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### Case Report

## How to deal with LM disease in an NSTEMI patient: PCI or CABG?

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#### ARTICLE INFO

#### ABSTRACT

Keywords: Background: In acute coronary syndrome, the left Main coronary artery (LMCA) has been associated Left Main disease: with significant deaths and morbidity. Urgent CABG is recommended for patients with LM disease Percutaneous Coronary Intervention; accompanied by ACS, but requires special preparation and adequate facilities. not all hospitals are Acute coronary syndrom; ready. PCI on left main coronary artery is a high risk procedure which requires special preparation like Non ST Elevation Segment Myocardial IVUS and FFR. Meanwhile, the ACS case is an emergency that needs to be treated immediately. Interventional management is mandatory in this setting, but the concern is whether the action is infacrtion; Unstable Angina Pectoris: carried out in an emergency or an elective procedure. Coronary Artery Bypass Graft Surgery. Objective: This study aimed to describe the management of LM disease in NSTEMI patients. Case Illustration: We will discuss a 69-year-old male brought to our hospital because of chest pain while doing moderate activity. The patient was previously referred from a private hospital and was assessed as NSTEACS. from angiography there was Stenosis dd Thrombus at LM, the cardiologist suggest him to be referred to RSSA for CVCU admission and will be underwent Urgent revascularisation. Clopidogrel and aspirin were routinely consumed as dual antiplatelet therapy. We treat the patient with an unfractionated heparin (UFH) bolus, continued with continuous infusion until revascularization. No event of subsequent acute coronary syndrome was observed. Conclusion: Although the management of patients with LM disease requires some preparation before action is taken, urgent revascularization in Acute coronary syndrome cases must still be carried out immediately.

#### 1. Introduction

Globally, cardiovascular disease is the primary cause of death.<sup>1</sup> STEMI incidences are decreasing and NSTEMI incidences are increasing, respectively. In 2015, the rate of ST-elevation myocardial infarction incidence (STEMI) in Sweden was 58 per 100 000 people, making it the country with the most comprehensive STEMI. While the incidence of NSTEMI has remained steady or slightly increased, the reported adjusted incidence rates from the United States have fallen from 133 per 100,000 in 1999 to 50 per 100,000 in 2008.<sup>2</sup>

Acute coronary syndromes (ACS) are a group of diseases defined by acute myocardial ischaemia caused by severe coronary artery stenosis or occlusion due to thrombosis; this can manifest as either an NSTE-ACS, such as unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI), or an ST-elevation myocardial infarction (STEMI).<sup>3</sup> Clinical characteristics suggestive of myocardial ischaemia can be referred to as a myocardial infarction (MI) if there is evidence of myocardial necrosis. After the heart muscle is injured, specific indicators are discharged into the bloodstream.<sup>1,3</sup>

Significant LMCA disease can be identified as an angiographic narrowing of greater than 50 percent.<sup>4</sup> Until recent years, LMCA disease was the lesion subset with the highest risk of ischemic heart disease.<sup>5</sup> LMCA diease is a disorder that, when it appears in the context of ACS, demands immediate therapy. The Left Main percutaneus intervention is a difficulty for operator because significant ischemic damage could result from main percutaneous interventions. A comparison of unprotected LMCA lesions linked with acute myocardial infarction presenting as acute coronary syndromes (ACS), including NSTEMI, to those associated with stable angina, there was no consensus.<sup>6,7</sup> In this situation, invasive procedures like a coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) are musts. Although PCI approaches were feasible, the decisional algorithm was complicated by a number of factors, including the high prevalence of both short- and long-term major adverse cardiac events, which are especially high in the elderly and in cases where revascularization had to be done quickly.8

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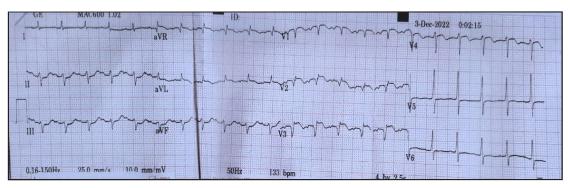


Figure 1. ECG performed at hospital showed normal Sinus rhythm. OMI Anteroseptal.

