

# Symptoms to Balloon time Dependent ST-Segment Resolution Post Primary Percutaneous Coronary Intervention and its Impact on Mortality

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## ABSTRACT

**Background:** The ST-segment elevation myocardial infarction (STEMI) is an emergency manifestation of coronary artery disease (CAD) that occurs when one epicardial coronary artery is completely blocked. Study aims to test whether symptom-onset-to-balloon time correlates with in-hospital outcomes after primary percutaneous coronary intervention (PPCI) among patients with STEMI.

**Methodology:** under the Hospital Ethical and Research Committee's approval, NICVD's Department of Interventional Cardiology conducted a prospective cohort study that lasted for 6 months. Patients fulfilling the criteria of ST elevation, i.e.,  $\geq 1$  mm in limb leads and  $\geq 2$  mm in precordial leads, aged  $> 18$  and  $< 80$  years, were included. ST segment elevations and time of symptoms onset were interpreted from the patient's ECG, performed for 30 to 60 minutes. Based on the symptom onset to balloon time, the patients were divided into 2 groups, i.e.,  $< 6$  and  $> 6$  hours with follow-up till discharge and 30 days after discharge. An analysis of multivariate logistic regression was conducted to determine if ST-segment resolution and in-hospital mortality were influenced by the time from symptom onset to balloon time.

**Results:** The results showed that Patients with double or triple vessel disease had longer symptom onset to balloon time ( $p=0.041$ ). Symptom onset to balloon time delayed increased ST-segment resolution by  $<50\%$  ( $p=0.000$ ). Symptom onset to balloon time was an important prognosticator of ST-Segment Resolution ( $< 50\%$  Resolution) but not for mortality.

**Conclusion:** The current study concluded that the association between ST-segment resolution and symptom onset to balloon time shows the significance of symptom onset to balloon time among STEMI patients after PPCI.

**Keywords:** Symptoms to Balloon Time, ST Segment Resolution, Primary percutaneous Coronary Intervention

## INTRODUCTION

Worldwide, coronary artery disease (CAD) is the leading cause of death<sup>1,2</sup>. ST-segment elevation Myocardial Infarction (STEMI) is one emergency presentation of CAD involving complete blockage of one of the epicardial coronary arteries. Mechanical opening of the blocked coronary artery via Primary Percutaneous Coronary intervention is the preferred method of treatment<sup>3-5</sup>.

The Current Guidelines Recommendation for PPCI is to perform it within 12 hours of the onset of symptoms, provided that Door to balloon Time is kept to less than 90 minutes<sup>3,4</sup>. However, studies show that there is time-dependent myocardial necrosis occurring as an ischemic wave front from endocardium to epicardium<sup>6</sup>, so the time from onset of symptoms, i.e., Chest pain to opening the artery via balloon or stent, should be kept as low as possible to minimize myocardial injury and subsequent scar<sup>7</sup>.

The ST-segment resolution post reperfusion therapy is an imperative prognosticator of potency to artery and associated event and actual microcirculatory perfusion. The investigation of electrocardiogram (ECG) for resolution of ST-segment involves an easy and low-cost tool that can document the feat of the tissue and epicardial after primary PCI<sup>8</sup>. When ST-segment elevation persists despite normalizing epicardial flow, patients face a poor prognosis, and are more likely to die from cardiovascular events and have a larger infarct size<sup>9</sup>.

ST segment resolution failure has been shown to be related to prolonged ischemic times, i.e., from symptoms onset to ballooning, diabetes mellitus, and chronic renal failure<sup>10</sup>. Resolution of more than 70% of the ST segment from baseline after PPCI has been shown in multiple studies to be correlated with a very good short- and long-term prognosis, while failure to do so has been associated with both short- and long-term mortality<sup>11</sup>. After STEMI symptoms are manifested, timing of artery opening has been associated with larger infarct sizes,<sup>7</sup> higher mortalities, and higher adverse cardiac events, such as poorly resolved ST segments following PPCI<sup>10</sup>. Serum Cardiac Troponins after an uncomplicated percutaneous coronary intervention (PCI) is elevated in 4 to 45 percent of patients<sup>8</sup>. A study by Song et al.<sup>12</sup>

reported ST-segment resolution  $<50\%$  in 16.7% vs. 19.2% of the patients with symptoms to balloon time of  $< 6$  hours and 6 to 12 hours, respectively.

