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Original Article

Early versus late intervention in patients with high-risk non-'ST'-elevation myocardial infarction

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Abstract

Introduction
With improvements in percutaneous coronary intervention and the advent of novel adjunctive pharmacotherapy agents (such as GP 2b/3a inhibitors, new antiplatelet agents, and intensive statin regimens), the safety and efficacy of early Percutaneous coronary intervention (PCI) in acute coronary syndrome (ACS) has improved significantly (1). Therefore, the current guidelines recommend a routine invasive strategy (angiography and revascularization if applicable) (2) in high-risk patients with non-'ST'-elevation ACS (NSTE-ACS).

Aim
The aim was to compare the results of early versus late intervention in patients with high-risk NSTE myocardial infarction (MI).

Patients and methods
This study was carried out on 60 patients who presented to the Emergency Department in the National Heart Institute with high-risk NSTEMI with GRACE score greater than 140 during the time period from December 2020 to July 2021. The patients fulfilled the following criteria: they had typical chest pain; they had ECG changes in the form of 'ST'-segment depression, 'T'-wave inversion, or even with normal ECG; they had elevated cardiac biomarkers; their estimated GRACE score was greater than 140. The eligible patients were divided into two groups: (there were no specific selection criteria for early or late intervention, but the selection was done randomly). Group A: included 30 patients with early treatment strategy as the angiography was performed as early as possible and within 12 h from the ischemic pain. Group B: included 30 patients with delayed treatment strategy as the angiography was performed after 48 h of intensive medical treatment.

Conclusion
Based on individual and careful patient and lesion assessments, early intervention in high-risk non-STEMI patients reduced the risk of in-hospital mortality and minor bleeding and consequently the time of hospital stay. It also decreased the occurrence of refractory angina, recurrent MI, and hospitalization for cardiac cause. It also helped to improve the ejection fraction.

Keywords: ECG, NSTEMI, PCI

Introduction

With improvements in percutaneous coronary intervention and the advent of novel adjunctive pharmacotherapy agents (such as GP 2b/3a inhibitors, new antiplatelet agents, and intensive statin regimens), the safety and efficacy of early PCI in ACS has improved significantly [1].

Therefore, the current guidelines recommend a routine invasive strategy (angiography and revascularization if applicable) [2] in high-risk patients with non-'ST'-elevation acute coronary syndrome (NSTE-ACS).

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Aim

The aim was to compare the results of early versus late intervention in patients with high-risk NSTE myocardial infarction (MI).

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Patients and methods

This study was carried out on 60 patients who presented to the Emergency Department in the National Heart Institute with high-risk NSTEMI with GRACE score.

Greater than 140 during the time period from December 2020 to July 2021.

The patients fulfilled the following criteria:

(1) They had typical chest pain.
(2) They had ECG changes in the form of 'ST'-segment depression, 'T'-wave inversion, or even with normal ECG.
(3) They had elevated cardiac biomarkers.
(4) Their estimated GRACE score was greater than 140.

The eligible patients were divided into two groups: (there were no specific selection criteria for early or late intervention, but the selection was done randomly).

Group A: included 30 patients with early treatment strategy as the angiography was performed as early as possible and within 12 h from the ischemic pain.

Group B: included 30 patients with delayed treatment strategy as the angiography was performed after 48 h of intensive medical treatment.

All patients were subjected to the following:

(1) Full history taking for detection of risk factors, including hypertension, diabetes mellitus, dyslipidemia, and smoking, as well as past history of prior MI or stroke.
(2) General and local cardiac examination.
(3) Laboratory investigation: including cardiac biomarkers (Treponin I and CK-MB), serum creatinine, lipid profile, complete blood count, and liver enzymes.
(4) Twelve-lead ECG.
(5) Transthoracic echocardiography.
(6) Assessment of the patient risk according to GRACE score.
(7) Coronary angiography and percutaneous coronary intervention:
    (a) Clinical in-hospital follow-up regarding.
    (b) Periprocedural MI.
    (c) Cardiogenic shock.
    (d) Stroke.
(8) Early assessment during hospital stay, including cardiac enzymes, bleeding complications, recurrent chest pain, and hemodynamic and echo data.
(9) Three months of clinical follow-up regarding MACE (major adverse cardiac events), including urgent revascularization, recurrent MI, death, and stroke.

Calculation of GRACE score for in-hospital mortality

Eight parameters are used for calculating GRACE score that include patient's age, heart rate, systolic blood pressure, Killip class, serum creatinine level, cardiac arrest at hospital admission, ST-segment deviation in ECG, and elevated cardiac marker.

