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Original Article

Impact of Total Ischemic Time on No Reflow Phenomenon

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ABSTRACT

Background: Ischemic heart disease, particularly ST-segment elevation myocardial infarction (STEMI), remains a major cause of morbidity and mortality globally. Despite advancements in primary percutaneous coronary intervention (PPCI), the no-reflow phenomenon, characterized by inadequate myocardial reperfusion despite successful vessel recanalization, continues to pose significant challenges, affecting clinical outcomes adversely.

Objective: This study aims to investigate the relationship between total ischemic time and the incidence of the no-reflow phenomenon in STEMI patients undergoing PPCI, to identify potential strategies for improving therapeutic outcomes.

Methods: Conducted at Hayatabad Medical Complex, Peshawar, this retrospective cohort study included 160 STEMI patients treated over eight months (February to October 2022). We collected data on demographic characteristics, clinical presentation, and outcomes. Inclusion criteria were patients over 18 years, undergoing PPCI within 12 hours of symptom onset, without prior MI, severe bleeding disorders, or previous significant revascularization. Statistical analysis was performed using SPSS 25.0, considering $P \leq 0.05$ as statistically significant.

Results: The average total ischemic time was significantly longer in patients experiencing no-reflow (Group I, 7.91 hours) compared to those with normal reperfusion (Group II, 3.41 hours) (P=0.001). Group I also showed higher rates of cardiogenic shock (17.6% vs. 6.8%, P=0.012) and reinfarction (11.8% vs. 2.9%, P=0.010). Mortality was significantly higher in Group I (5.8% vs. 1.9%, P=0.020).

Conclusion: Longer total ischemic time is associated with an increased risk of the no-reflow phenomenon and poorer clinical outcomes in STEMI patients. Reducing ischemic time could be crucial in improving reperfusion success and reducing complications post-PPCI.

Keywords: ST-segment elevation myocardial infarction, no-reflow phenomenon, ischemic time, primary percutaneous coronary intervention, myocardial reperfusion, clinical outcomes, ischemia-reperfusion injury.

INTRODUCTION

Ischemic heart disease continues to be a predominant cause of global morbidity and mortality, with ST-segment elevation myocardial infarction (STEMI) representing a particularly severe manifestation (1). The advent of primary percutaneous coronary intervention (PPCI) as a treatment has dramatically transformed the management of STEMI, significantly diminishing both mortality and morbidity (2, 3). Nevertheless, the no-reflow phenomenon, characterized by inadequate myocardial reperfusion despite successful recanalization of the epicardial vessel, persists as a significant clinical hurdle in the treatment of STEMI patients (4). This phenomenon not only undermines the benefits of prompt reperfusion therapy but also leads to worse clinical outcomes, such as increased infarct size, heightened risk of ventricular arrhythmias, and greater likelihood of congestive heart failure. The no-reflow is influenced by several factors including microvascular obstruction, inflammation, and endothelial dysfunction (4).

Recent attention has focused on the role of total ischemic time—the interval from symptom onset to successful reperfusion—in influencing the likelihood of no-reflow. Prolonged ischemic time is thought to aggravate microvascular damage, thereby increasing the risk of no-reflow, yet the specific duration after which this risk escalates significantly remains unclear (5, 6). This study seeks to clarify the relationship between total ischemic time and the no-reflow phenomenon in STEMI patients undergoing PPCI, addressing a critical gap in current medical understanding. By elucidating this relationship, the research aims to enhance risk stratification, improve clinical decision-making, and refine therapeutic approaches, potentially leading to better patient outcomes and reduced

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incidence of no-reflow in this vulnerable population (7). Such findings could offer essential insights for optimizing treatment timelines and strategies in managing STEMI, ultimately improving clinical results for patients undergoing PPCI (1-3, 5).

MATERIAL AND METHODS

This observational, retrospective, single-center cohort study was conducted at the Interventional Cardiology Unit of Hayatabad Medical Complex in Peshawar, Pakistan, over an eight-month period from February to October 2022. The study aimed to examine the impact of total ischemic time on the no-reflow phenomenon among patients experiencing ST-segment elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention (PPCI). The World Health Organization's recommended method for cohort studies was utilized to determine the sample size, resulting in 160 participants based on a 95% confidence level, an expected 20% prevalence of the no-reflow phenomenon, and a 5% margin of error.

