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# Percutaneous coronary intervention in unprotected left main coronary artery stenosis patients. A Retrospective Study from Palestine

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## ABSTRACT

**Objective:** The study aimed to assess the results of stenting in unprotected left main coronary artery disease (uLMCAD) at a tertiary hospital center. **Methods:** We assessed all patients who received stenting for uLMCAD, including stable patients who underwent elective, urgent, or emergent procedures. Data were gathered by reviewing hospital records and coronary angiograms and calculating SYNTAX scores. Patient follow-up was conducted via clinic visits and phone calls. **Results:** Percutaneous coronary intervention (PCI) was performed on seventy patients with uLMCAD, all of whom had successful revascularization. During their hospital stay, only one patient (1.4%) died from a noncardiac cause and no patient experienced target lesion failure. After an average follow-up of 17.4 ± 12.36 months, four patients (5.7%) died, with three of the deaths being noncardiac. Eight patients (11.4%) also experienced major adverse cardiac events, and six (8.6%) required target vessel revascularization. The crush technique was associated with a lower rate of target lesion failure than the noncrush technique (0% vs. 14%, $p$=0.03). Furthermore, patients with one- to two-vessel disease had lower rates of target lesion failure than those with three-vessel disease (2.5% vs. 16.7%, $p$=0.048). Other variables, such as the Syntax score and the lesion site (distal and nondistal left main disease), did not appear to affect target lesion outcomes. **Conclusions:** In our center, the stenting procedure for uLMCAD resulted in favorable outcomes during hospitalization and at the long-term follow-up, comparable to the results of large clinical trials.

**Keywords:** Left Main, Stenting, Unprotected, Outcome.

## INTRODUCTION

The left main coronary artery (LMCA) is one of the two major arteries supplying the heart. It is anatomically divided into three regions: the ostium, the midshaft, and the distal portion. The distal LMCA always terminates in a bifurcation, giving rise to the left anterior descending (LAD) and left circumflex (LCx) arteries. It supplies 75% of the left ventricular mass in patients with the right-dominant type and 100% in the case of the left-dominant type. Severe unprotected left main coronary artery disease (uLMCAD) will reduce flow to a large portion of the myocardium mass, placing the patient at high risk for left ventricle dysfunction and arrhythmias (1-5). When the LMCA has no patent graft to the left anterior descending (LAD) or circumflex (Cx), it is known as an uLMCA, which is generally a more challenging decision during percutaneous coronary intervention (PCI) (6).

Approximately 4-6% of all patients who underwent angiography were found to have significant stenosis in the LMCA (7), and most of them (60-80%) had distal lesions at the origin of the LAD and Cx (8).

Modalities in the management of uLMCAD have been developing over the years. Initially, revascularization by coronary artery bypass grafting (CABG) surgery was regarded as the standard treatment for uLMCAD (9). PCI is an alternative method for patients who are not candidates for surgery. Later, observation and the randomized trial showed equivalent outcomes for these 2 approaches. These findings apply to patients with mild-to-moderately complex lesions using newer drug-eluting stents (10-12). However, PCI carries a higher rate of revascularization (13).

The outcome of PCI for uLMCAD varies and depends on many factors, including the size of the lesion, whether it involves bifurcation or not (14), stent type (15), and stent technique used (16-18). Ostial or mid-shaft LMCA disease has a better outcome than distal bifurcation lesions and a lower rate of target vessel revascularization (14). The 2-stent strategy was also associated with lower target lesion failure than the 1-stent strategy (19).

In our hospital, a tertiary cardiology center in Palestine, we started performing PCI for uLMCAD in 2014. After the diagnosis of significant LMCA disease, a heart team discussion is usually conducted, which includes interventional cardiologists and cardiac surgeons, before the plan is discussed with the patients and their families. There is no reported data about the outcomes of uLMCAD stenting in Palestine. This article will present our experience at An-Najah National University Hospital in the stenting of uLMCAD.

## METHODS

### *Study design and population*

This retrospective cohort study was carried out for patients who underwent stenting for uLMCAD. Data were collected from a single center (An-Najah National University Hospital, NNUH), a tertiary center on the west bank capable of stenting uLMCAD. All patients who had significant uLMCAD and underwent stenting for uLMCAD were enrolled. It included patients who underwent the procedure as elective, urgent, or emergency from 2014 to 2020. The lesions' complexity was assessed using synergy between percutaneous coronary intervention with Taxus and cardiac surgery (SYNTAX) score. Patients with uLMCAD with mild-to-moderately complex lesions (SYNTAX score <33) typically undergo PCI.

