

Original Research Article

**“MOST CRUCIAL ARE TOTAL ISCHEMIC TIMES THAN DOOR TO BALLOON TIMES IN STEMI PATIENTS”**

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**Abstract**

**Objectives:** The present study was done to assess total ischemic time and door-to-balloon time in patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) and to assess prognostic impact and mortality rate in patients undergoing primary PCI for STEMI at a tertiary healthcare center in India.

**Methods:** In this single-center interventional study done between October, 2020 to December, 2021 at a tertiary healthcare center (Ramesh Hospital, Guntur) in India, consecutive patients with STEMI were included. Demographic parameters of patients were evaluated. Multivariate logistic regression analysis was done on various parameters using SPSS software, version 23.

**Results:** A total of 190 patients were included with the mean age of  $57.99 \pm 10.59$  years. Majority of the population was male (85.3%). The most common risk factors observed were diabetes mellitus (51.6%), hypertension (47.9%) and family history of coronary artery disease (6.7%). Acute anterior wall myocardial infarction and acute inferior wall myocardial infarction was observed in 57.4% and 28.9% patients, respectively. Mean ischemic time was  $470.02 \pm 528.94$  minutes. Patients with total ischemic time more than 480 minutes ( $P=0.05$ ) showed significant mortality. The mean door to balloon time was  $66.26 \pm 25.05$  minutes, where 154 (81.1%) patients had door to balloon time  $<90$  minutes.

**Conclusion:** Our data suggest that more efforts are needed to reduce Total Ischemic time, door-to-balloon time; like improving patients' awareness of symptoms, reducing the interval from the time of symptom onset to treatment and decreasing the transfer time between medical facilities can help achieve the goal.

**Key words:** Total Ischemic time; percutaneous coronary intervention; STEMI

## Introduction

Primary percutaneous coronary intervention (PCI) is an effective treatment option for acute ST-segment–elevation myocardial infarction (STEMI). Reduction in the frequency of total stroke, reinfarction, and an increase in the incidence of infarct-related artery patency, with an improved in-hospital and long-term survival, made PCI a primary therapeutic option compared to thrombolytic therapy<sup>1</sup>. Time to treatment plays a vital role in the survival of patients with primary PCI.

Total ischemic time was defined as the time from the onset of chest pain to the first balloon inflation during primary PCI. The time from symptom onset until reperfusion occurs is one estimate of total ischemic time. Several experimental studies and now human clinical studies have confirmed that infarct size and mortality are strongly correlated with the total ischemic time and much less so with its subintervals like door-to-balloon time.<sup>2</sup>

Door-to-balloon (D2B) is a time measurement in emergency cardiac care for treating patients with STEMI. The interval starts upon the patient's arrival to the hospital and ends with a catheter guide wire crossing the culprit lesion in the cardiac catheterization lab. Delay in treating a myocardial infarction enhances the amount of cardiac muscle damage due to localized hypoxia.<sup>3</sup> According to guidelines issued by the American Heart Association (AHA) and the American College of Cardiology (ACC), the door-to-balloon interval should not be more than 90 minutes.<sup>4</sup> It has become a significant performance measure in various settings.

Some of the factors linked to delays in Total Ischemic time, D2B time are female gender, contraindication to thrombolytic therapy, patients aged above 65 years, atypical symptoms, lack of chest pain at the time of presentation,<sup>5</sup> environmental issues like providing timely care on weekends, holidays, and off-hours<sup>6,7</sup>. At present, around 50% of patients with STEMI are receiving PCI<sup>8</sup>. Among them, less than 50% of STEMI patients are receiving primary PCI within the timeframe. Higher mortality rates were recorded in patients undergoing PCI beyond 120 minutes.<sup>9,10</sup>

Early recognition, decreasing pre-hospital time delays and procedural delays help to achieve optimal clinical results in the acute phase of STEMI. The relationship between symptom onset-to-balloon time and mortality is weak, and few long-term data are available. Hence, this study is an attempt to fill up the research gap. The present study was done to assess total ischemic time is more crucial than door-to-balloon time in patients undergoing primary PCI for STEMI and to assess prognostic impact and mortality rate in patients undergoing primary PCI for STEMI at a tertiary healthcare center in India.