We present an ACS case in a male patient with LMCA disease, emergent PCI consisted of 1 DES implantation at osteal LM to proximal LCx and 1 DES implantation at distal LAD (overlapped with prevously stent), the procedure was complicated; However, it worked, and the patient was saved.

#### 2. Case Illustration

A 69-year-old male Javanese was brought to our hospital on November 6, 2022, because of chest pain while doing moderate activity. Previously, the patient suffered from chest pain for 3 days before RSSA admission (November 3, 2022, 7 p.m.), while he was sitting at home after doing his daily activities. The chest pain was a heavy-like sensation at his mid-chest with a VAS of 8/10 and a duration of more than 30 minutes. Due to the persistent pain, his family brought her to an emergency room at a private hospital near his house.

He arrived at ER Private Hospital with persisting chest pain (VAS 6/10) and general weakness. From ECG performed, he was assessed and treated as NSTEACS and underwent Invasive Strategy following day. He was observed in the ICU for 3 days. During the observations, he still complained of shortness of breath. Because of this condition, the cardiologist suggests that he be referred to RSSA for CVCU admission and staging PCI.

He had history severe chest pain (October 4, 2022) that was not relieved by rest and felt like heaviness sensation on her left chest radiated to the back accompanied with diaphoresis (VAS 9/10). He was diagnosed with acute coronary syndrome but refused PCI because of financial issues. He was then treated with conservative management for nine days. 2 Weeks after initial hospitalization (October 18, 2022), he complained chest discomfort manifested at mild activity and was not relieved by rest. His family then took him to a private hospital. He underwent PCI thereafter with 1 DES implantation on proximal mid LAD coronary artery.

The patient was physically active and works as a farmer. He initially complained chest pain related with activity since 8 months prior admission. The chest pain had increased in frequency and intensity and was accompanied by leg swelling since 3 months prior to admission. He didn't seek medical consultation because he felt the chest pain was relieved by rest.

He was diagnosed with diabetes mellitus since 3 years ago, and didn't routinely control. He was an active smoker, smoking 1 pack a day, and had quit smoking since his prior hospitalization. On physical examination, it was found that blood pressure (BP) 128/76 mmHg, HR 69 bpm, RR 18 tpm, T 38°C, saturation (SpO2) 99% on nasal canule 4 liter per minute (lpm), with appropriate urination. Anemia was found with sing of pale conjungtiva. Jugular venous pressure (JVP) was R + 3 cm H20. There was not heart enlargement finding from auscultation with palpable apex cordis at intercostalis (ICS) V 2 cm medial. An abnormal lung sound was not heard from auscultation. Cold acrals were not found in the extremities. The electrocardiography (ECG) examination showed a sinus rhythm with Q pathological at V1-V3. ST Elevation Persistent at V1-V3. bibasic T wave at V1-V4, as seen in (Figure 1). An X-ray examination revealed normal dimensions with congestive pulmonum and pneumonia (Figure 2).

Laboratory examination at our ER showed normal leucocyte ( $6150/\mu$ L), haemoglobin (7.3 g/dL), platelets (427,000/uL), ureum (66), creatinine (1.47), sodium (135), potassium (4.09), chloride (110), partial prothrombin time (10) and activated partial thromboplastin time (28.1). The HbA1C was high (9.6%) without insulin treatment. He was given Clopidogrel and Aspirin as treatment. Notably, the patient had a decreased systolic function with an estimated ejection fraction of 39%, a creatinine clearance of 40 mL/min, and a diminished functional capacity.

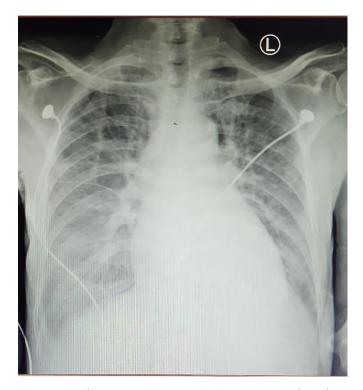


Figure 2. Thoracic antero-posterior (AP) X-ray imaging showed cardiomegaly, congestive pulmonum and pneumonia.