On the other hand, severe-complex lesions (SYNTAX score >33) were recommended for GABG according to the European Society of Cardiology (ESC) 2018 guidelines on myocardial revascularization (20). However, for many reasons, including the risk of invasive surgery and patient preference, the discussion between an interventional cardiologist and a cardiac surgeon was conducted for the best choice. Patients who presented with cardiogenic shock or underwent CABG surgery with grafts from the LM to the LAD or Cx were excluded.

### *Procedures and medications*

The procedure was conducted in the catheterization laboratory at NNUH. All patients were fasting. Details of the procedure were explained to the patients and their families, who agreed to sign and consent. Radial or femoral access was used depending on the hemodynamic state and the expected need for additional procedures. A bolus of heparin 80 international units (IU)/kg was given during the procedure, and the lesions were crossed using a floppy guide wire, then predilection with an inflating balloon if needed, followed by deployment of a stent (20). The result was optimized by the proximal optimization technique (one of the post-dilation methods to modify a regular stent to match the specific anatomy of a bifurcation) (21). The interventional cardiologist decided on the PCI stent type, size, and strategy according to the anatomical lesions. One stent strategy using the crossover technique and two using the crush or tap technique were used. An infusion of heparin and glycoprotein IIb/IIIA was used 24 hours after the procedure and sometimes felt to improve Thrombolysis In Myocardial Infarction (TIMI) flow based on angiographic findings (20). All patients who underwent successful PCI were discharged on dual antiplatelet (aspirin and clopidogrel) and high-dose statins (22, 23).

### *Measurement tool and follow-up*

A data abstraction sheet using an Excel sheet was constructed to collect relevant data from patients' files during the hospitalization period and follow-up at the cardiology clinic visit. All patients were also contacted at the time of data collection.

### *Endpoint and definition*

The outcomes that were measured were death (including cardiac and noncardiac death), major adverse cardiac events (MACE), which is a composite of death, myocardial infarction, and target vessel revascularization (TVR) (24), and target lesion failure (TLF). TVR was defined as repeating percutaneous coronary intervention in the same vessel, either at the same site of the stent or another part

of the same vessel (25). TLF was defined as the combination of cardiac death, target vessel myocardial infarction (MI), or clinically driven target lesion revascularization (26). Two cardiologists calculated The SYNTAX score based on the ESC 2018 guidelines on myocardial revascularization. The lowest score is 0, and more complex coronary anatomy has a higher score (no upper limit) (20). If there was a discrepancy, a third opinion was taken for the final result.

### *Ethical considerations*

Ethical approval was obtained from the institutional review board (IRB) at An-Najah National University. All data were kept confidential and stored in a locked file cabinet inside locked offices. The primary investigator and co-investigators had access to the original data forms. The principal investigator was responsible for reporting all serious or unexpected adverse events that influenced the safety of the research participants.

### *Statistical analysis*

This study used the statistical package of social science (SPSS) for data analysis. Demographic characteristics of the sample are presented using tables and/or figures as appropriate. The percentage of each study variable and the success rate were calculated. The significant difference between groups was assessed using the chi-squared test, Fisher exact test, and Mann-Whitney U test, as appropriate. The difference was considered significant when the P-value was $\leq 0.05$.

## RESULT

Baseline characteristic information for patients who underwent stenting for uLMCAD is presented in Table 1.

**Table (1):** Baseline characteristics of patients with uLMCA disease underwent PCI.

| ***Characteristic*** | **Frequency(%)** | **Mean**±SD |
|---|---|---|
| ***Age*** *(mean ± SD)* | | 65.4±11.3 |
| ***Gender*** | | |
| Male<br>Female | 53 (75.7)<br>17 (24.3) | |
| ***Smoker*** | | |
| Yes<br>No | 36 (51.4)<br>34 (48.6) | |
| ***Diabetes*** | | |
| Yes<br>No | 46 (65.7)<br>24 (34.3) | |
| ***Hypertension*** | | |
| Yes<br>No | 55 (78.6)<br>15 (21.4) | |
| ***Previous Ischemic heart disease*** | | |
| Yes<br>No | 33 (47.1)<br>37 (52.9) | |
| ***CKD*** | | |
| Yes<br>No | 15(21.4)<br>55(78.6) | |

***SD****; standard deviation,* ***CKD****; Chronic kidney disease*

Approximately 75.7% of patients were male, and 51.4% were smokers. The mean age of the patients was 65.4 years (ranging from 33 to 89 years), approximately 78.6% of the patients had hypertension (HTN), and 65.7% of the patients had type II diabetes mellitus (DM). Previous ischemic heart disease existed in 47.1% of patients. Heart failure was found in approximately 40% of patients at admission, with a mean EF of 50% ± 11.9. Approximately 78% of patients had normal kidney function, and the remaining patients had chronic kidney disease, including end-stage renal disease, on renal replacement therapy.

