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Original Article

Timing percutaneous coronary interventions and cardiovascular events in non-ST-elevation myocardial infarction patients

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Abstract: Background: The timing of coronary angiography in patients with non-ST elevation myocardial infarction (NSTEMI) needs to be well defined. In this study, based on the timing of percutaneous coronary intervention (PCI), we evaluated the incidence of major adverse cardiovascular events (MACE) in NSTEMI patients. Methods: In this longitudinal study, we included 156 NSTEMI patients who underwent a PCI at three time points, including <12 hr. (n = 53), 12-24 hr. (n = 54), and ≥24 hr. (n = 49) and followed them for one, three, and six months to monitor major cardiovascular events. The data analyses were conducted using SPSS version 20. Result: Four patients (2.56%) were hospitalized during the one-month follow-up, and only one patient (0.06%) had NSTEMI. The incidence of complications, such as readmission, acute coronary syndrome (ACS; 4 patients [2.56%]), and unstable angina (UA; 3 patients [1.92%]) did not differ significantly among the three intervention times. The occurrence of NSTEMI, UA, and recurrent PCI was 2.56%, 3.20%, and 5.12% in four, five, and eight patients, respectively, and no significant differences were observed among the aforementioned times. In the follow-up after six months, the incidence of STEMI, stroke, TLR, and other all-course deaths was observed in one person (0.06%), which all occurred within 12-24 hours. The difference among the three intervention times was non-significant. Conclusion: Our findings revealed an insignificant difference between the incidence of complications and the three-intervention time.

Keywords: Percutaneous coronary intervention, non-ST elevation myocardial infarction, complication, timing, follow-up

Introduction

Despite significant advancements in understanding the pathology and clinical management of cardiovascular diseases, acute coronary syndrome (ACS) remains a leading cause of morbimortality worldwide [1]. Non-ST-elevation myocardial infarction (NSTEMI)-ACS has a pathophysiological mechanism similar to acute ST-segment elevation (STEMI). According to clinical guidelines, percutaneous coronary intervention (PCI) and revascularization are the first-line treatment strategies for NSTEMI patients, with well-established evidence of their role in reducing major adverse cardiovascular events (MACE) [2, 3]. However, the optimal timing of an invasive procedure in NSTEMI-ACS is controversial. Early invasive management of NSTEMI has been shown to reduce MACE due to the swift reversal of ischemia. Moreover, coronary plaque stabilization in NSTEMI with medical management could provide an optimal substrate for late (delayed) invasive management, thereby reducing the risk of MACE [4, 5]. Early invasive methods have been shown to improve clinical outcomes, although they may increase infarct size [6]. Conversely, a delayed invasive strategy may yield benefits through plaque passivation by optimal medical treatment, followed by intervention on more stabilized plaques; this

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potential advantage may be counterbalanced by a higher risk for events while waiting for angiography [7, 8].

The global burden of cardiovascular disorders, particularly NSTEMI, is a major health concern. Among various strategies to enhance patient outcomes, those contributing to reducing adverse cardiovascular events are paramount. While previous studies have provided insightful information on these methods, further investigation is needed. The intervention time in PCI is a significant factor for NSTEMI patients and requires careful consideration. In this non-surgical method, timing, a crucial aspect of treating patients, can significantly impact patient outcomes [9]. However, the evidence lacks the specificity to determine the appropriate PCI to reduce MACEs. In light of this, our research aimed to address this information gap while focusing on different factors that affect MACE results [10].

PCI and revascularization are generally regarded as methods with favorable safety outcomes. However, risk factors, often influenced by the medical staff's expertise and the patient's prior medical condition, should be considered in employing these methods. It is crucial to emphasize that deciding to proceed with these procedures should be taken only after carefully weighing all pertinent factors. In the present study, we thoroughly assessed the interactions between variables affecting MACE outcomes and the timing of PCI in NSTEMI patients. Our methodology involves a comprehensive assessment of multiple variables, including patient demographics, medical history, comorbidities, surgery details, and post-procedural care, which could increase the risk of MACE. By comprehensively examining these features and intervention time, we hope to gain insight into improving the current most effective practices for managing NSTEMI.

Methods

Demographic characteristics of subjects

From June 2017 to June 2022, we analyzed the clinical records of 156 NSTEMI patients referred to the Rajaie Cardiovascular, Medical, and Research Institute (Tehran, Iran). Clinical and demographic data of the patients and the date of coronary angioplasty were collected from the medical records. Patients who had previously undergone angioplasty were monitored for one, three, and six months to detect any significant cardiovascular events. The local ethics committee approved the study protocol, and all the patients provided their written consent before the initiation of the study.