Figure 3. Coronary angiography of a patient with 70% stenosis in the LM osteal

Diagnostic coronary angiography revealed Significant LMCA disease, with a diffuse narrowing approximated at 70% a diffuse calcified stenosis from the osteal to the distal Left main Coronary artery, and stenosis of 80% in the distal LCx. We discovered the dominant right coronary artery from the angiography results, with a maximum narrowing of 70% in the proximal RCA (Figure 3). The LAD artery in this patient had previously been stented with two lengthy continuous stents, the first beginning nearly 3 mm after the ostium until to mid and the second 2.5 mm after mid until to distal.

The patient had history a heart attack, so the first DES stent was implanted with provisional stenting at osteal mid LAD on October 18th. After the first installation, the complaint improved for about the first 10 days. then the chest pain reappeared and did not improve, so the patient went back to the nearest hospital and was diagnosed with a heart attack again. The patient underwent PCI, and a second Des stent was implanted in the mid-distal LAD on November 3th. During the 3 days of treatment, complaints of chest pain did not improve. considering the patient's NSTEMI and LM disease, so the patient was referred to our hospital, and PCI was performed and a DES stent was implanted in the osteal LM to distal LCX on November 10th.

We decided provisional stenting on the LM and distal LCx coronary arteries as the target vessels. There was no visible tortuosity or intraluminal thrombus. A decision was made to perform emergent PCI. A single Stent DES was implantation in osteal LM until proximal LCx and single stent DES was implantation in distal LAD (Overlapped with previously stent). Cineangiography was then performed, with the results of TIMI flow of 3 and residual stenosis of 0%. After the procedure, we didn't find thrombosis intracatheter. No event of subsequent acute coronary syndrome was observed.

After the DES implantation, the monitor ECG showed a sinus rhythm with Q pathological at V1-V3. ST Elevation Persistent at V1-V3. Bipashic T wave at V1-V4. The chest pain was not complained by the patient during this procedure.

#### 3. Discussion

Acute chest pain in individuals who have acute coronary syndrome may present with the following symptoms: prolonged (lasting more than 20 minutes), restless chest pain, acute de novo Angina (3 months) (class II or III of the Canadian Cardiovascular Society classification), Angina post-myocardial infarction, or "crescendo angina," is the recent destabilization of previously stable angina showing at least Class III angina characteristics (MI).<sup>9</sup>

Patients with acute chest pain that persists for more than twenty minutes but no persistent ST-elevation. This condition is known as non-ST-segment elevation acute coronary syndrome (NSTACS) and is typically caused by the complete obstruction of a minor coronary artery or the partial obstruction of a main coronary artery. Symptoms may be identical to STEMI, but cardiac damage is significantly less severe.9,10 Myocardial infarction (MI) can be used when there is obvious myocardial necrosis in addition to the clinical symptoms of myocardial ischaemia. As a consequence of myocardial damage, cardiac biomarkers are released into circulation. All patients suspected of having NSTEACS must have a biomarker of cardiomyocyte injury measured, with hs-cTn being the preferred choice. When compared to creatine kinase (CK), its myocardial band isoenzyme (CK-MB), and myoglobin, cardiac troponins are more sensitive and precise markers of cardiomyocyte injury. Increases in cardiac troponin that are more than 99th percentile dynamically indicate myocardial infarction.9

A significant left main coronary artery disease is characterized by a vascular narrowing of more than 50% on an angiogram. There are three treatment choices for LMCA disease: optimal medicinal therapy, percutaneous revascularization, or surgical revascularization. It was formerly the subgroup of coronary artery disease with the highest risk.<sup>5</sup> Arteriosclerotic plaques have been reported at regions of low endothelial shear stress on the carina-opposed lateral wall of the bifurcation, suggesting a connection between atherosclerosis development and flow haemodynamics in the LMCA. Endothelial shear stress is the tangential force generated by the friction of flowing blood on the endothelium surface, and it is a function of the shear rate at the wall and the viscosity of the blood. High shear stress is observed in the carina, while low shear stress in arterial regions with disturbed laminar

