein EL, Weintraub WS. Characteristics and long-term outcomes of percutaneous revascularization of unprotected left main coronary artery stenosis in the United States: a report from the National Cardiovascular Data Registry, 2004 to 2008. Journal of the American College of Cardiology. 2012 Feb 14;59(7):648-54.
24) Naganuma T, Chieffo A, Meliga E, Capodanno D, Park SJ, Onuma Y, Valgimigli M, Jegere S, Makkar RR, Palacios IF, Costopoulos C. Long-term clinical outcomes after percutaneous coronary intervention for ostial/mid-shaft lesions versus distal bifurcation lesions in unprotected left main coronary artery: the DELTA Registry (drug-eluting stent for left main coronary artery disease): a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. JACC: Cardiovascular Interventions. 2013 Dec;6(12):1242-9.
25) Giacoppo D, Colleran R, Cassese S, Frangieh AH, Wiebe J, Joner M, Schunkert H, Kastrati A, Byrne RA. Percutaneous coronary intervention vs coronary artery bypass grafting in patients with left main coronary artery stenosis: a systematic review and meta-analysis. JAMA cardiology. 2017 Oct 1;2(10):1079-88.
26) Rao SV, Hess CN, Dai D, Green CL, Peterson ED, Douglas PS. Temporal trends in percutaneous coronary intervention outcomes among older patients in the United States. American heart journal. 2013 Aug 1;166(2):273-81.
27) Cornwell LD, Omer S, Rosengart T, Holman WL, Bakaeen FG. Changes over time in risk profiles of patients who undergo coronary artery bypass graft surgery: the Veterans Affairs Surgical Quality

Improvement Program (VASQIP). JAMA surgery. 2015 Apr 1;150(4):308-15.

28) Lee PH, Ahn JM, Chang M, Baek S, Yoon SH, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, Park DW. Left main coronary artery disease: secular trends in patient characteristics, treatments, and outcomes. Journal of the American College of Cardiology. 2016 Sep 13;68(11):1233-46.