IMPACT OF TOTAL ISCHEMIC TIME ON THE RECOVERY OF REGIONAL WALL MOTION ABNORMALITY AFTER STEMI IN THE MODERN REPERFUSION ERA

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Abstract

Introduction: Total ischemic time (TIT) plays a critical role in determining the recovery of regional wall motion abnormalities (RWMA) in STEMI patients treated with primary percutaneous coronary intervention (PCI).

Objectives: To evaluate the impact of TIT on RWMA recovery using advanced diagnostic modalities in STEMI patients undergoing reperfusion therapy.

Materials and Methods: This prospective study included 200 STEMI patients treated with PCI at multiple centers including Rashid Latif Medical University Lahore, Pakistan and Sindh Institute of Cardiovascular Diseases (SICVD) Hyderabad, Pakistan. Patients were categorized based on TIT: ≤3 hours, 3–6 hours, and >6 hours. Speckle-tracking echocardiography and cardiac magnetic resonance imaging were applied to evaluate RWMA and left ventricular function.

Results: Shorter TIT (≤3 hours) was associated with significant improvement in RWMA and left ventricular ejection fraction (LVEF). Prolonged TIT (>6 hours) led to higher rates of adverse remodeling and complications, including heart failure.

Conclusion: Reducing TIT is critical for optimizing RWMA recovery and improving outcomes in STEMI patients.

Keywords: STEMI, total ischemic time, reperfusion therapy, regional wall motion abnormality, left ventricular function.

INTRODUCTION

The need to introduce the Total Ischemic Time concept in understanding the recovery of RWMA following STEMI in the modern reperfusion era can not be done without assessing post-MI critical factors affecting cardiac recovery (1). Total Ischemic Time is the time point between the onset and

successful reperfusion and has a significant impact on the myocardial save along with the ventricular function (2). Even with newer reperfusion therapies, including the primary PCI, a subset of patients with STEMI will continue to manifest persistent RWMAs, the consequence of which have adverse effects on survival and health-related quality of life (3). Prompt reperfusion is a foundation of STEMI treatment that involves reintroducing blood flow and decreasing ischemic damage. However, delayed reperfusion is associated with worse myocardial necrosis, adverse remodeling, and a higher risk for residual RWMAs (4). Advanced imaging techniques like CMR and speckle tracking echocardiography in STEMI patients have come up as powerful aids toward assessing myocardial damage as well as functional recovery (5). These techniques enable the quantitative evaluation of left ventricular strain and offer new data regarding the continuous processes of myocardial remodeling and recovery (6).

The consequences of ischemia on myocardial tissue are tenderoniary, where Total Ischemic Time has been demonstrated to have an inverse relationship with the extent of irreversible myocardial damage (7). It was reported that myocardial salvage during reperfusion is inversely related to TIT in the large-scale echocardiographic series (8). Further, the experimental models have shown that the duration of ischemia affects the structure and function of myocardial tissue, thereby underlining the need for early intervention in patients. The ischemia-reperfusion injury, the formation of oxidative stress, and inflammation add more pressure to the quest for myocardial recovery post-STEMI (10). Maintaining timely reperfusion is a challenge in poor nations like Pakistan because of the disparities in patient travel distances and availability to medical facilities (11)(12). The results of this study highlight the necessity for treatment-specific approaches for maximizing TIT and improving the rates of recovery. Other experimental treatments, including supersaturated oxygen therapy, have also proved useful in reducing/reducing ischemia-reperfusion injury and enhancing myocardial salvage and functional recovery in experimental models (13).

To identify all potential factors that influence the outcome of RWMA treatment, a detailed assessment of clinical, procedural, and patient characteristics must be provided. It was established that the extent of functional recovery depends on the interaction between the regimes of ischemia, reperfusion, and characteristics of the individual myocardium (14). Thus, further examination of the possibilities of using new diagnostic and therapeutic technologies, such as imaging and new cardioprotective compounds, may create the basis for individual methods of STEMI therapy (15). The purpose of this study is to demonstrate the effects of Total Ischemic Time on RWMA recovery in a contemporary reperfusion age, using new diagnostic techniques and reperfusion strategies. As a result of filling knowledge and practice deficits, it aims to promote better clinical outcomes and increase the quality of care for STEMI patients across various healthcare organizations.

Objective: To assess the influence of total ischemic time on the subsequent improvement of regional wall motion defects in STEMI patients treated with reperfusion therapy in the conditions of contemporary diagnostic technologies.

MATERIALS AND METHODS
Study Design: Prospective observational study.
Study setting: The study was carried out multiple centers including Rashid Latif Medical University Lahore, Pakistan and Sindh Institute of Cardiovascular Diseases (SICVD) Hyderabad, Pakistan
Duration of the study: The duration of the study was from November, 2023 to October, 2024.

Inclusion Criteria
The participants were patients 18 years and above, with symptoms of STEMI presented by ECG changes and increased levels of cardiac biomarkers. Patients subjected to reperfusion therapy were only included in the study if they received the treatment within the prescribed time. Participants had to give their consent, and subsequent assessments, including imaging studies, were also conducted.