Inclusion and exclusion criteria

The inclusion criteria were chest discomfort 24 hours before admission, increased cardiac troponin enzyme level, new ST-segment depression of 1 mV, and T-wave inversion in 2 contiguous leads. Patients with STEMI, shock, life-threatening ventricular arrhythmias, active bleeding, and posterior myocardial infarction were excluded. Overall, NSTEMI patients who exhibited the following symptoms were selected to participate in the present study:

1. Clinical symptoms: Chest pain or discomfort that may radiate to the arm, jaw, or back, as the most common symptoms; shortness of breath, nausea, vomiting, diaphoresis (excessive sweating), and dizziness are additional possible symptoms. These symptoms could help diagnose the disease better.

2. Electrocardiogram (ECG) findings: ST-segment depression, T-wave inversion, or abnormal Q waves. ECG is a crucial diagnostic tool for NSTEMI. Alterations in the ECG findings of NSTEMI, unlike STEMI, are often mild or nonspecific. Significant ECG changes in the inclusion criteria were new ST-segment depression of 1 mV and T-wave inversion in 2 contiguous leads.

3. Cardiac biomarkers: Troponin level, a crucial indicator of myocardial damage, is used to diagnose NSTEMI. Troponin is considered a vital biomarker for the diagnosis of MI. Cardiac biomarkers, similar to troponin, were tested to evaluate myocardial injury.

Patients must have experienced at least one of the following symptoms to meet the diagnostic criteria for NSTEMI: typical ischemia symptoms, significant new or suspected new ST-T wave alterations on ECG, and cardiac troponin levels above the 99th percentile upper reference limit.

Statistical analysis

SPSS version 20 was utilized to analyze the patients' data. Data are shown as mean (SD) for normal continuous variables, median (IQR)

Table 1. Demographic and clinical information of patients

Variable	Total n = 156	<12 hr. n = 52	12-24 hr. n = 54	>24 hr. n = 50	*P*-value
Sex, male n (%)	82 (52.56)	27 (51.92)	32 (59.25)	23 (26)	0.543
Age (mean ± SD)	58.48 ± 11.07	59.19 ± 10.53	60.78 ± 9.72	57.26 ± 12.43	0.133
HTN, n (%)	98 (62.82)	34 (65.38)	38 (70.37)	26 (52)	0.137
Smoking, n (%)	38 (24.35)	12 (23.07)	15 (27.77)	11 (22)	0.754
DM2, n (%)	54 (34.61)	17 (32.69)	21 (38.88)	16 (32)	0.630
ASA, n (%)	145 (92.94)	45 (86.53)	51 (94.44)	49 (98)	0.432
Clopidogrel, n (%)	151 (96.79)	49 (94.23)	53 (98.14)	48 (96)	0.224
ACE-ERB, n (%)	143 (91.66)	46 (88.46)	50 (92.59)	47 (94)	0.581
Statin, n (%)	144 (92.30)	47 (90.38)	52 (96.29)	45 (90)	0.394
Beta-blocker, n (%)	149 (95.51)	49 (94.23)	51 (94.44)	49 (98)	0.587
CCB, n (%)	33 (21.15)	10 (19.23)	12 (22.22)	11 (22)	0.917
Nitrate, n (%)	68 (43.58)	25 (48.07)	25 (46.29)	18 (36)	0.415
PPI, n (%)	120 (76.92)	38 (73.07)	42 (77.77)	40 (80)	0.697
Diuretics, n (%)	13 (8.33)	3 (5.76)	5 (9.25)	5 (10)	0.876
Previous PCI, n (%)	15 (9.61)	5 (9.61)	6 (11.11)	4 (8)	0.843
Previous CABG, n (%)	16 (10.25)	5 (9.61)	9 (16.66)	2 (4)	0.101
Time of PCI, n (%)	11 (7.05)	4 (7.69)	3 (5.55)	4 (8)	0.874
Occlusion					
LM	12 (7.69)	4 (7.69)	5 (9.25)	3 (6)	0.821
LAD	71 (4.55)	19 (3.65)	30 (55.55)	22 (44)	0.150
LCx	45 (28.84)	15 (28.84)	16 (29.62)	14 (28)	0.867
RCA	17 (10.89)	7 (13.46)	4 (7.40)	5 (10)	0.589
Graft	2 (1.28)	1 (1.92)	1 (1.85)	0	0.626

HTN: Hypertension; DM2: Diabetes Mellitus type 2; ASA: acetylsalicylic acid; ACE-ERB: angiotensin-converting enzyme; CCB: calcium channel blocker; PPI: Proton-pump inhibitors; PCI: Percutaneous coronary intervention; CABG: coronary artery bypass graft; LM: left main; LAD: left anterior descending; LCX: left circumflex artery; RCA: right coronary artery.

for non-normal continuous variables, and frequency (%) for categorical variables.