1. Age (years)	Score		
≤30	0		
30-39	8		
40-49	25		
50-59	41		
60-69	58		
70-79	75		
80-89	91		
2. Heart rate (beats/min)	Score		
≤50	0		
50-69	3		
70-89	9		
90-109	15		
110-149	24		
150-199	38		
3. Systolic blood pressure (mm Hg)	Score		
≤80	58		
80-99	53		
100-119	43		
120-139	34		
140-159	24		
160-199	10		
≥200	0		
4. Killip class	Score		
I (no heart failure)	0		
II (crackles audible in the lower half of lung field)	20		
III (crackles audible in whole lung field)	39		
5. Serum creatinine (μmol/l)	Serum creatinine (mg/dl)		Score
0-34	0-0.38	1	
35-70	0.39-0.79	4	
71-105	0.80-1.19	7	
106-140	1.2-1.58	10	10
141-176	1.59-1.90	13	13
177-353	2.0-3.99	21	21
≥354	≥4.0	28	28
6. Cardiac arrest at hospital admission	Score		Score
Absent	0		0
Present	39		39
7. ST-segment deviation in ECG	Score		Score
Absent	0		0
Present	28		28
8. Elevated cardiac markers	Score		Score
Absent	0		0
Present	14		14

Results

Demographic characteristics, risk factors, and comorbidities

There was no statistically significant difference between the two groups as regards age, sex, hypertension, diabetes, current smoking, previous stroke and dyslipidemia but morbid obesity was significantly more prevalent in the late group [Table 1].

Table 1: There are no statistically significant difference between the two groups as regards the demographic data and risk factors except for morbid obesity which was more significant in the late group

	Early (n=30) [n (%)]	Late (n=30) [n (%)]	Independent t-test/χ^2	P
Age (years)				
Mean±SD	69.47±3.53	67.20±5.88	1.810	0.075
Range	61-74	51-75		
Sex				
Male	21 (70)	16 (53.3)	1.763	0.184
Female	9 (30)	14 (46.7)		
BMI kg/m^2				
18-25	5 (16.7)	4 (13.3)		
25-30	25 (83.3)	16 (53.3)	12.087	0.002
>30	0	10 (33.3)		
Smoking				
Yes	16 (53.3)	14 (46.7)	0.267	0.606
No	14 (46.7)	16 (53.3)		
HTN				
Yes	25 (83.3)	27 (90)	0.577	0.448
No	5 (16.7)	3 (10)		
DM				
Yes	20 (66.7)	21 (70)	0.077	0.781
No	10 (33.3)	9 (30)		
Dyslipidemia				
Yes	18 (60)	21 (70)	0.659	0.417
No	12 (40)	9 (30)		

DM, diabetes mellitus; HTN, hypertension.

Table 2: Comparison between early and late groups regarding previous history of M.I. and stroke, family history of CAD and initial LVEF

	Early [n (%)]	Late [n (%)]	χ^2	P
Previous MI				
Yes	4 (13.3)	12 (40)	5.455	0. 20
No	26 (86.7)	18 (60)		
Previous stroke				
Yes	0	7 (23.3)	7.925	0.005
No	30 (100)	23 (76.7)		
Family history of CAD				
Yes	15 (50)	21 (70.0)	2.500	0.114
No	15 (50)	9 (30)		
Initial LVEF %				
Mean±SD	49.20±8.51	54.60±7.11	2.666	0.010
Range	30-65	45-65		

MI, myocardial infarction; CAD, coronary artery disease; LVEF, Left ventricular Ejection fraction

Previous history of MI or stroke

The rates of previous MI four (13.3%) in the early PCI group versus 12 (40%) in the late PCI group, P = 0.20, which is statistically insignificant, previous stroke was 0 (0.0%) in the

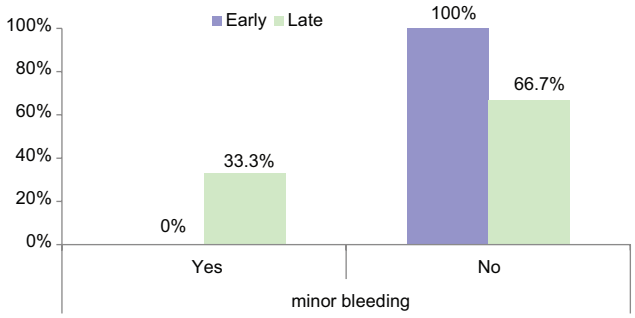

Figure 1: Minor bleeding.