Exclusion Criteria

Patients with previous myocardial infarction, severe valvular disease, or severe heart failure [New York Heart Association (NYHA) Class III/IV] were ineligible. Patients who were poor candidates for reperfusion therapy or those who could not generate good-quality image data were also excluded. Patients who refused consent or those who couldn't be traced for follow-up were excluded from the study.

Methods

It was important to obtain extensive information on the clinical, procedural, and imaging characteristics of STEMI patients who underwent reperfusion therapy. Sterile pyuria rate and any baseline characteristic affecting Blank were compared between patients allocated to each treatment arm to test the first study hypothesis. Patients undergoing PCI as the index procedure for STEMI and meeting the inclusion criteria received primary PCI as the standard reperfusion strategy. Total ischemic time was defined as the time from the onset of the symptoms to the restoration of coronary blood flow after PCI using TIMI 3 as the end-point. RWMA was evaluated by speckle-tracking echocardiography before discharge (within 24 h after reperfusion) and at three-month follow-up. LVEF and regional strain, which characterize the functional recovery of the left ventricle, were measured. To confirm the findings obtained in the study, patients benefited from techniques such as cardiac magnetic resonance (CMR). The analyses that have been used to understand the changes in the recovery of RWMA included correlation coefficients and regression models in relation to TIT. Qualitative data were analyzed manually, while quantitative data were analyzed using the Statistical Package for Social Sciences, version 26, with a significance level set at 5%.

RESULTS

Thus, a total of 200 patients suffering from STEMI and treated with primary PCI were included in the study. The average age was 58.3 ± 10.2 years, and 70% of the participants were male. The average total ischemic time was 270 ± 48 minutes or 4.5 ± 1.2 hours. Patients were categorized into three groups based on TIT, and classification was done into ≤ 3 hours (Group 1), $3 - 6$ hours (Group 2), and > 6 hours (Group 3). The data on comorbidity and risk factors did not differ between the first, second, and third groups at the baseline. The mean baseline LVEF was $44.5 \pm 7.1\%$ and was lower in Group 3 compared to Groups 1 and 2. RWMA scores were significantly different between the groups in both pre and post-intervention categories and illustrated the negative effects of prolonged TIT.

Table 1: Baseline Characteristics of Study Participants

Variable	Group 1 (≤3 hours)	Group 2 (3–6 hours)	Group 3 (>6 hours)	p-value
Number of Patients	70	90	40	-
Mean Age (years)	57.2 ± 9.5	58.9 ± 10.7	59.3 ± 10.1	0.12
Male (%)	71.4	68.9	70.0	0.45
Diabetes Mellitus (%)	34.3	36.7	35.0	0.39
Hypertension (%)	42.9	45.6	47.5	0.52

At the three-month follow-up, Group 1 exhibited the highest improvement in RWMA and LVEF (LVEF: $50.2 \pm 6.8\%$), followed by Group 2 (LVEF: $47.5 \pm 7.2\%$), and Group 3 (LVEF: $43.1 \pm 7.5\%$). The recovery rate of RWMA was really dependent with TIT whereby Group 1 had a better recovery rate by 70% from RWMA scores in comparison to Group 3 who emerged with only a 40% of the RWMA scores recovery rate.

Table 2: Echocardiographic Parameters at Baseline and Follow-up

Parameter	Group 1	Group 2	Group 3	p-value
Baseline LVEF (%)	46.7 ± 7.0	44.5 ± 7.2	42.5 ± 7.1	0.01
Follow-up LVEF (%)	50.2 ± 6.8	47.5 ± 7.2	43.1 ± 7.5	<0.001
RWMA Improvement (%)	70	60	40	<0.001

Adverse remodeling like complications were seen in 15% of Group 3 patients which was comparatively low than 5% in Group 1. The study examines the negative impact of late reperfusion on the heart's function.

Table 3: Incidence of Adverse Events

Event	Group 1 (n=70)	Group 2 (n=90)	Group 3 (n=40)	p-value
Adverse Remodeling	5 (7.1%)	10 (11.1%)	6 (15.0%)	0.03
Heart Failure (NYHA III/IV)	2 (2.9%)	6 (6.7%)	4 (10.0%)	0.04

Therefore, a decrease in TIT was also associated with better RWMA recovery and favorable cardiac prognosis in STEMI patients. The myocardium should be salvaged as soon as possible to minimize complications of the disease.

DISCUSSION

Importantly, the results point to the significance of Total Ischemic Time in RWMA healing post-STEMI in the contemporary reperfusion practice. Primary PCI, as the initial step in STEMI management, has been hailed as the reperfusion strategy with early success, which reduced mortality and improved the functional status. However, the degree of myocardial recovery is dependent on the duration of ischemia before intervention, and any prolonged TIT will impair regional and global cardiac function. The present discussion outlines the relevance of the findings of the present study and discusses them in relation to the previous literature, as well as the prospects of recovery strategies in the clinical context. This research supports the findings of the earlier studies that had shown an inverted-U curvilinear relationship between TIT and RWMA recovery. The patients with a duration of TIT less than or equal to 3 hours showed the best result in LVEF and RWMA scores improvements. These observations may be explained by several factors, including shorter ischemic times that have been shown to produce more minimal impairment of myocardial contractility and dispersion of wall motion abnormalities (1). These findings underscore the need for accurate and timely evaluation and treatment of STEMI patients.

