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A Comparison of Thrombolytic Therapy and Primary Angioplasty in Patients with Acute Myocardial Infarction

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ABSTRACT

Background and Objective: The standard treatment for patients with acute myocardial infarction is to reestablish blood flow in the blocked vessels, which is possible through angioplasty and thrombolytic therapy. However, even in developed countries, some patients still do not undergo coronary interventional therapy due to difficulties in accessing centers capable of performing primary angioplasty and the lack of prepared angiography departments, which can lead to undesirable consequences. Therefore, this study was conducted to compare the therapeutic outcomes of primary angioplasty and thrombolytic therapy.

Methods: This cross-sectional study was conducted on 291 patients with ST segment elevation myocardial infarction (STEMI) referred to medical centers under the auspices of Babol University of Medical Sciences. Patients undergoing Primary Percutaneous Coronary Intervention (PPCI) (n=213) or thrombolytic therapy (n=78) were evaluated and compared in terms of demographic and clinical information at the time of referral, mortality rate, major cardiovascular events, need for repeat PCI, and need for readmission.

Findings: The mean age of the patients was 60.55±11.90 years and 72% of the patients were male. Repeat single-vessel PCI was 11% (6 cases) in the Primary Percutaneous Coronary Intervention (PPCI) group and 23% (7 cases) in the thrombolytic therapy group. Readmission due to chest pain and shortness of breath was 30% (59 cases) in the PPCI group and 39% (38 cases) in the thrombolytic therapy group. The odds of mortality in patients treated with thrombolytic therapy compared to PCI were 1.38 times (p=0.56, OR=1.38), which was not significant. Furthermore, the odds of mortality decreased significantly with increasing EF (p=0.001, OR=14.64). Ejection Fraction (EF) and Functional Class (FC) were not significantly different between the two groups. The average time interval from onset of pain to hospital admission and thrombolytic therapy was 276±147 and 33±5 minutes, respectively, and in the PCI group it was 323±169 and 37±6 minutes, respectively. The odds of recurrent myocardial infarction (MI) in patients treated with thrombolytic therapy were 1.53 times higher than in patients treated with PPCI (OR=1.53, p=0.54), which was not significant.

Conclusion: According to the results of this study, treatment outcomes in both groups were better if the patient had visited the hospital within a short time from the onset of pain. The rate of recurrent MI and single vessel MI did not differ between the two groups.

Keywords: *Percutaneous Coronary Intervention, Thrombolytic Therapy, Myocardial Infarction*.

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Introduction

Irreversible death and necrosis of the heart muscle due to prolonged lack of blood supply (ischemia) is called acute myocardial infarction. This disease is relatively common, with 1.5 million cases occurring annually in the United States (1). The standard treatment for a patient with ST segment elevation myocardial infarction (STEMI) is to re-establish blood flow in the blocked vessels (reperfusion) with the aim of preventing myocardial necrosis, heart failure, and ultimately increasing the patient's life expectancy (2), which is performed by two methods: thrombolytic therapy and percutaneous coronary intervention (PCI).

Percutaneous transluminal coronary angioplasty (PTCA), or percutaneous coronary intervention (PCI) was first introduced in 1977 by Andreas Gruentzig in Zurich, Switzerland, as a catheter-based procedure that was an alternative to open heart surgery. Initially, this procedure was performed only on an elective and non-emergency basis, but after several decades of significant progress in this field, PCI is now considered the most effective approach in saving patients with acute myocardial infarction (3).

If PCI is not available, the next treatment option is thrombolytic therapy. This method uses clot-busting drugs to try to remove the blockage in the coronary artery. Thrombolytic therapy has the greatest benefit in terms of mortality reduction if administered within 12 hours of symptom onset and has the greatest absolute benefit if administered within 2 hours of symptom onset (4).

Based on this evidence and according to the European Society of Cardiology (ESC) guidelines as well as the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines, if PCI cannot be performed within 120 minutes of the diagnosis of STEMI, thrombolytic therapy is recommended as initial treatment in the absence of contraindications (5).