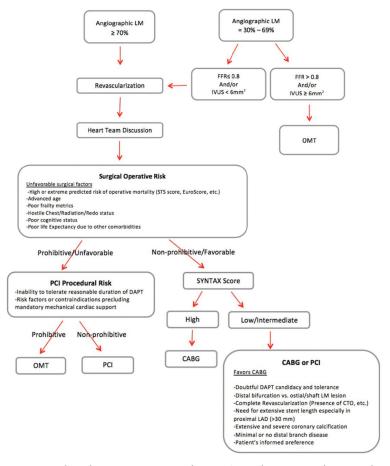


Figure 4. Algorithm management LM disease. (According to Ramadan R, et al. Management of Left Main Coronary Artery Disease)

flow promotes a therogenesis, a therosclerotic plaque creation and progression, and vascular remodeling. ^ $^{\rm 11}$ 

In patients with stable LMCAD, the first step is to determine the degree of stenosis which can be performed using non-invasive (CCTA, CMR, Stress ECG) and invasive modalities (invasive coronary angiography, IVUS and FFR). Sensitivity and specificity, which are determined by comparing test results to those of invasive coronary angiography, are two metrics used to gauge diagnostic accuracy. Table 1 lists the sensitivity and specificity (not corrected for referral bias) of popular noninvasive cardiac imaging methods.12 if the degree of stenosis is more than 70% then revascularization is indicated, especially by forming a heart team which is followed by discussions to choose CABG or PCI. if the degree of stenosis is less than 70% then proceed with IVUS and FFR modalities. The ischemic load of the LM lesion can be estimated with IVUS, and it is useful after Left main percutaneous coronary intervention. In the multicenter prospective LITRO study of intermediate LM stenosis between 25% and 60%, deferring revascularization of LM lesions with a minimal luminal area (MLA) of 6 mm2 (53% of lesions) was safe and affiliated with positive outcomes at 2 years of follow-up (cardiac death-free survival of 97.7%). IVUS is superior for assessing the anatomical importance of an LM stenosis, while FFR is superior for determining the hemodynamic significance of an LM stenosis. With an FFR 0.80, revascularization can be postponed for angiographic intermediate LM lesions, improving long-term results.13 The algorithm and management in patients with stable LMCAD are simply described in the following (Figure 4).

The gold standard therapy for stable CAD's LMCA disease historically has been CABG surgery.7,14 However, with the growth and development of interventional cardiology, PCI has emerged as a safe alternative management choice to CABG in certain patients.<sup>14</sup>

In contrast to patients with stable angina, data on the prognosis of patients undergoing unprotected Left Main percutaneous interventions with ACS and NSTEMI are limited.<sup>6</sup>

Table 1. Sensitivity and Specificity of Noninvasive Cardiac Imging

Test	Sensitivity	Specificity
Exercise ECG <sup>b</sup>	61%	70%-77%
Exercise stress echo	70%-85%	77%-89%
Exercise stress MPI	82%-88%	70%-88%
(SPECT, PET)		
CAC Scoring	98%	40%
CCTA	93%-97%	80%-90%
Pharmacologic stress	91%	81%
CMR Perfusion		
CMR angiography	87%-88%	56%-70%

Note; "Unadjusted for referral bias, <sup>b</sup>Accuracy in women lower. Diagnostic Acuracy is improved when non-ECG factors are considered

CABG is recommended in patients who are hemodynamically stable and have a low perioperative risk, such as those with low left ventricular function, diabetes, concurrent valve disease or mechanical problems, and multi-vessel disease with a high SYNTAX score.<sup>7</sup> In individuals with acute coronary syndrome, an organized protocol for the treatment of LMCA illness. Currently available evidence suggests that criteria that apply to patients with LM with stable CAD are guidelines (ESC/EACTS 2018 on myocardial revascularization) should also be applied to patients with NSTE-ACS with LMCAD.<sup>21</sup>