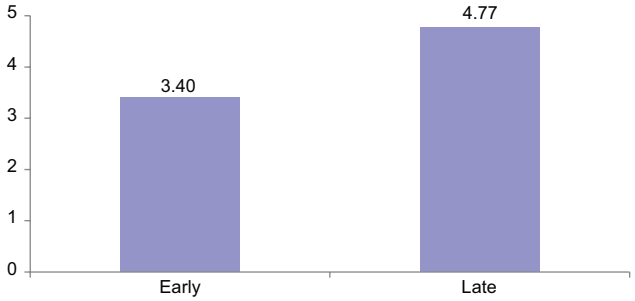

Figure 2: Coronary care unit (CCU) stay.

Table 3: The only statistically significant difference was in more consumption of contrast in the early group due to complete revascularization

	Early (n=30)	Late (n=30)	χ^2/t*	P
Access site				
Femoral	30 (100)	30 (100)	NA	NA
Site of lesion				
Single vessel	3 (10)	6 (20)		
Two vessels	20 (66.7)	14 (46.7)	2.588	0.274
Three vessels	7 (23.3)	10 (33.3)		
Contrast amount (ml)				
Mean±SD	73.33±19.22	53.67±15.86	4.322*	0.000
Range	40-100	35-80		
Total procedural duration (min)				
Mean±SD	44.47±11.47	31.50±12.74	4.143*	0.000
Range	20-70	15-50		
PCI				
Yes	27 (90)	30 (100)	3.158	0.076
No	3 (10)	0		

*0.001 highly significant

early PCI group versus seven (23.3%) in the late PCI group, $P = 0.005$, which is statistically highly significant, and family history of Coronary artery disease (CAD): 15 (50) in the early group versus 21 (70%) in the late group, $P = 0.114$, which is statistically insignificant (Table 2).

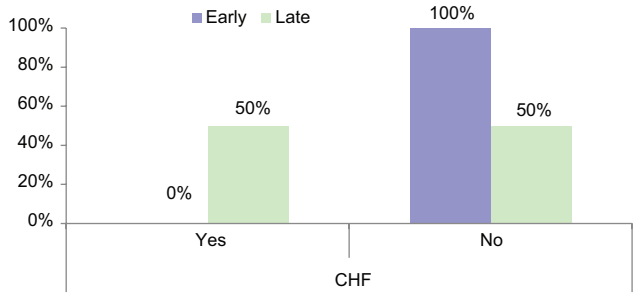

Figure 3: Congestive heart failure (CHF) rate.

Table 4: In-hospital complications

	Early ($n=30$)	Late ($n=30$)	χ^2/t*	P
Cardiac death				
Yes	0	1 (3.3)	1.017	0.313
No	30 (100)	29 (96.7)		
Noncardiac death				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		
Stroke				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		
CIN				
Yes	0	3 (10)	3.158	0.076
No	30 (100)	27 (90)		
Major bleeding				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		
Minor bleeding				
Yes	0	10 (33.3)	12.000	0.001
No	30 (100)	20 (66.7)		
Cardiogenic shock				
Yes	0	3 (10)	3.158	0.076
No	30 (100)	27 (90)		
Urgent CABG				
Yes	3 (10)	0	3.158	0.076
No	27 (90)	30 (100)		
Urgent PCI				
Yes	0	3 (10)	3.158	0.076
No	30 (100)	27 (90)		
[VF/VT]				
Yes	0	1 (3.3)	1.017	0.313
No	30 (100)	29 (96.7)		
CCU stay (day)				
Mean±SD	3.40±0.93	4.77±1.48	−4.283*	0.000
Range	2-5	3-10		

CIN, Contrast induced nephropathy. *0.001 highly significant.

Angiographic strategy

Coronary intervention was done in both groups using femoral approach (Table 3). The results show single-vessel disease three (10%) in early PCI group versus six (20%) in late PCI group, two vessels 20 (66.7%) in early versus 14 (46.7%) in late, and three vessels seven (23.3%) in the early PCI group versus 10 (33.3%) in the late PCI group, $P = 0.274$, which is statistically insignificant. Contrast amount (73.33 ± 19.22 in the early group vs. 53.67 ± 15.86 in the late group; $P = 0.000$). This may be due to total revascularization that was done in the early group.

Procedural time (44.47 ± 11.47 in the early group vs. 31.50 ± 12.74 in the late group).

PCI-procedure result was achieved in 27 (90%) of early group, compared with 30 (100%) in the late group ($P = 0.076$).

In-hospital complications

Complications were variable, but most of them were statistically insignificant between the early and late group: major bleeding and stroke (0 vs. 0%.). Regarding Contrast induced nephropathy (CIN) (0 vs. 3%, $P = 0.076$), early versus late, respectively, which was statistically insignificant. While the minor bleeding [0 vs. 10 (33.3%), $P = 0.001$], which was statistically highly significant. This may be due to the use of anticoagulants and antiplatelets in the late group till 5 days from admission.