Common thrombolytic drugs include streptokinase, alteplase, reteplase, and tenecteplase. Fibrin-specific plasminogen activators, including tenecteplase and reteplase, provide better thrombolysis in myocardial infarction (TIMI) flow grade 3 and reduce the chance of re-clotting compared with streptokinase, which is associated with a decrease in 30-day mortality (6). Fibrinolysis treatment should be administered within 15 minutes of the diagnosis of STEMI, and the effectiveness gradually decreases with increasing time to start treatment from the moment of clot formation. However, fibrinolysis treatment has limitations, and in 25% of cases, thrombolysis is not achieved despite timely administration, and in about a quarter of successful thrombolysis cases, clot re-formation and re-MI occur. Moreover, in elderly patients, the chance of cerebral hemorrhage with thrombolytic treatment increases (7). A study conducted in Peru in 2022 showed no difference in in-hospital outcomes between patients with STEMI who received thrombolytic therapy or PPCI, and similar results were found in propensity score matching (PSM), rates of cardiovascular mortality, post-infarction heart failure, and successful reperfusion (8).

Even in developed countries, some patients still fail to receive coronary intervention due to difficulties in accessing centers capable of performing primary angioplasty and the lack of prepared angiography departments, and sometimes there is a significant delay in the patient's treatment process, which can be associated with undesirable consequences. Considering the health care system and access to health services and the shortage of coronary intervention centers, the proportion of patients with STEMI who undergo PPCI is low. Therefore, the greater availability and simplicity of thrombolytic agent administration make this approach a reasonable alternative. In addition, no similar study has been conducted in our region in this regard. Therefore, the aim of this study was to compare the treatment outcomes of primary PCI versus thrombolytic therapy in health centers of Babol, Northern Iran.

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Methods

This cross-sectional study was conducted in a 3-year period after approval by the Ethics Committee of Babol University of Medical Sciences with the code IR.MUBABOL.HRI.REC.1398.033. The study was conducted on all patients diagnosed with STEMI in Babol medical centers who underwent primary PCI and thrombolytic therapy. Patients diagnosed with STEMI who underwent primary PCI or thrombolytic therapy were included in the study. In case of patient death before treatment, patients who were candidates for CABG (Coronary Artery Bypass Graft), patients with liver failure or severe renal failure (GFR<30), patients prohibited from long-term dual antiplatelet therapy or anticoagulant drugs, and lack of consent or cooperation from patients and their companions were excluded from the study.

Some data were extracted from the patients' records, including demographic information (age and gender) and clinical information (history of underlying disease, medications, time of chest pain onset, other clinical symptoms, and ECG changes). In addition, the average time interval from admission to emergency department until receiving thrombolytic therapy or primary PCI treatment was recorded in all patients. Duration of hospitalization, mortality rate, major adverse clinical events (MACE), need for repeat PCI up to one month later, and need for readmission were obtained from the patients.

The collected data were statistically analyzed using SPSS 23, and Chi-square and logistic regression tests. Continuous quantitative variables were expressed as mean±standard deviation and qualitative frequency distribution was expressed as percentage, and $p<0.05$ was considered significant.

Results

Among 337 patients with STEMI referred to Babol medical centers over a 3-year period, 8 died at the time of admission due to cardiogenic shock and hemodynamic instability, and 38 were unresponsive. Of the remaining 291 patients, 78 received thrombolytics and 213 underwent angiography.

Of the 78 patients who received thrombolytics, 11 (14%) died within 24 hours of admission. Five patients did not undergo angiography after admission due to advanced age and lack of chest pain or elevated creatinine. Five patients of the remaining 62 patients who underwent angiography and 47 patients of the 213 patients who underwent primary angioplasty at the time of admission were candidates for CABG and were excluded from the study, and 166 patients underwent PPCI. Two of the PPCI patients died on the first day (both were single-vessel). After angiography in thrombolytic recipients, 7 patients were candidates for drug therapy and did not undergo angioplasty. After receiving thrombolytics, 27 patients became asymptomatic and underwent elective PCI, and 23 patients underwent rescue PCI due to chest pain.

The mean age of the patients was 60.55±11.90 years. The mean age of the patients receiving thrombolytic therapy was 63.74±11.68 years and the mean age of the patients receiving PPCI was 58.36±10.82 years. In the PPCI group, 76.50% (127 patients) of the patients were male and 23.5% (39 patients) were female, and 63% (46 patients) of the patients in the thrombolytic group were male and 37% (27 patients) were female.