The clinical characteristics of the patients, angiography findings, and intervention strategy are presented in Table 2.

All patients were referred to our center for cardiac catheterization for the following indications: unstable angina was the main presentation (45.7% of the patients); other presentations, such as non-ST elevation myocardial infarction (NSTEMI) or stable angina, were less common (34.3% and 18.6%, respectively); and STEMI due to occlusion of uLMCAD was seen in one patient, as shown in Table 2.

**Table (2):** Clinical characteristics at presentation, angiography finding, and intervention (n=70).

| ***Characteristic*** | **Frequency(%)** | **Mean**±SD |
|---|---|---|
| ***Presentation*** | | |
| Stable Angina<br>Unstable angina | 13 (18.6)<br>32(45.7) | |
| NSTEMI<br>STEMI | 24 (34.3)<br>1 (1.4) | |
| ***Access*** | | |
| Radial<br>Femoral | 50 (71.4)<br>20(28.6) | |
| ***Left the main finding*** | | |
| Distal<br>Nondistal | 59 (84.3)<br>11 (15.7) | |
| ***Syntax score*** | | 20.7 (±7.9) |
| ***Tirofiban infusion*** | | |
| Yes<br>No | 6 (8.6)<br>64 (91.4) | |
| ***Heparin infusion*** | | |
| YES<br>No | 50 (71.4)<br>20 (28.6) | |
| ***Stent Technique*** | | |
| Crossover<br>Crush<br>Tap | 40 (57.1)<br>27 (38.6)<br>03 (4.3) | |
| ***Stent length*** | | 24.9 (±7.9) |
| ***Stent diameter*** | | 3.54 (±0.47) |
| ***IABP*** | 2 (2.9) | |
| ***OCT guided PCI*** | 3 (4.3) | |
| ***Follow-up period (Months)*** | | 17.5 (±12.3) |

***SD****; standard deviation,* ***IABP;*** *Intra-aortic balloon pump,* ***OCT;*** *optical coherence tomography.*

The timing of cardiac catheterization and PCI was performed according to the guidelines for NSTE-ACS and STEMI and within one day of hospitalization in cases of stable angina. Radial access was the main approach for cardiac catheterization used in approximately 71.4% of patients. Most patients had distal uLMCAD, which involves bifurcation lesions at the ostial LAD and Cx. Only 11 patients (15.7%) had nondistal lesions, which included ostial and/or mid-shaft lesions in the LMCA. The complexity of the lesion was variable, with a mean syntax score of 20.7 ± 7.9. After angiography, many patients were advised to undergo CABG according to the guidelines. However, it was not performed after a heart team discussion due to the comorbidities of the patients and the high risk of surgery. Moreover, two patients refused to undergo CABG, and one developed chest pain requiring urgent revascularization.

During the intervention, the 2-stent strategy was used in 30 patients (42.9%) using the crush or tap technique, and the crossover technique with a 1-stent strategy was used in the remaining patients. All the stents used in the PCI were drug-eluting stents (DES); the mean length was 24.9 ± 7.9, and the mean diameter was 3.5 ± 0.47. Optical coherence tomography (OCT)-guided PCI was used in 3 patients (4.3%). An infusion of heparin and tirofiban was sometimes used following the procedure to improve TIMI flow, and it was reported in 50 patients (71.4%) and 6 patients (8.6%), respectively. Figure 1 represents a patient who underwent stenting for the distal left main coronary artery.