The high number of PPCI performed in our institute requires methods to assess the outcome of patients after PPCI. Also, late presentation of patients in our setup for PPCI due to multiple issues puts them at higher risk for adverse outcomes. To address these issues, we need to have a local study to look at the percentage of complete vs. partial and no resolution of ST segment after PPCI and its correlation with the symptoms to balloon time and look at its impact on mortality. We examined the effect of symptom onset-to-balloon time on STEMI patient outcomes after PPCI in the present study.

## MATERIAL & METHODS

A six-month prospective cohort study was carried out at the Department of Interventional Cardiology at the National Institute of Cardiovascular Development, from 28<sup>th</sup> January 2021 to 27<sup>th</sup> July 2021. The Hospital Ethical and Research Committee approved the study protocol (Reference #ERC-04/2021; Dated January 27, 2021). Verbal informed consent was obtained, and data confidentiality was maintained. With an expected ST-segment resolution rate of 78% vs. 86% for the patients with symptoms to balloon time of 6 to 12 hours and  $< 6$  hours respectively<sup>13</sup>, with 80% power of test and 5% level of significance, the required sample size of  $n=100$  patients in each group, i.e., symptoms to balloon time of  $< 6$  hours and  $> 6$  hours, was calculated. The final cohort included 235 patients.

All STEMI patients fulfilling the criteria of ST elevation, i.e.,  $\geq 1$  mm in limb leads and  $\geq 2$  mm in precordial leads, aged  $> 18$  and  $< 80$  years, were included. At the same time, patients with pre-existing Left bundle branch block (LBBB), prior Myocardial Infarction (MI), and those with cardiogenic shock were excluded from the study.

ST segment elevations and time of symptoms onset were interpreted from the patient's ECG, performed for 30 to 60 minutes. The patients were divided into two groups, based on their onset to

balloon time, i.e., < 6 hours and > 6 hours. All patients were followed till discharge and 30 days after discharge by the attending physician or via telephonic interview if the patient did not visit on the scheduled follow-up visit.

A frequency or percentage was calculated for each qualitative variable. The mean and standard deviation were used to express quantitative data. In order to assess differences in baseline features and in-hospital outcomes based on symptomatology, Chi-square tests were used for categorical variables and independent sample T tests for continuous variables. Multivariate logistic regression analyses were conducted to assess the attuned effect of Symptom onset to Balloon Time on ST-segment resolution and in-hospital mortality. In order to be considered statistically significant, a p-value of < 0.05 was required.

that patients with double or triple vessel disease were more likely to have longer symptom onset to balloon time (p=0.041).

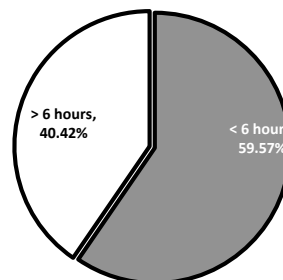


Figure 1: Proportions of symptom onset to balloon time.

**RESULTS**

There were mostly male patients (87.2%) in the cohort; their mean age was 53.99 ± 9.79 years.

The baseline, angiographic and clinical characteristics of symptom onset to balloon time are presented in **Table 1**, indicating

Table 1: Baseline, clinical and angiographic characteristics of the patients based on the symptom onset to balloon time.

Variables	Total (n=235)	Symptom onset to Balloon Time		p-value
		< 6 Hours (n=140)	> 6 Hours (n=95)	
Age (Years)	53.99±9.79	53.99±9.77	54.00±9.86	0.996
Gender	Female	30(12.8)	15(15.80)	0.253
	Male	205(87.2)	80(84.20)	
Diabetes	No	164(69.8)	101(72.10)	0.340
	Yes	71(30.2)	39(27.90)	
Hypertension	No	100(42.6)	63(45.00)	0.357
	Yes	135(57.4)	77(55.00)	
Smoking	No	151(64.3)	88(62.90)	0.587
	Yes	84(35.7)	52(37.10)	
Chronic Renal Failure	No	230(97.9)	137(97.90)	0.984
	Yes	5(2.1)	2(2.10)	
Acute Kidney Injury	No	226(96.2)	137(97.90)	0.102
	Yes	9(3.8)	6(6.30)	
Number Of Diseased Vessels	DVD	89(37.9)	47(33.60)	0.041*
	TVD	59(25.1)	32(22.90)	
	SVD	87(37.0)	61(43.60)	
Pre-Procedure TIMI Flow	TIMI 0	91(38.7)	49(35.00)	0.466
	TIMI I	49(20.9)	32(22.90)	
	TIMI II	76(32.3)	46(32.90)	
	TIMI III	19(8.1)	13(9.30)	

\*shows p<0.05 (statistically significant)

Table 2 provides information about the outcomes of patients in the hospital. A total of 11 (4.7%) patients died in hospital; in relation to the symptom onset to balloon time, 9.50% of patients with > 6 hours' symptom onset to balloon time died as compared to 1.40% of those with < 6 hours' time (p=0.004). Furthermore, ST-segment resolution < 50% increased as a symptom onset to balloon time delayed (p=0.000).