In PPCI patients, the average time interval from pain onset to hospital admission was 383±316 minutes and the average time interval from PPCI to hospital admission was 66±21 minutes. In the thrombolytic therapy group, in patients who underwent elective PCI, the average time interval from pain onset to hospital admission and the average time interval from thrombolytic administration to hospital admission were 276±147 minutes and 33±5 minutes, respectively. In patients who underwent rescue PCI, the average time interval from pain onset to hospital admission and the average time interval from thrombolytic administration to hospital admission were 323±169 minutes and 37±6 minutes, respectively.

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Among the 164 patients undergoing PPCI and 62 patients undergoing thrombolytic therapy who remained after the first day of treatment, the results showed that 59 patients (36%) in the PPCI group and 38 patients (61.3%) in the thrombolytic group were readmitted. Of these readmitted cases, 30% of the PPCI group and 39% of the thrombolytic group were readmitted due to shortness of breath and chest pain, which was not statistically significant between the two groups. 54 patients (32.9%) in the PPCI group and 30 patients (48.4%) in the thrombolytic group underwent repeat PCI, of which 6 patients in the PPCI group and 7 patients in the thrombolytic group underwent single-vessel PCI, which was statistically significant (Table 1) ($p<0.05$).

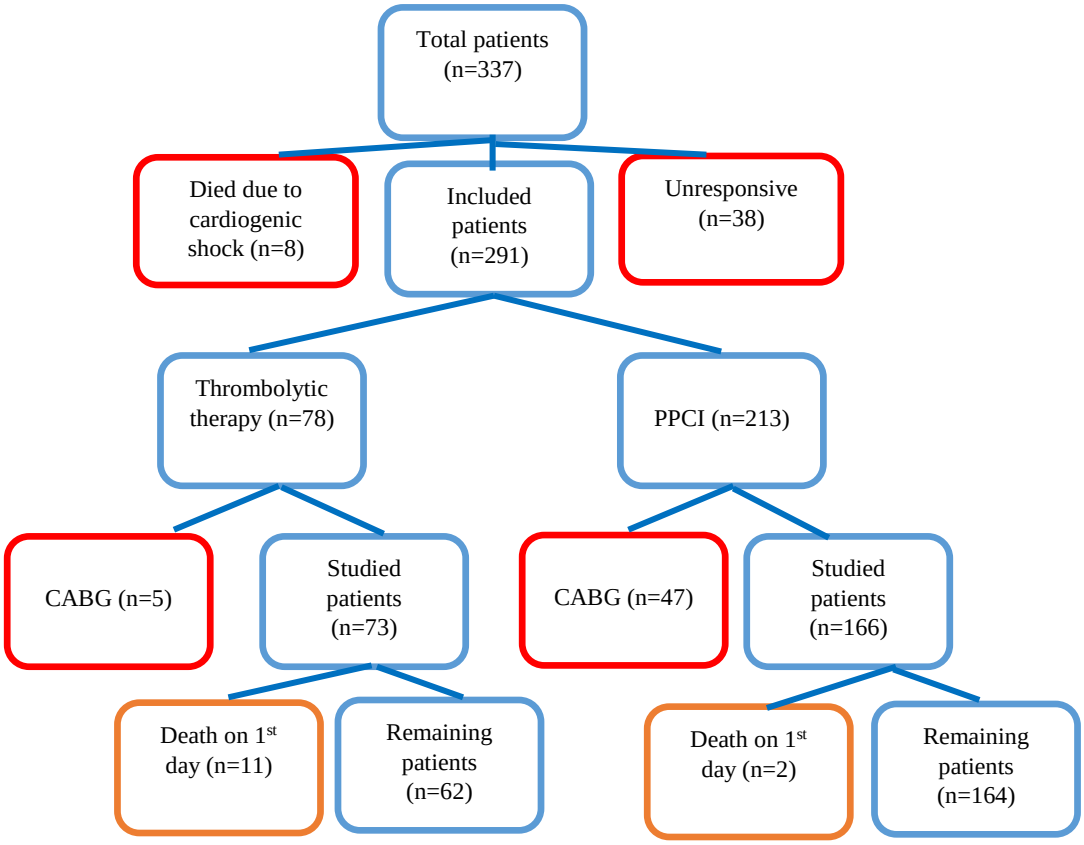

Figure 1. Systematic process of enrolling patients in the study

Table 1. Evaluation of the rate of readmission, repeat PCI, and repeat single-vessel PCI in patients in the two groups