Characteristics between subgroups were compared using the chi-square test for categorical variables, analysis of variance (ANOVA) for normal continuous data, and the Kruskal-Wallis test for non-normal continuous data. P<0.05 was considered statistically significant.

Results

Demographic features and subgroups

In this study, we analyzed the demographic and clinical data of 156 NSTEMI patients (**Table 1**) who underwent a PCI at three timeframes (<12 hr., 12-24 hr., and ≥24 hr.). Among these 156 patients, 53 cases were included in the group <12 hr., 54 patients in the 12-24 hr. group, and 49 cases in the group ≥24 hr. In the first group (<12 hr.), 27 patients (51.92%) were male, and the mean and standard deviation (SD) of age were 59.19 ± 10.53 years. In the 12-24 hr. and ≥24 hr. groups, 32 (59.25%) and 23 (26%) patients were males, with the mean (SD) ages of 60.78 ± 9.72 and 55.43 ± 12.43 years, respectively. The mean age of the patients in the three groups showed a significant difference in the death rate (P = 0.0543 and P = 0.003; **Table 1**).

Underlying disorders and habits

The prevalence of type 2 diabetes mellitus in the three groups of <12 hr., 12-24 hr., and ≥24 hr. was 17 (32.49%), 15 (27.77%), and 11 (22%), respectively (P = 0.137), and that of hypertension in the same groups was 34 (65.38%), 38 (70.37%), and 26 (52%), respectively, with a *p*-value of 0.137. The prevalence of smoking in the three study groups were 12 (23.07%), 15 (27.77%), and 11 (22%) patients, respectively (P = 0.745; **Table 1**).

Table 2. Frequency of complications of NSTEMI patients undergoing PCI in three time periods

Complication	Total (%) n = 156	<12 hr. (%) n = 52	12-24 hr. (%) n = 54	>24 hr. (%) n = 50	*P*-value
Within 1 month					
Hospitalization	4 (2.56)	2 (3.84)	1 (1.85)	1 (2)	0.773
ACS	4 (2.56)	2 (3.84)	1 (1.85)	1 (2)	0.773
NSTEMI	1 (0.06)	0	1 (1.85)	0	0.307
UA	3 (1.92)	2 (3.84)	0	1 (2)	0.353
PCI	4 (2.56)	2 (3.84)	1 (1.85)	1 (2)	0.773
MFU	4 (2.56)	2 (3.84)	1 (1.85)	1 (2)	0.773
After 3 Months					
Hospitalization	9 (5.76)	2 (3.84)	3 (5.55)	4 (8)	0.665
NSTEMI	4 (2.56)	2 (3.84)	0	2 (4)	0.337
UA	5 (3.20)	0	3 (5.55)	2 (4)	0.248
PCI	8 (5.12)	1 (1.92)	3 (5.55)	4 (8)	0.374
MFU	9 (5.76)	2 (3.84)	3 (5.55)	4 (8)	0.665
After 6 Months					
Hospitalization	19 (12.179)	7 (13.46)	4 (7.40)	8 (16)	
ACS	16 (10.25)	7 (13.46)	2 (3.70)	7 (14)	0.145
STEMI	1 (0.06)		1 (1.92)	0	0.366
NSTEMI	3 (1.92)	1 (1.92)	1 (1.85)	1 (2)	0.998
UA	12 (7.69)	5 (9.61)	1 (1.85)	6 (12)	0.124
STROKE	1 (0.06)	0	1 (1.85)	0	0.386
TLR	1 (0.06)	0	1 (1.85)	0	0.386
PCI	9 (5.76)	3 (5.76)	2 (3.70)	4 (8)	0.644
CABG	3 (1.92)	2 (3.84)	0	1 (2)	0.353
MFU	17 (10.89)	7 (13.46)	3 (5.55)	7 (14)	0.296
Other death	1 (0.06)	0	1 (1.85)	0	0.386
All-course death	1 (0.06)	0	1 (1.85)	0	

Past medical history

Among the 156 NSTEMI patients, 16 (10.25%) had a history of coronary artery bypass graft surgery and included 5 (9.61%), 9 (16.66%), and 2 (4%) cases in the <12 hr., 12-24 hr., and ≥24 hr. groups, respectively (P = 0.101). In addition, 13 (9.61%) patients, including 5 (9.61%) in the <12 hr. group, 6 (11.11%) in the 12-24 hr. group, and 2 (4%) in the ≥24 hr. group (P = 0.843), had a history of PCI. Regarding the prevalence of drug history, the highest frequency was related to clopidogrel (151 patients [96.79%]) and beta-blockers (149 patients [95.51%]), while the lowest frequency was associated with calcium channel blockers in 33 (21.15%) patients and diuretics in 13 (8.33%) patients. There was no significant difference in the incidence of drug history among the three intervention groups (**Table 1**).