Table 2: Comparisons of in-hospital outcomes based on symptom onset to balloon time.

Variables	Total (n=235)	Symptom onset to Balloon Time		p-value
		< 6 Hours (n=140)	> 6 Hours (n=95)	
ST Segment Resolution	< 50	57(24.3)	4(2.90)	0.000*
	> 50	156(66.4)	135(96.40)	
	None	22(9.4)	1(0.70)	
Post-Procedure Echo	Ef 25%	2(0.9)	1(0.70)	0.315
	Ef 30%	22(9.4)	11(7.90)	
	Ef 35%	101(43.0)	57(40.70)	
	Ef 40%	33(14.0)	20(14.30)	
	Ef 45%	35(14.89)	22(15.71)	
	Ef 50%	28(11.9)	16(11.40)	
	Ef 55%	10(4.3)	10(7.10)	
	Ef 60%	4(1.7)	3(2.10)	
Heart Failure	No	205(87.2)	125(89.30)	0.253
	Yes	30(12.8)	15(15.80)	
Re-Admission	No	208(88.5)	128(91.40)	0.089
	Yes	27(11.5)	12(8.60)	
Mortality	No	224(95.3)	138(98.60)	0.004*
	Yes	11(4.7)	2(1.40)	

\*shows p<0.05 (statistically significant)

I found a significant correlation between the time from symptom onset to balloon bursting and the ST-Segment Resolving (< 50% Resolution) but not for mortality.

Table 3: Multivariate logistic regression analysis to assess the relation between Symptom onset to Balloon Time and (A) in-hospital mortality, and (B) ST-segment resolution.

Variable	Symptom onset To Balloon Time	
	< 6 hours	> 6 hours
Mortality	1.0	0.44(0.07-2.72)
ST Segment Resolution (< 50% Resolution)	1.0	0.01(0.00-0.03)*

\*shows  $p < 0.05$  (statistically significant)

## DISCUSSION

The present study showed an overall mortality rate of 4.7%, reduced symptom onset to balloon time was significantly associated with decreased mortality rate and better survival among STEMI patients. Song et al. also stated a progressive increase in the mortality rate with increased symptom onset to balloon time<sup>12,14</sup>. Furthermore, Rollando et al. also concluded that shorter symptom onset-to-balloon time amongst STEMI patients could predict lower mortality<sup>15</sup>. The registries from the United States, Japan, Korea, and also global registry from twelve different countries reported a medium symptom onset to balloon time of 2.25, 4.6, 3.9, and 3.8 hours, respectively<sup>16-18</sup>. The National Registry conducted in the USA, including 20,000 MI patients, concluded that door-to-balloon time is a better predictor of in-hospital mortality when compared with symptom onset to balloon time<sup>16,19</sup>.

We have also observed a significant association between several diseased vessels and symptom onset to balloon time; patients with longer time were more likely to have double or triple vessel disease. Other studies report that female gender, diabetes, and multivessel disease had longer symptom onset to balloon time than the counterpart<sup>20,21</sup>. Our study, however, did not find any significant relationship between the onset of symptoms and balloon time based on gender or diabetes. The early arrivers had grade III TIMI, supported by another study<sup>14</sup>.

ST-segment resolution is listed among the significant predictors of adverse cardiovascular events and target vessel revascularization and is also determined as a well-known myocardial reperfusion indicator<sup>22</sup>. Longer symptom onset to balloon time was associated with ST-segment resolution < 50% (< 6 hours: 2.90%; > 6 hours: 55.80%;  $p=0.000$ ) and it was found as its significant predictor. Similarly, Song et al. reported that symptom onset to balloon time for > 12 hours is an independent risk factor for < 50% ST-segment resolution<sup>14</sup>. This association between ST-segment resolution and symptom onset to balloon time shows the significance of symptom onset to balloon time among STEMI patients.

**Study limitations:** Our study has few terms of analysis based on observational results and might be attributable to biases because of unmeasured factors, as we cannot exclude the likelihood of confounding by other hospital factors allied with door-to-balloon time or mortality.

## CONCLUSION

I conclude it from the current study that the association between ST-segment resolution and symptom onset to balloon time indicates the significance of symptom onset to balloon time among STEMI patients after PPCI. In addition, we found that patients undergoing primary percutaneous coronary intervention had an advantage by reducing the time spent from door-to-balloon.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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