Treatment group	Readmission Number(%)	Repeat PCI Number(%)	Repeat single-vessel PCI Number(percentage from repeat PCI)
PPCI (n=164)	59(36)	54(32.9)	6(11.1)
Thrombolytic (n=62)			
Elective PCI (n=27)	19(70.4)	16(59.3)	4(25)
Rescue PCI (n=23)	16(69.6)	14(16.9)	3(21.4)
Drug therapy after angiography (n=7)	2(28.6)	0(0)	0(0)
No angiography (n=5)	1(20)	0(0)	0(0)
Total	38(61.3)	30(48.4)	7(23.3)

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In patients receiving thrombolytics, 11 patients died within the first 24 hours after receiving thrombolytics in the hospital, and 5 patients developed drug-related complications including gross hematuria (one patient), gastrointestinal bleeding (GIB) (one patient), and intracranial hemorrhage (ICH) (three patients). Also, two PPCI cases died on the first day (both were single-vessel). In this study, patients who died during the first day in the hospital were excluded from the study, and the remaining deaths occurred after discharge from the hospital (up to one month later) and were included in the study.

In PPCI patients, out of 20 (12.2%) deaths after 24 hours, 9 (45%) were due to cardiac disease. Also, 2 patients had drug-related complications (one patient had hematuria and one had gastrointestinal bleeding). Eight (4.9%) patients had recurrent MI, of which 4 (50%) had recurrent single-vessel MI. 24 hours after starting thrombolytic therapy, out of 10 (16.1%) patients who died, 6 cases (60%) were due to cardiac disease. Six (9.7%) patients had recurrent MI, of which 3 (50%) had recurrent single-vessel MI. The results showed no significant relationship between the two groups (Table 2).

In Elective PCI patients, 4 patients (14.8%) died, 3 patients (75%) had cardiac disease, and 3 patients (11.1%) had recurrent MI, and 1 patient (33.3%) had recurrent single-vessel MI. In Rescue PCI patients, 2 patients (8.7%) died, which was not due to cardiac disease, and 2 patients (8.7%) had recurrent MI, and 1 patient (33.3%) had recurrent single-vessel MI. There was no statistically significant difference between the two groups in terms of mortality, recurrent MI, and recurrent single-vessel MI (Table 2).

In patients receiving thrombolytics, 5 patients developed drug-related complications, including gross hematuria (one patient), GIB (one patient), and ICH (three patients).

In PPCI patients, 116 (70.7%) had FC1 and the mean EF of the patients was 45.1±8. In patients receiving thrombolytics, 31 (50%) had FC1 and their mean EF was 42.6±8.6. In patients who underwent elective PCI, 17 (63%) had FC1 and their mean EF was 43.3±9.7. In patients who underwent rescue PCI, 11 (47.8%) had FC1 and their mean EF was 42.4±8.4. The results obtained between the two groups were not significant (Table 3) ($p<0.05$). The highest rate of coronary artery involvement was related to LAD with 106 cases, followed by RCA with 86 cases and LCX with 40 cases (Figure 1).

Table 2. Assessment of the rate of complications, death, and recurrent MI in patients in the two groups

Treatment group	Death Number(%)	Deaths from heart disease Number(percentage from cases of death)	Non-cardiac complications Number(%)	Recurrent MI Number(%)	Recurrent single vessel MI Number(percentage from recurrent MI)
PPCI (n=164)	20(12.2)	9(45)	2(1.2)	8(4.9)	4(50)
Thrombolytic (n=62)					
Elective PCI (n=27)	4(14.8)	3(75)	2(7.4)	3(11.1)	1(33.3)
Rescue PCI (n=23)	2(8.7)	0(0)	1(4.3)	2(8.7)	1(50)
Drug therapy after angiography (n=7)	1(14.3)	1(100)	1(14.3)	0(0)	0(0)
No angiography (n=5)	3(60)	2(66.7)	1(20)	1(20)	1(100)
Total	10(16.1)	6(60)	5(8.1)	6(9.7)	3(50)