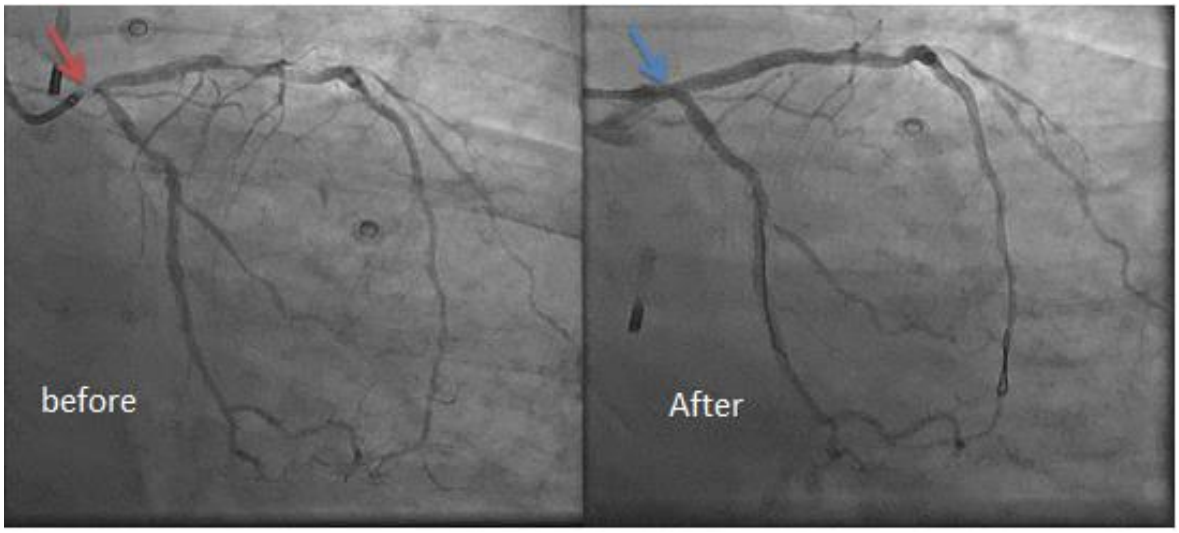


**Figure (1):** Cardiac catheterization of the left coronary system; the left side represents the left coronary system before stenting, which showed significant stenosis in the bifurcation of the distal left main artery (red arrow), and the right side represents the left coronary system after stenting of distal left main artery (blue arrow).

All patients who underwent successful PCI were discharged on dual antiplatelet (aspirin 100 mg once daily and clopidogrel 75 mg once daily) and high-dose statins for one year and then continued on aspirin and statins afterward. Approximately 34 patients (48.6%) were discharged on clopidogrel 75 mg twice daily for 2 weeks and continued the same conventional treatment.

Outcomes after stenting uLMCAD are presented in Table 3. Most patients underwent successful PCI to uLMCAD and were discharged in good general condition. Only 1 patient (1.4%) died due to septic shock before discharge. The mean duration of follow-up after the procedure was 17.5 ± 12.3. Only three patients (4.3%) died during follow-up; two died from COVID-19 pneumonia, and one died during cardiac CABG surgery.

**Table (3):** Clinical outcome after stenting *uLMCAD.*

| ***Characteristic*** | **In-hospital** | **From intervention till the time of follow-up** |
|---|---|---|
| ***Death from any cause*** | 1 (1.4) | 4(5.7) |
| Cardiac | 0 (0) | 1 (1.4) |
| Noncardiac | 1 (1.4) | 3 (4.3) |
| ***Target lesion failure*** | 0 (0) | 6 (8.6) |
| Cardiac death | 0 (0) | 1 (1.4) |
| Target vessel revascularization | 0 (0) | 6 (8.6) |
| ***Major Adverse Cardiac Event*** | 1 (1.4) | 8 (11.4%) |

Most patients reported improvement in their condition regarding shortness of breath or chest pain. During follow-up, 19 patients (27.1%) developed a clinical picture that required cardiac investigations. Seventeen patients underwent angiography; most (64.7%) had a patent stent in the left main artery. Only six patients (8.6%) found stent restenosis in the left main stent required target lesion revascularization. The mean duration for angiography follow-up was 10.65 ±7.73 months.

There was no association between MACE and any variable included in the analysis, as shown in Table 4. However, target lesion failure was statistically associated with the stent technique and the number of diseased vessels (Table 5).

The rate of target lesion failure was higher with the non-crush technique than with the crush technique (14% vs. 0%, P=0.03). In addition, the 3-vessel disease had a higher rate of target lesion failure than the 1-2-vessel disease (16.7% vs. 2.5%, P-value 0.048). Other variables, including syntax score and site of left main disease, had no statistically significant association with our outcomes.