Extending TIT results in permanent myocardial damage and adverse remodeling, as indicated in the present study among patients with TIT>6h. The remodeling is unfavorable, resulting in ventricular enlargement and fibrosis and not only affecting the regional contractile performance but also putting patients at risk of developing heart failure and arrhythmias (2). Luisi et al. focused on the correlation between Ischemia lasting longer than 48 hours and profound dysfunction of left ventricular strain that precedes adverse remodeling (3). Some of these changes have been elucidated by advanced imaging, such as cardiac magnetic resonance (CMR), in terms of the degree of damage to the myocardium and the capacity to rebuild it (5). There is also the question of ischemia-reperfusion injury in relationship to RWMA recovery. While reperfusion is necessary for the salvage of the myocardial tissue, extra harm is realized from it through oxidative stress, inflammation, and microvascular dysfunction. Ahmed et al. discussed the effect of reperfusion on left ventricular function and proposed further approaches to ameliorate reperfusion injury in order to improve results (4). Additional experimental research by Radike et al. has also demonstrated that the degree of reperfusion damage is influenced by the duration of ischaemia, which emphasises the importance of early intervention (9).

However, prospects for the recovery of RWMA in addition to TIT depend on patient-specific factors. Diabetes, hypertension, and prior cardiovascular events have been observed to influence the myocardial tolerability to ischemia and reperfusion therapy, respectively. Therefore, inherent to STEMI pathology, predictors of functional recovery were described by Talha et al. using speckle-tracking echocardiography, signifying the role of patient-specific risk stratification in this condition (6). Along the same line, Aparicio-Ortiz et al. comprehensively discussed a separate aspect of mechanical complications following myocardial infarction with a focus on the relationship between ischemic time, patient profile, and prognosis (7). From a clinical point of view, this study has some implications. First, management of pre-hospital time is still considered a direction in STEMI treatment. Increased public health initiatives, better ambulance services, and earlier sign recognition can greatly reduce the time between the onset of symptoms and percutaneous revascularization. The work by Tsega et al., in a low-resource context, reveals that Controlling TIT is one of the strategies of HC system readiness in enhancing its outcomes among diverse populations worldwide (11).

Second, it becomes essential to investigate whether improvements in therapeutic approaches may add to the benefits of timely reperfusion in RWMA recovery. For example, new concepts like intracoronary supersaturated oxygen that was used by Kaluza et al. proposed to reduce ischemia-reperfusion injury and increase myocardial salvage (15). Consequently, pharmacological agents that are related to oxidative stress and inflammation could help decrease the negative consequences of reperfusion and may enhance functional recovery (10). The limitations of this study should be acknowledged. Such limitations include a Small sample Size, Time constraints, and Self-Administration of questionnaires. Although we have brought out specific facts that supported the research questions about the role of TIT in RWMA recovery, the study is limited by the fact that it is a single-center study. Further, applying techniques, such as CMR, that yield high-resolution images was not routine in some centers, which could have caused variability in evaluating myocardial injury. Future studies that use data from more centers and apply more stringent criteria for image acquisition could give a better insight into RWMA recovery in STEMI patients.

These results also have important implications for the timing of intervention in patients with STEMI who presented late. Wang et al. proposed a new grading system for ischemia-reperfusion injury and concluded that early and late presenters could receive precise treatment (14). More investigation is required to enhance the understanding of the sub-group's risk profiles, and management strategies are developed further. Finally, this study underscores the importance of TIT in the identification of the recovery of RWMA in STEMI patients receiving primary PCI. Myocardial salvage and functional recovery are best when treatment is received within the golden window of three hours, as anything beyond this leads to poor outcomes. Current practical management of acute myocardial reperfusion includes measures to lower TIT, limit ischemia-reperfusion injury, and tailor the therapy in relation to the patient's individual condition. Thus, by dealing with these difficulties, clinicians are able to enhance the prognosis for adequate results and patients' life quality in the case of STEMI.

CONCLUSION

This study also focuses on the effectiveness of TIT in predicting RWMA in the setting of patients with STEMI receiving reperfusion therapy. The greatest benefits were derived when treatment commenced in the first three hours, most notably with respect to left ventricular function and myocardial salvage. Ischemic times more than 120—180 minutes were associated with adverse remodeling, reduced functional recovery, and increased risk of complications such as heart failure and ventricular dysfunction. In conclusion, our observations affirm the need for a general rise of public awareness, improvements in the healthcare organization, and effective pre-hospital structures to mitigate TIT. Furthermore, improved therapeutic approaches such as new cardioprotective drugs and high-technology imaging also may improve outcomes of delayed presenters. This approach, which focuses on early intervention and individualized treatment, allows clinicians to enhance risk, quality of life, and STEMI survival in the modern reperfusion age.

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