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Table 3. FC and EF evaluation in patients in two groups

Treatment group	FC1 Number(%)	FC2 Number(%)	FC3 Number(%)	FC4 Number(%)	EF Mean±SD
PPCI (n=164)	116(70.7)	42(25.3)	7(4.22)	1(0.6)	45.1±8
Thrombolytic (n=62)					
Elective PCI (n=27)	17(63)	7(25.9)	2(7.4)	1(3.7)	43.3±9.7
Rescue PCI (n=23)	11(47.8)	9(39.1)	2(8.7)	1(4.3)	42.4±8.4
Drug therapy after angiography (n=7)	2(28.6)	4(71.4)	0(0)	0(0)	47.1±4.9
No angiography (n=5)	1(1.4)	3(4.2)	1(1.4)	0(0)	34±8.2
Total	31(50)	23(37.1)	5(8.1)	2(3.2)	42.6±8.6

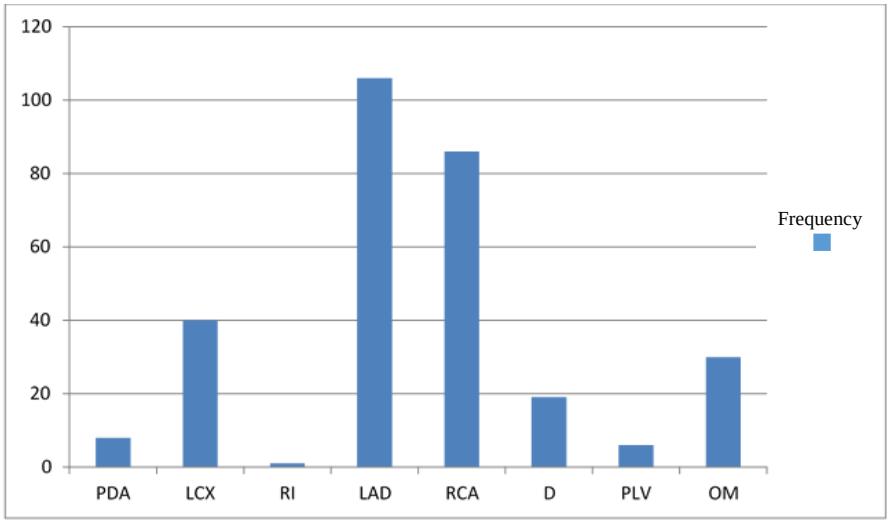

Figure 2. Frequency of coronary arteries in patients

PDA: Posterior Descending Artery, LCX: Left Circumflex, RI: Ramus Intermedius, LAD: Left Anterior Descending, RCA: Right Coronary Artery, D: Diagonal Branches, PLV: Posterior Left Ventricular, OM: Obtuse Marginal

In the comparison of thrombolytic and PPCI groups, the odds of repeat PCI in patients receiving thrombolytic therapy were twice as high as in patients undergoing PPCI ($p<0.05$). The chance of death in the thrombolytic therapy group was 1.38 times higher than in the PPCI group ($p=0.56$, OR=1.38), which was not statistically significant. Also, with increasing EF, the odds of death significantly decreased ($p=0.001$, OR=14.64), and with increasing time interval from pain onset to hospital visit, the odds of death significantly increased ($p=0.02$, OR=1.20). For patients receiving thrombolytic therapy, the odds of recurrent MI were 1.53 times higher than in patients undergoing PCI, which was not statistically significant ($p=0.54$, OR=1.53).