Three patients developed cardiogenic shock in the late group: patients developed PCI-related MI, 0 (0.0%) versus 0, three patients needed urgent PCI in the late group, while no patient needed urgent PCI in the early group with $P = 0.076$, which is statistically insignificant (Figs. 1–3 and Table 4).

Table 5: Three months' outcomes

	Early [n (%)]	Late [n (%)]	χ^2	P
Cardiac death				
Yes	0	1 (3.3)	1.017	0.313
No	30 (100)	29 (96.7)		
Noncardiac death				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		
MI				
Yes	0	3 (10)	3.158	0.076
No	30 (100)	27 (90)		
CHF				
Yes	0	15 (50)	20.000	0.001
No	30 (100)	15 (50)		
Stroke				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		
Refractory angina				
Yes	0	9 (30)	10.588	0.001
No	30 (100)	21 (70)		

MI, myocardial infarction; CHF, congestive heart failure; CCU, Coronary care unit

Three months' outcomes

Clinical follow-up was performed for 3 months to document major adverse cardiac events (MACE) comprising all-cause mortality, recurrent MI, heart failure (HF), stroke, and refractory angina. Despite the 3-month cardiac mortality tended to be decreased in the early group, but this decrease was nonsignificant, 0 versus 3.3%, $P = 0.313$, between the early and late, respectively. There was no noncardiac mortality in both groups. There was an increase in recurrent MI (early, 0% versus 3 (10%), $P = 0.076$), which is statistically insignificant, HF 0 in the early PCI group versus 15 (50%) in the late PCI group with $P = 0.001$, which is statistically highly significant and stroke 0 versus 0% between the early and late group, respectively, which is statistically insignificant. The early group were highly significantly less suffering from refractory angina 0 versus 30%, $P = 0.001$ (Table 5).

Subsequent revascularization

About 13.3% of late-group patients had recurrent ischemia versus 0% in the early group with $P = 0.038$, which is statistically significant and 0% of patients referred to Coronary artery bypass grafting (CABG), target vessel revascularization, 0 versus 0% (Table 6).

Table 6: The rate of recurrent ischemia was more significant in the late group

	Early [*n* (%)]	Late [*n* (%)]	χ^2	*P*
Repeat revascularization				
Yes	0	0	NA	NA
No	0	0		
Recurrent ischemia				
Yes	0	4 (13.3)	4.286	0.038
No	30 (100)	26 (86.7)		
CABG				
Yes	0	0	NA	NA
No	30 (100)	30 (100)		

CABG, Coronary artery bypass grafting

Table 7: Re-hospitalization for cardiac cause was more significant in the late group and LVEF improvement was more significant in the early group

	Early (*n*=30)	Late (*n*=30)	χ^2/*t**	*P*
Rehospitalization for cardiac cause				
Yes	0	12 (40)	15.000	0.001
No	30 (100)	18 (60)		
Follow-up EF % 3 months				
Mean±SD	60.07±3.86	53.23±8.22	4.120	0.001
Range	55-65	35-65		

*P value = 0.001

Study of left ventricular function

The Left ventricular Ejection fraction (LVEF)% significantly improved in the early group ($P < 0.001$) as shown in Table 7.

Discussion

There is a debate about the optimum time for revascularization in patients with non-ST-segment-elevation myocardial infarction (NSTEMI) [3]. The 2014 AHA/ACC NSTE-ACS Guidelines and the 2015 ESC guidelines recommended an early invasive strategy (<24 h) in patients with at least one of the following high-risk criteria:

(1) Rise in cardiac troponin compatible with MI.
(2) Dynamic ST- or T-wave changes (symptomatic or silent).
(3) GRACE score greater than or equal to 140.

These recommendations arose from the meta-analyses of early invasive strategy that was associated with a statistically significant lower risk of recurrent ischemia [4].

In our study, we demonstrated that the early PCI group was significantly less suffering from refractory angina, 0 versus 30%, $P = 0.001$.

Despite the recurrent MI tended to be more in the late PCI group, but this increase was nonsignificant. Previous study conclusions suggested that NSTE-ACS patients initially hospitalized in non-PCI centers show the largest benefit from early angiography and revascularization [5].

In our study, we reported no significant difference between early and late intervention in high-risk non-STEMI as regarding rates of previous MI (13.3 vs. 40%, $P = 0.20$) and family history of CAD, 50 versus 70.0%, respectively, and $P = 0.114$ that was concordant with Thiele *et al.* [6] (24 vs. 20%, $P = 0.43$), and Mehta *et al*. [7] (19.7 vs. 20.9%, $P = 0.41$).