**Table (4):** Major Adverse Cardiac Event with background and clinical characteristics.

| *Characteristic* | Major Adverse Cardiac Event | | P-value* |
|---|---|---|---|
| | No (62) | Yes (8) | |
| ***Gender*** | | | |
| Male | 47 (88.7%) | 6 (11.3%) | 0.649 |
| Female | 15 (88.2%) | 2 (11.8%) | |
| ***Smoker*** | | | |
| Yes | 32 (88.2%) | 4 (11.8%) | 0.612 |
| No | 30 (88.9%) | 4 (11.1%) | |
| ***Diabetes*** | | | |
| Yes | 41 (89.1%) | 5 (10.9%) | 0.706 |
| No | 22 (91.7%) | 02 (8.3%) | |
| ***Hypertension*** | | | |
| Yes | 47 (85.5%) | 8 (14.5%) | 0.619 |
| No | 15 (100.0%) | 0 (0.00%) | |
| ***CKD*** | | | |
| Yes | 12 (80.0%) | 3 (20.0%) | 0.355 |
| No | 50 (90.9%) | 5 (9.1%) | |
| ***Left the main finding*** | | | |
| Distal | 52 (88.1%) | 7 (11.9%) | 0.632 |
| Nondistal | 10 (90.9%) | 1 (9.1%) | |
| ***Vessels*** | | | |
| One or two | 38 (95.0%) | 2 (5.0%) | 0.066 |
| Three | 24 (80.0%) | 6 (20.0%) | |
| ***Stent Technique*** | | | |
| Crossover | 36 (85.0%) | 6 (15.0%) | 0.132 |
| Tap | 2 (66.7%) | 1 (33.3%) | |
| Crush | 26 (96.3%) | 1 (8.6%) | |
| ***Syntax*** | 20.1(±7.7) | 24.8(±8.6) | 0.115** |
| ***Number of stents*** | | | |
| One | 34 (85.0%) | 6 (15.0%) | 0.452 |
| Two | 28 (93.3%) | 2 (6.7%) | |

***** *Fisher exact test, **Mann–Whitney U test*

**Table (5):** Target lesion failure with background and clinical characteristics.

| *Characteristic* | Target lesion failure | | P-value* |
|---|---|---|---|
| | No (62) | Yes (8) | |
| ***Gender*** | | | |
| Male | 48 (60.6%) | 5 (9.4%) | 0.547 |
| Female | 16 (94.1%) | 1 (5.9%) | |
| ***Smoker*** | | | |
| Yes | 34 (91.7%) | 3 (8.3%) | 0.635 |
| No | 31 (91.2%) | 3 (8.8%) | |
| ***Diabetes*** | | | |
| Yes | 42 (91.3%) | 4 (8.7%) | 0.666 |
| No | 22 (91.7%) | 2 (8.3%) | |

| *Characteristic* | Target lesion failure | | P-value* |
|---|---|---|---|
| | No (62) | Yes (8) | |
| ***Hypertension*** | | | |
| Yes | 49 (89.1%) | 6 (10.9%) | 0.221 |
| No | 15 (100.0%) | 0 (0.00%) | |
| ***CKD*** | | | |
| Yes | 14 (93.3%) | 1 (6.7%) | 0.381 |
| No | 50 (90.9%) | 5 (9.1%) | |
| ***Left the main finding*** | | | |
| Distal | 53 (89.8%) | 6 (10.2%) | 0.580 |
| Nondistal | 11 (100.0) | 0 (0.00%) | |
| ***Vessels*** | | | |
| One or two | 39 (97.5%) | 1 (2.5%) | 0.048 |
| Three | 25(83.3%) | 5 (16.7%) | |
| ***Stent Technique*** | | | |
| Crossover | 35 (87.5%) | 5 (12.5%) | 0.037 |
| Tap | 2 (66.7%) | 1 (33.3%) | |
| Crush | 27 (100.0%) | 0 (0.00%) | |
| ***Syntax*** | 20.2(±7.7) | 25.7(±8.9) | 0.393** |
| ***Number of stents*** | | | |
| One | 35 (87.5%) | 5 (12.5%) | 0.115 |
| Two | 29 (96.7%) | 1 (3.3%) | |

***** *Fisher exact test, **Mann–Whitney U test.*

## DISCUSSION

Stenting of uLMCAD has been developing in the last two decades. Different techniques, newer generations of DES, varying anatomic complexity, and patient selection play a major role in the reported outcomes of stenting uLMCAD. In our institution, in-hospital mortality and MACE were reported in only one patient (1.4%) who underwent stenting for uLMCAD, the same as the 30-day event rate. This is consistent with other studies that reported almost the same rate. In a systemic review, mortality and MI during hospitalization were 2.3% and 2.5%, respectively (27). Moreover, in the most recent trial (the EXCEL trial), it was reported that 30-day mortality was 1% and MACE was 4.3% (28). These outcomes resulted from a good selection of patients who are candidates for intervention, using the newer generation of stents, highly skilled interventional cardiologists in our department, and high-quality medical care during the hospitalization period.