LMCA LESION	Favours CABG	Favours PCI
<sup>*</sup> Left main with SYNTAX score ≤22	1 (Level of evidence – B)	1 Level of evidence – B)
<sup>*</sup> Left main with SYNTAX score 23–32	1 (Level of evidence – B)	2a (Level of evidence – B)
<sup>*</sup> Left main with SYNTAX score >32	1 (Level of evidence – B)	3 (Level of evidence – B)
<sup>a</sup> Left main (isolated or 1 VD, ostium/shaft)	1 (Level of evidence – A)	2a (Level of evidence – B)
<sup>a</sup> Left main (isolated or 1 VD, distal bifurcation)	1 (Level of evidence – A)	2b (Level of evidence – B)
<sup>a</sup> Left main + 2 VD or 3 VD, SYNTAX score ≤32	1 (Level of evidence – A)	2b (Level of evidence – B)
<sup>a</sup> Left main + 2 VD or 3 VD, SYNTAX score $\geq$ 33	1 (Level of evidence – A)	3 (Level of evidence – B)

LMCA, Left main coronary artery; CABG, Coronary artery bypass graft; PCI, Percutaneous coronary; VD, Vessel disease; SYNTAX, Synergy between percutaneous coronary intervention with taxus and cardiac surgery.

\* According to 2014 European Society of Cardiology Guidelines in Myocardial Revascularisation.

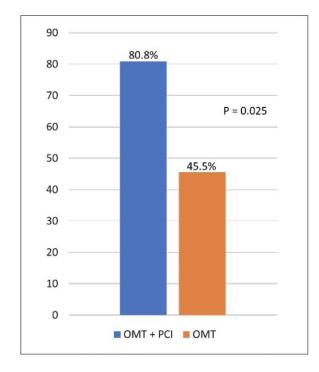
<sup>a</sup> According to 2010 European Society of Cardiology Guidelines in Myocardial Revascularisation.

Table 2. Indication for coronary bypass graft surgery vs. percutaneous coronary intervention in the stable angina patients withlesions suitable for both procedures. (According to Karabulut et al. Treatment strategies in the left main coronary artery disease associated with acute coronary. J Saudi Hear Assoc. 2015)

The optimal revascularization approach for ACS patients whose disease was caused by LMCA culprit lesions is not clear. The presenting thrombolysis in myocardial infarction (TIMI) 0/1 flow status is the primary factor in determining treatment selection. Since TIMI flow can be restored more quickly through percutaneous intervention, it is possible that PCI should be the standard therapy. When a patient's hemodynamic status is stable, either PCI or surgery can be performed in accordance with recommendations for stable patients.<sup>7</sup>

The SYNTAX score could be used to forecast the likelihood of mortality or MACE in patients with complex lesions like LMCAD or 3VD. In patients with a SYNTAX score of more than 22, according to the guidelines, CABG is recommended rather than PCI. This is as shown in the following (Table 2).<sup>7,15</sup> based on research conducted by Wella at al, The quality of life and physical limitations of CCS patients receiving OMT were improved by myocardial revascularization by PCI. OMT plus PCI was associated with improved QoL in patients with SYNTAX > 22 (Table 3).<sup>16</sup>

Table 3. Good quality of life outcome among patients with SYNTAX score of more than 22.