In our study, we found a significant difference between early and late intervention in high-risk non-STEMI as regarding rates of previous stroke. Previous stroke, 0 (0.0%) versus seven (23.3%), $P = 0.005$, respectively, that was concordant with Deepak and colleagues as they found that the stroke rate was 6.4 versus 14.3%, respectively, between the two groups with $P = 0.001$. This was in concordant with Badings and colleagues, where the difference was 1.1 versus 4.5%, respectively, and $P = 0.228$, and in Mehta and colleaguesit was 7.2 versus 7.5%, respectively, and $P = 0.71$, which is statistically insignificant.

In our study, there was a statistically nonsignificant difference in the percent of patients transferred to GABG in the early PCI group (10%) compared with 3.3% in late PCI group with $P = 0.31$ that was concordant with Montalescot and colleagues, where it was 4.1 versus 4.6% in the early versus late groups, and Thele and colleagues as CABG was 13% in both groups.

In our study, complications were variable, but most of them were statistically insignificant between the early and late group: major bleeding and stroke (0 vs. 0%). As regarding

CIN (0 vs. 3%, $P = 0.076$), early vs late, respectively, which was statistically insignificant, while the minor bleeding [0% in the early group vs. 10 (33.3%) in the late group, $P = 0.001$], which was statistically significant. This may be due to using anticoagulant and antiplatelet in the late group.

In our study, three patients developed cardiogenic shock (10%) in late PCI group vs no patients in the early PCI group (0%) with $P = 0.07$ and it was concordant with Deepak and colleagues, which was 2.3 versus 2.6% in the early versus the late groups. This may be due to rapid revascularization in early group that led to restoration of blood flow within few hours of coronary occlusion, which resulted in myocardial salvage, while in the late group, there was stunning or hibernation of the myocardium.

In our study, as regards in-hospital mortality, only one patient died in the late group, which represents 3.3% with $P = 0.313$, which is insignificant. This was not concordant with Milosevic *et al*. [8], where it was 4.3% in the early group versus 13.0% in the late group with $P = 0.008$.

This may be explained by the small number of our studied patients (60) versus (323 NSTEMI) in Milosevic and colleagues.

In our study, the LVEF% significantly improved in the early PCI group 60.07 ± 3.86 versus 53.23 ± 8.2 ($P < 0.001$).

In our study, clinical follow-up was performed for 3 months to document major adverse cardiac events (MACE) comprising all-cause mortality, recurrent MI, HF, stroke, and refractory angina. Despite the 3-month cardiac mortality tended to be less in the early group, but this decrease was nonsignificant, 0 versus 3.3%, $P = 0.313$, between the early and late, respectively. This was concordant with Mehta and colleagues when the mortality was 4.8% in the early PCI group versus 5.9% in the late PCI group with $P = 0.19$. This was also concordant with Badings and colleagues as they approved that mortality was 1.1% in the early PCI group versus 1.1% in the late PCI group ($P > 0.99$).

In our study, there was no noncardiac mortality in both groups, but as regards recurrent MI [early 0% vs. late 3 (10%) with $P = 0.076$], which was statistically insignificant. These findings were concordant with Badings and colleagues, who showed 1.1% recurrent MI in the early PCI group versus 2.3% in the late PCI group with $P = 0.329$, and Milosevic and colleagues who showed 0.6% recurrent MI in the early PCI group versus 4.3% in the late PCI group with $P = 0.07$.

In our study, it is important that our analysis confirmed that the early PCI group was significantly less suffering from refractory angina, 0 versus 30% in late PCI group with $P = 0.001$. This was in agreement with Mehta and colleagues and Thiele and colleagues who confirmed that refractory angina in the early PCI group was 1% versus 3.3% in the late PCI group (in Mehta and colleagues) and it was 0 versus 10% (in Thiele and colleagues) with $P = 0.001$.

In our study, there were significant differences in recurrent ischemia 0% in early versus 13.3% in late group with $P = 0.038$, that agreed with Badings and colleagues, who show 2.3% in the early PCI group versus 18.2% in the late PCI group with $P = 0.030$.

Conclusion

Based on individual and careful patient and lesion assessments, early intervention in high-risk non-STEMI patients reduced the risk of in-hospital mortality and minor bleeding and consequently the time of hospital stay. It also decreased the occurrence of refractory angina, recurrent MI, and hospitalization for cardiac cause. It also helped to improve the ejection fraction. It is clear that further research in this area should be directed to search for criteria according to which it would be possible to choose the most effective and safe time for intervention in high-risk no- STEMI patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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