Regarding long-term outcomes, a systematic review reported MACE in 14.7% (6.2%-23.2%), death in 4.1% (1.7%-6.6%), and TVR in 6.7% (27). Our results were comparable to those reported in the systemic review, as shown in Table 4, despite our median follow-up being longer (17 months in our patients compared to 10 months in the systemic review). Additionally, the one-year outcome in the recent Excel trial had a MACE of 12.7%, a mortality rate of 3.4%, and a TVR of 7% (28), which is very close to our result, although we have a longer duration of follow-up. Another observational trial for 2 years of outcomes of stenting uLMCAD stenting showed MACE of 11.6%, death of 2.6%, and TVR of 6.5% (29). Therefore, our outcome is acceptable when compared with trials worldwide. They just need to follow them more to see the long-term outcome.

The last ESC guidelines, which were published in 2018 regarding the management of uLMCAD, reported a class I indication for PCI if the syntax score is ≤ 22 and class IIa if the syntax score is > 22 and < 33, while it recommended going for CABG if the syntax score is ≥ 33 (20). This was based on the recent EXCEL, PRECOMBAT, SYNTAX, and NOBLE trials (11, 28, 30, 31). However, our study had no linear - statistically significant - association between the syntax score and the primary outcome. In addition, there was no significant association between stenting

highly complex lesions compared to low-intermediate lesions and target lesion failure. However, this could be due to the small sample size. Other studies reported worse outcomes with bifurcation (distal) than nondistal lesions (14). In our study, although all patients with target lesion failure were in the distal lesion group, the difference between the two groups was not statistically significant, possibly due to the small sample size.

The optimal stenting technique is debated, mainly in bifurcation lesions, and early studies suggested better outcomes with a one-stent strategy than a 2-stent strategy (16). However, the recently published DKCRUSH-V randomized trial found that the 2-stent strategy has a lower rate of target lesion failure than the 1-stent strategy (17). After an average of 17 months of follow-up, target lesion failure occurred more frequently with a 1-stent strategy than a 2-stent strategy; it was statistically significant with the crush technique only.

There were many limitations encountered in our study. First, it was a retrospective study with many data points that could be missed, and we cannot observe each outcome at different times. Second, our sample size was too small to obtain a reliable association between outcomes and variables. Third, it represents a single center, which will affect the external validity of our results. Finally, an observational study over a longer period is needed to confirm our findings.

## CONCLUSION

Revascularization of uLMCAD is a complex decision that requires appropriate lesion assessment and heart team discussions. However, based on our data, we think stenting of uLMCAD in our center is effective with excellent immediate and long-term outcomes.

### Abbreviations

uLMCAD: unprotected left main coronary artery disease, CABG: coronary artery bypass graft, PCI: percutaneous coronary intervention, MACE: major adverse cardiac event, TVR: target vessel revascularization, TLF: target lesion failure, LMCA: left main coronary artery, LAD: left anterior descending, Cx: circumflex, HTN: hypertension, DM: diabetes mellitus, STEMI: ST elevation myocardial infarction, NSTEMI: non-ST elevation myocardial infarction, DES: drug-eluting stent, TIMI: thrombolysis in myocardial infarction, ESC: European society of cardiology.

## DECLARATION

### Consent for publication

No images or other personal data might compromise the anonymity of the patients.

### Ethics approval and consent to participate

The international review board of An-Najah National University approved the study archived number (3) Sep. 2019.

### Availability of data and materials:

All data supporting the study are presented in the manuscript or available upon request from the corresponding author.

### Competing interest

The authors state that they do not have any conflicting interests.

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### Authors' contributions

YD, YI, and HH designed the study and its protocol. HH, ZN, RY, AK, and AA collected the data. All authors participated in the drafting of the manuscript. All authors read and approved the final manuscript.

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