Discussion

The results of this study show that the incidence of complications and clinical outcomes in the PPCI group was low and included two cases of minor bleeding. In the study of Rashid et al., cerebral hemorrhage was mentioned in the two groups in a similar way; in a study of 980 patients who underwent PCI or thrombolytic therapy, they reported that the incidence of mortality, re-infarction, and stroke was not significantly different, but the tendency to bleed was significantly higher in thrombolytic therapy (9). In the

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present study, the rate of cerebral hemorrhage was higher in the medical treatment condition than in PPCI. The mortality rate on the first day of hospital admission (within the first 24 hours of admission) was 11 after thrombolytic therapy and 2 after PPCI, which was higher than the short-term mortality in the study by Roule et al. (10).

The long-term mortality in this study was similar in the two groups, which is consistent with the study by Roule et al. (10). According to the study by Roule et al., compared with the PPCI group, thrombolytic therapy was associated with increased cardiovascular death, decreased risk of cardiogenic shock, increased risk of stroke, and increased hemorrhagic stroke, but the 1-year mortality and major bleeding rates were similar in the two groups (10). The overall prognosis depends on the extent of muscle damage. Good results are seen in patients who receive initial thrombolytic-perfusion therapy within 30 minutes of admission or PCI within the first 90 minutes (11).

Low left ventricular ejection fraction is a well-known predictor of in-hospital mortality (12-14). In a study aimed at determining factors associated with in-hospital mortality in patients with AMI in Tehran, Salarifar et al. found a significant inverse relationship between mean left ventricular ejection fraction and the frequency of in-hospital mortality; a decrease in mean left ventricular ejection fraction increased the frequency of in-hospital mortality (12). The results of our study indicated that there was no statistically significant difference in mean EF between PCI group and thrombolytic therapy group, and when comparing EF in these two treatment methods according to the location of MI, no significant difference was observed; however, mortality was significantly reduced with an increase in EF (p=0.001, OR=14.64), which is consistent with the study by Berrocal et al. (15).

In another study by Safi et al. comparing the results of emergency coronary angioplasty with thrombolytic therapy in patients with acute myocardial infarction in 2009, 144 patients were in the thrombolytic therapy group and 143 patients in the PPCI group. The EF rate in the thrombolytic therapy group was 43.8±11.9 and in the PPCI group was 42.19±9.8 (p=0.02), which was consistent with our study (16).

The results of our study showed that recurrent angina was less in patients undergoing PPCI than in the thrombolytic therapy group, and the odds of death significantly increased with increasing time from onset of pain until hospital admission (p=0.02, OR=1.20).

In our study, the highest level of involvement was related to the LAD vessel, followed by the RCA vessel, and then the LCX vessel. In addition, patients with more than one vessel involved had a significantly more than 10-fold odds of repeat PCI. The anatomical location of myocardial infarction is one of the factors predicting survival (17, 18). As observed in a number of studies, the prognosis between types of myocardial infarction differs based on their location, such that anterior myocardial infarction has a worse prognosis than inferior myocardial infarction (19-21).

In our study, patients receiving thrombolytics had a 1.5-fold higher risk of recurrent MI than those receiving PCI, but this was not statistically significant, which may be due to the small sample size. Previous studies after successful thrombolysis have shown evidence of early recurrence of ischemia (pain or ST-segment elevation) in 20–30% of patients (22, 23), coronary re-occlusion in 5–15% (24, 25), and re-infarction in 3–5% (26, 27). Re-infarction is associated with higher rates of in-hospital, short-term, and long-term mortality.

Patients treated with thrombolytic therapy were significantly more likely to undergo repeat PCI than those treated with PCI. Patients receiving thrombolytic therapy were 1.38 times more likely to die than those receiving PCI. According to the Survival and Ventricular Enlargement Trial, the most important predictor of long-term survival was patency of the infarcted artery, even after adjustment for ejection fraction, ventricular volume, and the presence of comorbidity (25, 27, 28), which our study also confirmed.

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In both studied groups, the results were better if the patient was admitted to the hospital within a short time after the onset of pain. Repeat single-vessel PCI was performed more often in the thrombolytic group than in the PPCI group. In both groups, the most frequent readmissions were due to chest pain and shortness of breath, and the rest were due to PCI of other vessels. ICH was more common in the thrombolytic therapy group, but hematuria and GIB were similar in the two groups. There was no significant difference in the rates of recurrent MI and single-vessel MI between the two groups.

Conflict of Interest: The authors declare that there are no conflicts of interest.

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