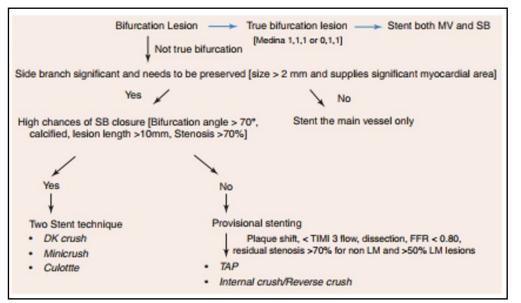
The ACCF/AHA Coronary Artery Bypass Surgery 2011 Guideline suggests Emergency CABG for Patients with Acute Myocardial Infarction, Class I When 1) first percutaneous coronary intervention (PCI) has failed or cannot be performed, 2) the coronary anatomy is favorable to CABG, and 3) there is persistent ischaemia of a substantial region of resting myocardium and/or hemodynamic instability unresponsive to nonsurgical therapy.(Level of Evidence: B).<sup>17</sup>

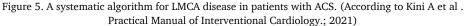
The clinical and angiographical data can be used to assess the patient risks. In this patient, the estimated TIMI score was 6, resulting in a 41% chance of incidents requiring medical attention following 14 days (Overall mortality, acute or recurrent myocardial infarction, or severe recurrent ischaemia necessitating immediate revascularization). The estimated Syntax-score for this patient was 23, translating to a major cardiac event risk between 28.6% and 32.1%. This patient has left main disease and a Medina-type bifurcation lesion, and the Syntax score, which is entirely anatomical, is particularly important in him or her (1,0,1). The Syntax-score II was calculated at 52, which produced a mortality rate of 36.2% after PCI, and at 43.6, which produced a mortality rate of 19.9% after CABG.

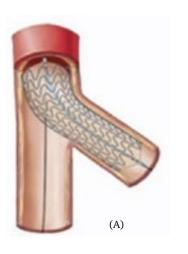
Patients with LMCA disease have similar outcomes following PCI and CABG, according to latest studies. According to a study conducted by Barsoum et al., CABG exceeds PCI for MACCE in individuals with NSTE-ACS and TVD. In patients with NSTE-ACS with MVD and left main CAD at 30 days revascularized by PCI or CABG, there were no statistically significant differences in MACE and all-cause death. In comparison to CABG, PCI was linked to a greater incidence of MACE, myocardial infarction, and repeat revascularization during long-term follow-up (3-5 years).<sup>18,19</sup> However, percutaneous coronary intervention (even with drug-eluting stents) was related to increased rates of subsequent revascularization. Gregg et al found that PCI was as effective as CABG in reducing mortality after treating unprotected LMCA disease. In individuals with mild to moderate anatomical complexity LMCA disease.<sup>20</sup>

In patients with a confirmed diagnosis of NSTEACS, an invasive strategy is suggested at a time determined by individual risk stratification. According to the recently announced European Guidelines for the care of patients with NSTEACS, coronary angiography should be done on high-risk patients presenting with NSTEACS within 24 hours of hospital admission. because in the ACS setting, the use of dual antiplatelets (aspirin and clopidogrel) and anticoagulants (unfractional heparin or lMWH) is mandatory in patients prior to reperfusion.<sup>22</sup>

Current recommendations for these individuals call for immediate coronary artery bypass grafting (CABG). Given the unexpected nature of the presentation, an emergency bypass may be logistically more difficult to execute because of the need for extensive resource mobilization in order to prepare and coordinate the operative







team. due to the lack of adequate facilities and teams in performing emergency CABG, we made deccission to perform emergency PCI or invasive strategy.  $^{23}$ 

We discovered the dominant right coronary artery from the angiography results, with a maximum narrowing of 70% in the proximal RCA. Patented RCA vessels provide benefits for LM interventions. Several operators are deterred from doing PCI of the LM due to the lack of RCA support for the left coronary circulation. This is due to a significantly increased risk of potentially fatal postoperative complications. According to general consensus, in these conditions, the emergence of substantial problems during PCI of LM might lead to the complete deprivation of blood flow to the entire myocardium and may put the patient at an intolerably high risk.<sup>24</sup> We didn't use IABP before PCI in this patient. The routine use of IABP in MI without cardiogenic shock is not supported by any data. Additional studies powered to clinical outcomes ought to be taken into consideration, especially in high-risk subgroups.<sup>25</sup> The current guidance recommendations for the IABP are set out in the following (Table 4).



(B)

Figure 6. (A) illustration of Left main stenting procedure, (B)Results after performing left main stenting in patients with NSTEMI.