## Methods

The present study was a single-center, interventional study done on 190 patients with STEMI between October, 2020 and December, 2021 at a tertiary healthcare center in India. The patients were analyzed for trends in total ischemic time, D2B time, associated factors and in-hospital mortality of patients undergoing primary PCI.

The patients were evaluated for demographic parameters like age, gender, comorbid conditions like diabetes, hypertension, arrhythmias, hypothyroidism, cancers, chronic obstructive pulmonary disorder (COPD), shortness of breath (SOB) and other parameters like BMI, D2B time, serum creatinine, hemoglobin, total ischemic time, types of MI. Institutional ethics committee approval was taken before the initiation of the study. A signed informed consent form was taken from each patient participating in the study. Purpose of the study, benefits and all the study details were explained to participants in their local, easily understandable language. All 190 patients had given their consent to participate in the study through their signatures or thumb impression.

## Statistical analysis

The categorical variables were presented as number and percentage. The continuous variables were presented as mean and standard deviation. Chi square test was done to access the association between categorical variables. The statistical analysis was done by SPSS software version 23.

## Results

Results of 190 participants of the study were evaluated. The mean age of the population was  $57.99 \pm 10.59$  years. Of the 190 participants, 65 patients were in the age group 56-65 years, the detailed age distribution of patients is depicted in Figure 1. Majority of the population were male (85.3 %). Out of 190 patients, 165 patients (86.8%) had LV dysfunction. Most of the study participants are in the body mass index (BMI) range of 25-29.9 kg/m<sup>2</sup> (over weight). The BMI distribution is shown in Figure 2. Mean ischemic time was around 470 min in 190. Patients with total ischemic time more than 480 minutes (P=0.05) showed significant mortality. Mean D2B time was  $66.26 \pm 25.05$  min. The detailed demographic details of patients are given in Table 1.

Majority of the patients had acute anterior wall myocardial infarction (57.4%) followed by acute inferior wall myocardial infarction (28.9%). Left ventricular dysfunction was reported in 86.8 % patients. The mean door to balloon time was  $66.26 \pm 25.05$  min. The detailed presentation of patients presented with myocardial infarction is shown in Table 2.

All 190 patients in the study were treated with stent implantation and most of them were having a family history of coronary artery disease. 8 patients died in the duration with increased total Ischemic time >8 hours due to underlying complications like arrhythmia (2patients) and pump failure (6 patients).Arrhythmia is the most common associated comorbid condition followed by diabetes mellitus. Many patients with STEMI were having left ventricle dysfunction when assessed by the 2D echo.

## Tables

**Table 1: Demographic details of patients**

<b>Characteristics</b>	<b>N=190 patients</b>
Age, mean $\pm$ SD (years)	57.99 $\pm$ 10.59
Male, N (%)	162 (85.3)
Diabetes mellitus, n (%)	98 (51.6)
Hypertension, n (%)	91 (47.9)
Smoking, n (%)	5 (2.6)
Family history of coronary artery disease, n (%)	12 (6.7)
Chronic obstructive pulmonary disease, n (%)	7 (3.7)
HbA1c, mean $\pm$ SD (%)	8.32 $\pm$ 1.72
Creatinine, mean $\pm$ SD (mg/dl)	0.99 $\pm$ 0.62
Haemoglobin, mean $\pm$ SD (%)	13.56 $\pm$ 1.89
External shortness of breath, n (%)	18 (9.5)
Denovo diabetes, n (%)	5 (2.4)
Arrhythmias, n (%)	11 (5.8)
CHB, n (%)	5 (2.4)
Ventilator, n (%)	21 (11.1)
Use of balloon, n (%)	13 (6.8)
Stents, n (%)	190 (100)
Intra-aortic balloon pump, n (%)	21 (11.1)
Hypothyroidism, n (%)	9 (4.8)