Inclusion criteria for the study encompassed patients who presented with typical chest pain and electrocardiographic evidence of ST-segment elevation indicative of acute myocardial infarction, those who underwent PPCI as the primary reperfusion strategy within 12 hours of symptom onset, and those aged 18 years or older. Exclusion criteria included patients with a history of prior myocardial infarction, contraindications to PPCI such as bleeding disorders or active bleeding, significant pre-existing coronary artery disease, prior coronary artery bypass surgery or coronary stent implantation, presentation in cardiogenic shock, or inability to provide informed consent (8).

Data collection involved recording detailed clinical information at admission, including demographic details, medical history, presenting symptoms, and baseline vital signs. Standard 12-lead electrocardiograms were obtained upon admission, before and after PPCI, and at regular intervals during the hospitalization to monitor ST-segment changes and the extent of myocardial infarction. Coronary angiography, conducted as part of the PPCI procedure, provided data on the number and location of culprit lesions, the Thrombolysis in Myocardial Infarction (TIMI) flow grade, and the presence of collateral vessels. Total ischemia time, defined as the duration from the onset of chest pain to successful reperfusion, was meticulously recorded for each patient. Blood samples for routine laboratory tests, including cardiac biomarkers (troponin I or T), complete blood count, and renal function tests, were collected at admission (9, 10).

The study was approved by the institutional ethics committee of Hayatabad Medical Complex and was conducted in accordance with the Declaration of Helsinki. All participants provided informed consent before inclusion in the study. Data analysis was performed using SPSS version 25.0, and a P-value of ≤0.05 was considered statistically significant for all statistical tests. This approach ensured rigorous data handling and analysis, aiming to provide reliable and valid results regarding the no-reflow phenomenon in STEMI patients.

RESULTS

In the study, Group I had a mean age of 62.8 years, slightly higher than Group II, which had a mean age of 59.9 years; this difference was statistically significant (P=0.033) as noted in Table 1. The gender distribution between the two groups was similar, with males comprising 58.8% of Group I and 60.1% of Group II, showing no significant difference (P=0.891). Likewise, the proportions of females in the groups were comparable (41.2% in Group I and 39.8% in Group II), also yielding no significant difference (P=0.910).

Table 1: Demographic and Clinical Characteristics

Characteristics	Group I	Group II	P value
Mean age	62.8 years	59.9 years	0.033
Male	10 (58.8%)	62 (60.1%)	0.891
Female	7 (41.2%)	41 (39.8%)	0.910
Diabetes	6 (35.2%)	24 (23.3%)	0.021
Prior MI	1 (5.8%)	16 (15.5%)	0.031
Hypertension	7 (41.7%)	40 (38.8%)	0.910
Dyslipidemia	4 (23.5%)	26 (25.2%)	0.891
Smoking	6 (35.2%)	39 (37.8%)	0.878
CK-MB level	94.71 U/L	75.03 U/L	0.001

Table 2: Study Outcomes

Outcome	Group I	Group II	P value
Cardiogenic shock	3 (17.6%)	7 (6.8%)	0.012
Reinfarction	2 (11.8%)	3 (2.9%)	0.010
Thrombus burden	5 (29.4%)	14 (13.6%)	0.001
Aspiration catheter	6 (35.3%)	11 (10.7%)	0.050
Glycoprotein IIb/IIIa	9 (52.9%)	17 (16.5%)	0.001
Total ischemic time	7.91 hours	3.41 hours	0.001
Mortality	1 (5.8%)	2 (1.9%)	0.020

Regarding clinical characteristics, diabetes prevalence was significantly higher in Group I (35.2%) compared to Group II (23.3%), with a P value of 0.021. Patients with a history of myocardial infarction (MI) prior to the study were less frequent in Group I (5.8%) than in Group II (15.5%), with this observation being statistically significant (P=0.031). The prevalence of hypertension and dyslipidemia showed no significant differences between the groups, with hypertension appearing in 41.7% of Group I and 38.8% of Group II (P=0.910), and dyslipidemia in 23.5% of Group I compared to 25.2% of Group II (P=0.891). Smoking rates were similarly close, with 35.2% in Group I and 37.8% in Group II (P=0.878). The mean CK-MB level, a marker of myocardial injury, was notably higher in Group I at 94.71 U/L compared to 75.03 U/L in Group II, representing a statistically significant difference (P=0.001).