Indication		AHA and ACC guidelines		ESC guidelines
STEMI with cardiogenic shock	lla/B	Consider for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy <sup>a</sup> [27 <sup>•</sup> ].	IIb/B	Consider IABP in patients with cardiogenic shock <sup>a</sup> [28].
STEMI without cardiogenic shock.	-	-	IIIA	Not recommended in the absence of haemodynamic impairment [29].
Mechanical complications of AMI	-	IABP can be used to provide temporary circulatory support [27 <sup>■</sup> ].	IC	IABP recommended for those with cardiogenic shock with mechanical complications [29].
Intractable ventricular arrhythmia	-	-	-	-
High-risk PCI	llb/C	Elective IABP may be considered in selected high-risk patients [30].	-	-
High-risk CABG	lla/B	Preoperative IABP is reasonable in high-risk patients (LVEF <30% or left main disease) [31].	-	-

Table 4. Current Guideline recommendation for IABP Accros various indications. (According to Ihdayhid AR et al. Intra-aortic balloon pump: Indications, efficacy, guidelines and future directions. Curr Opin Cardiol. 2014)

From the Algorithm Bifurcation lession in figure 5, Patients with bifurcation lesions in the LM, it is necessary to clarify whether the lesion is a true bifurcation or not. if there is significant narrowing in the Side branch and Main branch with medinaa (1-1-1-1 or 0-1-1), then it can be considered using the 2-stent technique. If it is not a true bifurcation lesion, then we need to evaluate whether the sidebranch is significant and needs to be secured (> 2mm in size and provide significant supply to the myocardial area). If the side branch is significant, it is necessary to evaluate whether the high-risk side branch is closed (bifurcation angle > 70, calcified, and the lesion is > 10mm long with stenosis > 70%). If not, we can consider provisional stenting.26 In this patient, provisional stenting was performed from the osteal LM to the distal LCX because the distal main vessel (osteal proximal LAD) was experiencing ACS and had been previously secured. (Figure 6).

Based on these risk scores, data from recent research, our knowledge of the patient's anatomy, and what we know about how things worked in the past, we think that PCI is a good first choice, especially when surgery is difficult or there aren't enough facilities and teams to do an emergency CABG. In the context of ACS (NSTEACS), an invasive strategy must be chosen according to risk stratification. postponement of action or elective procedures are not in accordance with ACS management recommendations. For an improved outcome and reduced risk, the attending team should consider the guideline recommendations, the patient's individual circumstances, and the available operative technique when deciding between medical treatment, PCI, and CABG.

#### 4. Conclusion

The evidence suggests that PCI of the left main is safe for some patients. Clinical cardiologists, interventional cardiologists, and cardiac surgeons should all be involved in the choice to move forward with PCI or CABG. Patient goals and preferences, co-morbidities, anticipated surgical risk, coronary anatomy complexity, and the patient's capacity to comply with dual antiplatelet therapy are all factors to be taken into account.

Urgent CABG is more beneficial than PCI for individuals with LM disease and ACS. Urgent CABG is available at a relatively small number of institutions; however, there is evidence that percutaneous coronary intervention (PCI) yields similar outcomes to CABG. When surgical risk is assessed to be high and the technique is anticipated to be challenging, percutaneous coronary intervention (PCI) for LMCA disease should be considered as an alternative to CABG.

#### 5. Declarations

5.1. Ethics Approval and Consent to participate

This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involvement in the study.

- 5.2. Consent for publication Not applicable.
- 5.3. Availability of data and materials

Data used in our study were presented in the main text.

- 5.4. Competing interests
- Not applicable.

5.5. *Funding source* Not applicable.

#### 5.6. Authors contributions

Idea/concept: DIS, SA. Design: DIS, SA. Control/supervision: SA, AR, MSR, IP. Literature search: SA, AR, MSR, IP. Data extraction: DIS, SA. Statistical analysis: DIS, SA. Results interpretation: DIS, SA. Critical review/discussion: NK, IP, CT, BS. Writing the article: DIS, SA. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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