**Table 2: Types of myocardial infarction and other procedure related details of patients**

<b>Types of MI</b>	<b>N=190 patients</b>
Acute anterior wall MI, n (%)	109 (57.4)
Inferior wall MI	55(28.9)
Inferoposterior wall MI	12(6.3)
Anterolateral wall MI	5(2.6)
Lateral wall MI	3(1.6)
Inferolateral wall MI	3(1.6)
Posterolateral wall MI	2(1.1)
Inferoposterior lateral wall MI	1(0.5)
<b>Other parameters</b>	
Left ventricular apical clot, n (%)	3(1.6)
Left ventricular Dysfunction, n (%)	165 (86.8)

Total Ischemic Time, mean $\pm$ SD (min)	470.02 $\pm$ 528.94
Door to balloon time, mean $\pm$ SD (min)	66.26 $\pm$ 25.05
Door to balloon time >90 minutes, n (%)	36 (18.9)
Door to balloon time <90 minutes, n (%)	154 (81.1)

MI- myocardial infarction

**Table 3: Total Ischemic time with relation to mortality**

Total Ischemic Time	Alive	Deaths	Total
<3 hours	51(28%)	1(12.5%)	52(27.4%)
3-6 hours	57(31.3%)	2(25%)	59(31.1%)
6-9hours	27(14.8%)	1(12.5%)	28(14.7%)
>9 hours	47(25.8%)	4(50%)	51(26.8%)
Total	182	8	190

P Value: 0.4; NS

With the increase in total Ischemic time >9 hours, the mortality has been increased by 50%.

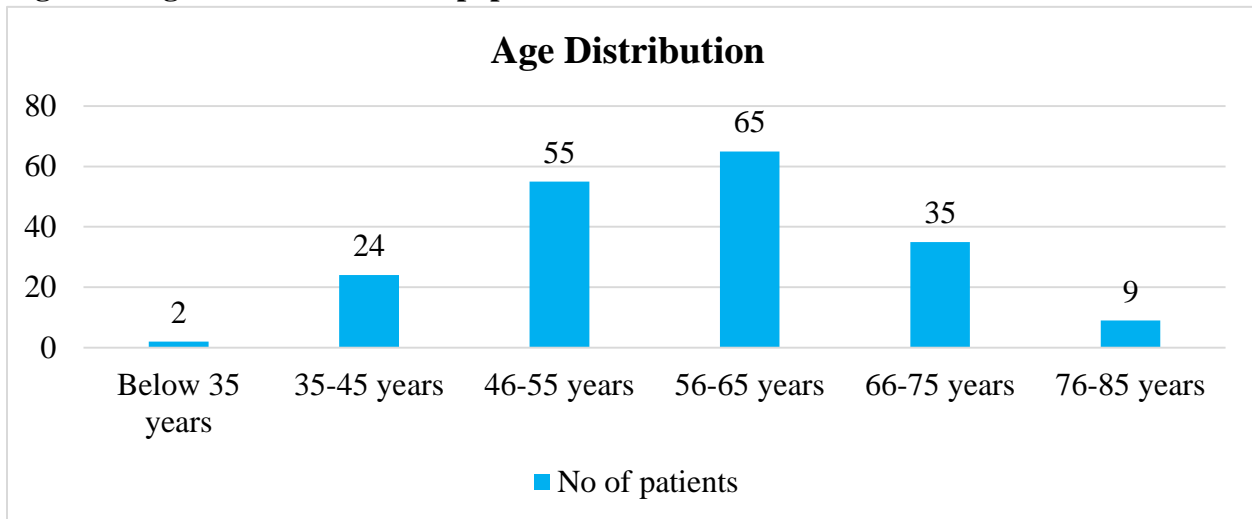
**Table 4: Univariable analysis.**

S.NO	Variable	Alive	Deaths	P Value
<b>AGE in Years</b>				
1	<35	2	0	0.2
	36-45	24	0	
	46-55	54	1	
	56-65	59	6	
	66-75	34	1	
	76-85	9	0	
<b>D2B time</b>				
2	<30mins	8	0	0.1
	30-59mins	67	6	
	60-89mins	70	2	
	>90mins	37	0	
<b>Total Ischemic Time</b>				
3	<120 mins	20	1	0.05

121-240 mins	50	1
241-360 mins	38	1
361-480 mins	20	0
481-600 mins	14	3
601-720 mins	6	1
721-840 mins	12	0
841-960 mins	6	1
>960 mins	16	0

Total Ischemic time showed statistical significance ( $p=0.05$ ) in relation to mortality of the patients. Patients with more than 8 hours of total ischemic time had higher chances of mortality.