Complications

Most vessel involvement was observed in the left anterior descending artery in 71 (40.55%) patients and the left circumflex artery in 45 (28.84%) patients. The lowest incidence of vessel involvement was observed in the left main vessel (12 patients [7.69%]) and graft (2 patients [1.28%]). Right coronary artery involvement was found in 17 patients (10.89%). **Table 2** shows the frequency of complications among the study groups during one month and after three and six months. Within the first month, the frequency of hospitalization in the <12 hr., 12-24 hr., and ≥24 hr. groups were 5 (3.20%), 2 (3.84%), and 1 (1.85%) (P = 0.773), respectively. During the same month, the lowest prevalence of complications was observed in 1 patient (0.06%), which occurred in the 12-24 hr. group. The one-month prevalence of

complications such as hospitalization, ACS, PCI, and MFU was comparable in all the groups (4 patients [2.56%]), and there were no significant differences in any of the groups. After three months, the incidence of complications such as hospitalization, NSTMI, unstable angina, PCI, and MFU was observed in 9 (5.76%), 4 (2.56%), 5 (3.20%), 8 (5.12%), and MFU 9 (5.76%) patients, respectively. The frequency distribution of all complications among the three patient groups over three periods was not significantly different. The highest prevalence of complications after six months was related to hospitalization (19 patients [12.17%]) and ACS (16 patients [10.25%]), and the lowest prevalence was associated with STEMI, TLR, and stroke (1 patient [0.06%] each; **Table 2**).

Discussion

The present study evaluated the complications of NSTEMI patients undergoing PCI during time intervals of 12 hours, 12 hours, 12-24 hours, 24 hours, and 24 hours. This study showed that complications during the first month were significantly higher than in three-month and six-month follow-ups. The results also indicated that the frequency of each complication in <12, 12-24, and ≥24 hr. groups was not significantly different. Herein, we examined the frequency of patients' complications within one month and after three and six months. In various studies, patients were divided into intervention time (early and late) groups. Rasmussen et al.'s study, classified 496 NSTEMI patients into two groups based on intervention timing: early (<2 hr.) and late (<72 hr.) and reported no significant difference in the incidence of complications such as mortality, reinfarction, and readmission between the groups [11]. Mahendiran et al. categorized patients into time groups <2 hr. and 12-24 hr. and followed them for one year. They found no significant difference in the incidence of complications between the two groups [12]. In contrast to our study and the study conducted by Yoshida et al. [13], a three-year follow-up survey showed that patients undergoing PCI in less than 24 hours had fewer complications than those undergoing 24-hour intervention [13, 14]. In a similar study to ours conducted on NSTEMI patients, the rapid intervention of fewer than 2 hours significantly reduced ischemic events compared to patients undergoing intervention between 12 and 72 hours [14]. Unfortunately, many studies represented much variation during the follow-up period, which could be a reason for the discrepancy between the results. Jobs et al. investigated eight clinical trial studies and reported that early intervention could decrease six-month mortality in NSTEMI patients [15]. The investigations above demonstrate wide heterogeneity between the optimal timing of PCI and the incidence of potential complications based on the duration of follow-up. These discrepancies in the results of these studies may be due to various factors, including variations in demographic characteristics, severity of coronary artery involvement, definitions of early and late intervention, and disparities in follow-up duration.

In the current study, we examined the complications of NSTEMI patients undergoing PCI within three-time windows: <12 hr., between 12 and 24 hr., and ≥24 hr., and obtained interesting results. Complications were substantially more prevalent in the first month after treatment than in the three- and six-month follow-up periods. Moreover, no significant differences were observed in the frequency of specific complications among the three intervention groups. It is important to note that there are potential biases within the sample population and variations in treatment regimens across various medical facilities. Hopefully, future studies will improve these findings by expanding the study to include a more extensive and varied patient group. Multicenter studies should also be conducted to cover a broader range of patients and intervention settings. Investigating the impact of patients' characteristics, such as age, underlying medical conditions, and medication use, on the outcomes of different time intervals could provide valuable insights into improving PCI therapies for NSTEMI patients.

Conclusion

The present study discovered that NSTEMI patients who were followed for one, three, and six months for major cardiovascular events did not demonstrate any significant correlation between PCI timing and cardiovascular events. In other words, the incidence of complications in patients at the time of the intervention did not differ significantly between the two groups. In this study, we address a crucial knowledge

gap by investigating the relationship between the timing of PCI and the risk of MACE in NSTEMI patients. Moreover, we provide essential information that could aid clinical decision-making and lead to new strategies to reduce adverse cardiovascular events in this vulnerable patient population by considering multiple factors influencing patient outcomes.

Disclosure of conflict of interest

None.

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