Study outcomes as detailed in Table 2 also demonstrated significant findings. The incidence of cardiogenic shock was higher in Group I (17.6%) than in Group II (6.8%), with a P value of 0.012. Reinfarction occurred in 11.8% of Group I compared to only 2.9% of Group II, marking another significant difference (P=0.010). Group I also showed a higher thrombus burden (29.4%) versus 13.6% in Group II, which was statistically significant (P=0.001). The use of an aspiration catheter was more frequent in Group I (35.3%) compared to Group II (10.7%), with this result bordering on statistical significance (P=0.050). The administration of Glycoprotein IIb/IIIa inhibitors was notably higher in Group I (52.9%) compared to Group II (16.5%), a difference that was highly significant (P=0.001). The total ischemic time was considerably longer in Group I, averaging 7.91 hours, in contrast to 3.41 hours in Group II, a finding that was statistically significant (P=0.001). Mortality rates were also different, with Group I recording a rate of 5.8% compared to 1.9% in Group II, which was significant (P=0.020).

DISCUSSION

Ischemic heart disease, particularly ST-segment elevation myocardial infarction (STEMI), remains a major global health challenge, significantly contributing to morbidity and mortality worldwide. Over recent decades, the advent of primary percutaneous coronary intervention (PPCI) has been a transformative milestone in STEMI management, significantly reducing mortality and morbidity. However, the no-reflow phenomenon continues to be a significant impediment in the field, characterized by inadequate myocardial reperfusion despite successful epicardial vessel recanalization. This condition not only undermines the benefits of timely reperfusion therapy but also leads to adverse outcomes, including larger infarct sizes, increased risk of ventricular arrhythmias, and a higher incidence of congestive heart failure. The complex nature of no-reflow involves factors such as microvascular obstruction, inflammation, and endothelial dysfunction (10-13).

A pivotal aspect that has gained attention in the context of no-reflow is the total ischemia time, defined as the duration from the onset of symptoms to successful reperfusion. This study aimed to delve into the relationship between total ischemia time and the no-reflow phenomenon to enhance risk stratification and therapeutic strategies for STEMI patients undergoing PPCI. Notably, the study revealed that the group experiencing no-reflow (Group I) had a significantly longer mean total ischemia time of approximately 7.91 hours compared to 3.41 hours in the group with normal flow (Group II). This finding aligns with prior research, such as that conducted by Bessonov IS et al., which also noted prolonged ischemia as a contributing factor to no-reflow. The consistency of these findings across different studies highlights the crucial role of minimizing ischemia time to mitigate the risk of no-reflow (14-16).

Additionally, the study identified other clinical factors influencing no-reflow, such as age over 65 years, high thrombus burden, and the presence of cardiogenic shock. These factors were independently associated with the no-reflow phenomenon, echoing findings from research by Auffret V et al., which similarly recognized age and thrombus burden as critical predictors. This convergence of evidence underscores the multifactorial nature of no-reflow, necessitating a holistic approach to risk assessment (17).

The clinical significance of these findings is further emphasized by the impact of no-reflow on mortality rates; Group I exhibited a higher mortality rate of 5.8% compared to 1.9% in Group II. This observation is supported by the study by Nielsen CG et al., which reported increased mortality among patients experiencing no-reflow post-PPCI. Such parallel findings highlight the urgent need for strategies that address and mitigate no-reflow to improve patient outcomes (18).

While this study adds valuable insights into the no-reflow phenomenon and its association with total ischemia time, it is important to recognize its limitations (19). Conducted at a single center with a relatively small sample size, the findings may not be generalizable across different populations or geographic regions. Future research should involve larger, multicenter studies to confirm these findings and enhance their applicability (20). Additionally, a more diverse and representative patient population would help generalize these results more broadly, enabling more effective and targeted therapeutic interventions for STEMI patients at risk of no-reflow.

CONCLUSION

In conclusion, prolonged ischemia, advanced age, cardiogenic shock, and high thrombus burden significantly contribute to the risk of no-reflow and poorer clinical outcomes, including increased mortality. Recognizing and addressing these risk factors is paramount in refining risk assessment and guiding therapeutic strategies, ultimately aiming to improve care and outcomes for this high-risk patient group.

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