**Figure 1: Age distribution of the population**



**Figure 2: Body mass index distribution of the population**

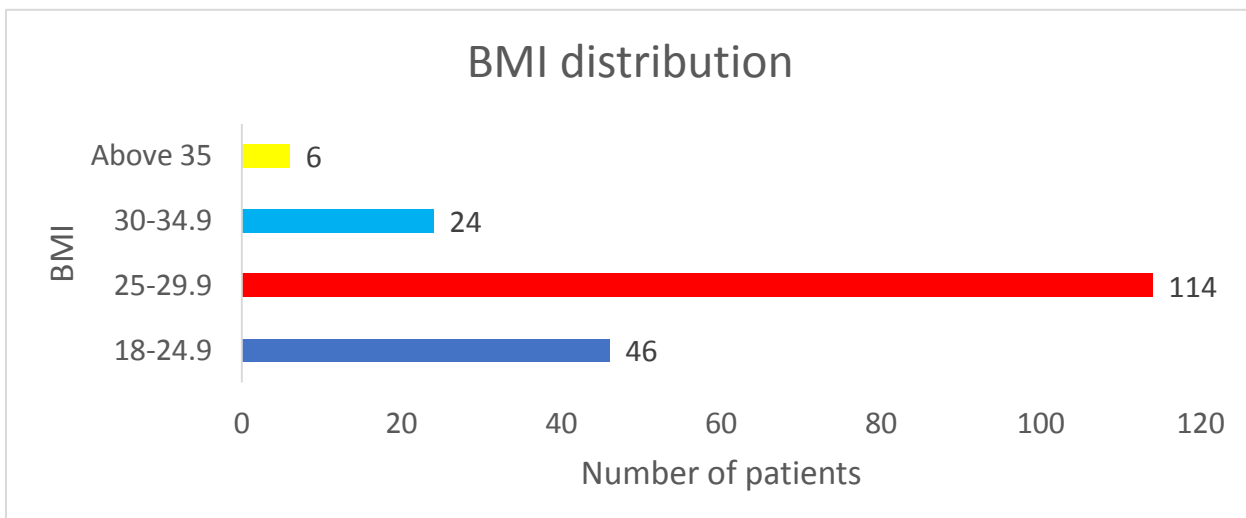
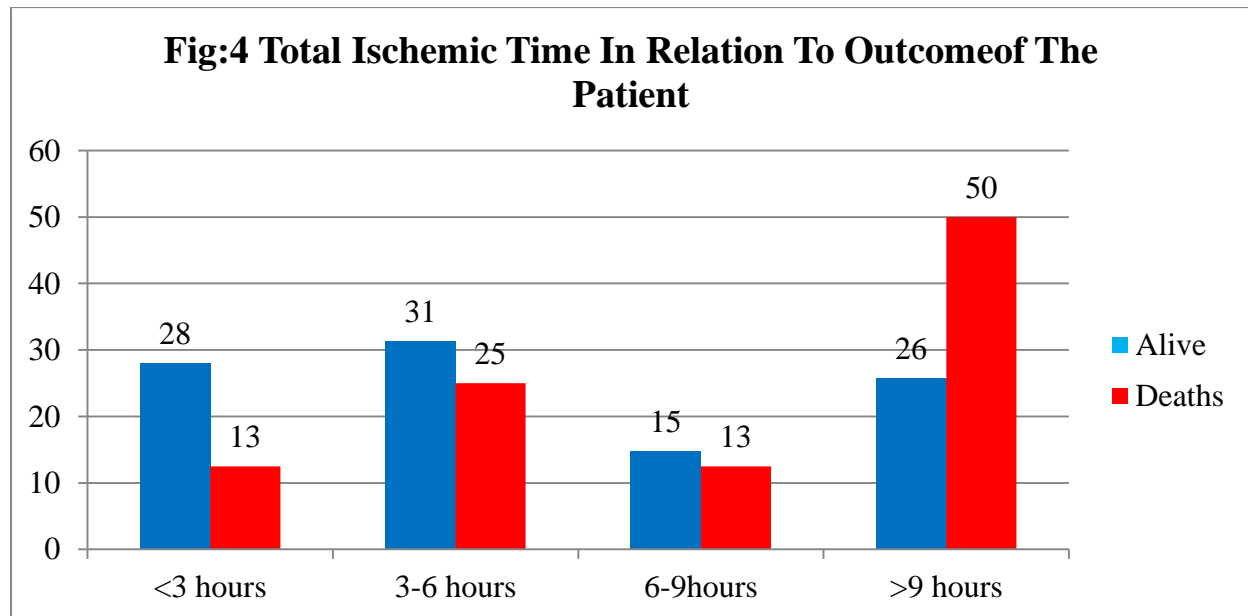
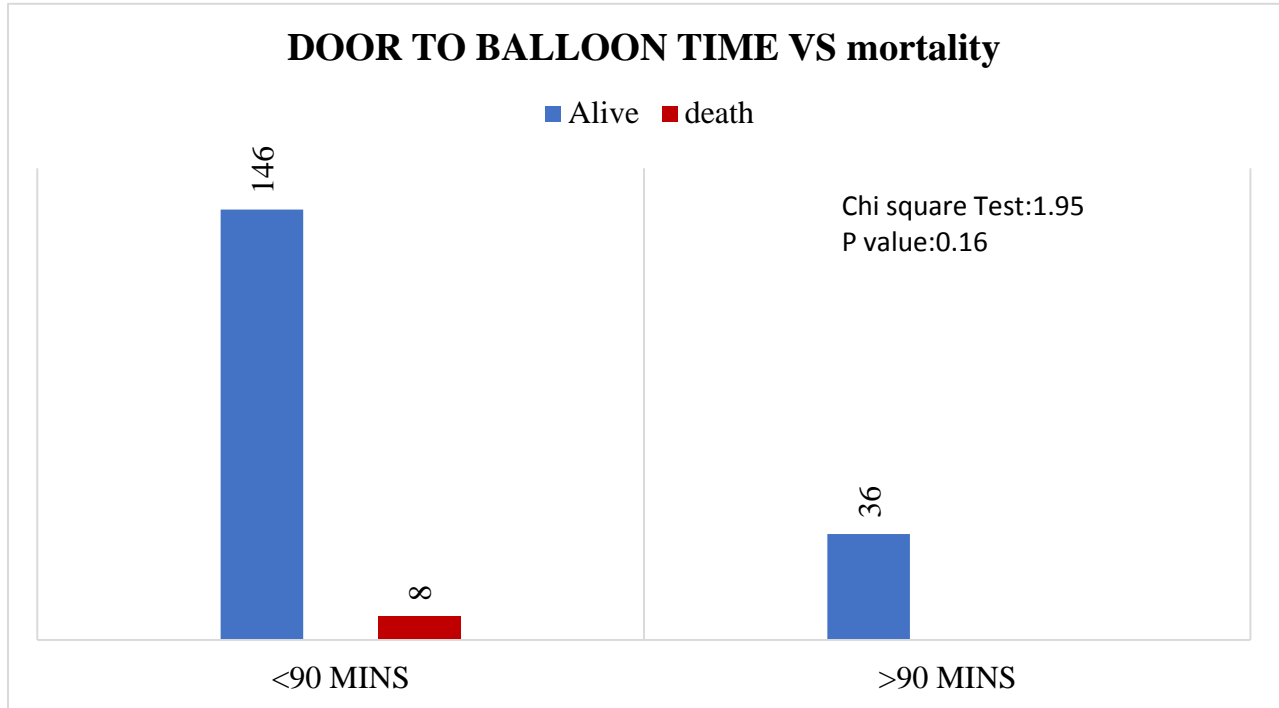


Figure 3: Door to balloon time and mortality



## Discussion

Total ischemic time and Door-to-balloon time are the major focus in qualitative care assessment for patients undergoing primary PCI for ST-segment elevation myocardial infarction. Patients with total ischemic time more than 480 minutes ( $P=0.05$ ) showed significant mortality. In our study, more than 81% of patients undergoing primary PCI for ST-segment elevation myocardial infarction reached the goal mentioned in the ACC/AHA clinical practice guidelines of a door-to-balloon time of 90 minutes or less.

In our study, D2B time is not related to mortality rates. In the study done by Berger et al. 30-day mortality rate was lower among patients with a door-to-balloon time of less than 60 minutes.<sup>11</sup> In the study done by Brodie et al<sup>12</sup>, improved door-to-balloon times were not associated with a mortality benefit at 1 month or 6 months.

Animal studies done on dogs and pigs have proved a time-dependent wave front of ischemic cell death linked to arterial occlusion, showing that the degree of myocardial salvage is significantly decreased after prolonged periods of ischemia.<sup>13, 14</sup> Thus, total ischemic time may be a more important clinical parameter than door-to-balloon time.

Some researchers suggest the link between door-to-balloon time and mortality may be affected by an “immigration bias”.<sup>15</sup> Healthier patients are likely to have shorter door-to-balloon times compared to sick patients with more comorbid conditions, for whom treatment may be delayed because of the time needed for medical stabilization.<sup>16</sup> And, hospitals with more patient volumes are having better equipment than other settings, which reduces door-to-balloon times along with other improved performance measures.<sup>17</sup> So, good clinical outcomes could be the result of institutional or operator experience and expertise.

In the study done in 2008 by Gibson et al<sup>18</sup>, in an analysis of data from the National Registry of Myocardial Infarction, they reported a significant reduction in mortality, from 8.6% to 3.1%, linked with a decline in door-to-balloon times from 111 minutes in 1994 to 79 minutes in 2006. In another analysis of data from the National Registry of Acute Myocardial Infarction<sup>19</sup> that included 27,080 patients, the least mortality rate was seen in patients undergoing PCI within 60 minutes from the presentation, and higher mortality rates were observed in patients undergoing PCI beyond 120 minutes.

In the study published in the journal *Circulation* by Bradley et al<sup>20</sup> researchers identified 8 themes that were specific to major hospitals like commitment to a goal to improve door-to-balloon time motivated by internal and external pressures, proper support from the senior management, innovative protocols, flexibility in refining certain protocols, good clinical leaders, collaborative supporting teams, data feedback.

In the Guidelines Applied to Practice (GAP)<sup>21</sup> intervention that is aimed at enhancing the quality of care for patients with acute coronary syndromes, data collection was followed by interventions like hospital site visits by project leaders, development of appropriate standings orders, simple hospital discharge contracts etc.<sup>17</sup> These interventions improved the quality of care but they were unsuccessful in improving door-to-balloon time for primary PCI.



In study done by Caputo et al<sup>22</sup>, he reported that interventions like avoidance of pre-evaluation by cardiologists, proper education of emergency department staff, transport persons, rapid transport to the catheterization laboratory and target time of 30 minutes for staff performing first balloon inflation after xylocaine administration etc. significantly decreased D2B time.

### **Limitations of the present study:**

We cannot preclude the possibility of confounding factors like prior peripheral vascular disease, pre hospital system delay. Larger observational studies involving more patients are more likely to be the best way to evaluate the effect. This study included patients who were undergoing primary PCI. So, the results cannot be generalized to all patients with ST elevated myocardial infarction and patients with different ethnic and geographical backgrounds.

### **Conclusion**

Remarkable improvement in clinical outcomes can be achieved by a multidisciplinary collaboration. Our data suggest that more efforts are needed to reduce total ischemic time and door-to-balloon time. More efforts like improving patients' awareness of symptoms, reducing the interval from the time of symptom onset to treatment, and decreasing the transfer time between medical facilities can help achieve the goal. 8 patients died in the duration with increased total Ischemic time >8 hours & D2B<90mins due to underlying complications like arrhythmia (2patients) and pump failure (6 patients). Hence Total ischemic time must be taken as the most crucial factor than D2B.

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