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Original Article

Is symptom to balloon time a better predictor of outcomes in acute ST-segment elevation myocardial infarction than door to balloon time?

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Abstract: Introduction: Current guidelines for the treatment of ST-segment elevation myocardial infarction (STEMI) recommend early revascularization with a door-to-balloon (D2B) time of 90 minutes or less in patients undergoing primary percutaneous coronary intervention (PPCI). The focus of most studies has been D2B time. Because of the large variability in the time between symptom onset and presentation, we sought to determine the effect of symptom-to-balloon (S2B) time on presentation and outcomes as a potentially more clinically relevant parameter. Methods: We conducted a retrospective study of 106 patients who were diagnosed with an acute STEMI, had a documented S2B time and who underwent a PPCI at a tertiary hospital from the period of January 2014 to December 2014. S2B time was defined as the time interval beginning from the episode of chest pain that led the patient to present to the emergency department to the time of the first balloon inflation. We categorized our patients into 2 main groups depending on whether S2B time was greater or less than 240 minutes. They were further subdivided into 2 groups depending on the site of the culprit lesion (left anterior descending LAD vs. non-LAD). Results: There was no difference between the two main groups in regard to the left ventricular ejection fraction (EF) on presentation, length of stay, and readmission with heart failure or chest pain. However, when S2B time was greater than 240 min, there was a statistically significant difference in left ventricular ejection fraction (EF) between LAD and non-LAD stenosis with a mean of 38.4% and 49.3% respectively (P=0.01). No relationship was found between S2B time and gender or age. Conclusion: Although D2B time is a well-established clinical parameter, S2B time may be expected to be a more accurate predictor of outcomes. However, in our study, S2B time of >240 minutes only predicted a significant worse EF (and presumably mortality) when the culprit vessel was the LAD. Further studies are needed to better elucidate the relation of S2B time to clinical outcomes.

Keywords: Acute myocardial infarction outcomes, symptom to balloon time, left anterior descending vessel lesion

Introduction

In today's practice of cardiology, primary percutaneous coronary intervention (PPCI) is the treatment of choice for acute ST-segment elevation myocardial infarction (STEMI). In the current literature, observational studies have shown a strong association between prompt performance of primary PCI as measured by the door to balloon (D2B) time and improved patient outcomes [1]. D2B time is defined as the time interval from the patient's arrival at the hospital to the first balloon inflation in order to restore coronary blood flow [2, 3].

Based on the available data, current joint clinical practice guidelines of the American College of Cardiology and the American Heart Association (ACC-AHA) endorse a D2B of 90 minutes or less as the goal, giving it a Class I recommendation [4]. Due to this recommendation, D2B time has become the focus of local, regional, and national quality-improvement initiatives and is currently recorded by a number of clinical registries [5, 6]. D2B times are also publicly reported and have financial implications, since they are linked to reimbursements from the Centers for Medicare and Medicaid Services (CMS) [7].

Previous studies have shown inconsistent results regarding the effect of symptom onset to balloon time compared with door to balloon time on clinical outcomes in patients with STEMI undergoing PPCI [1, 3, 8, 9]. Although a clear relationship has been demonstrated in the literature between mortality and time delay

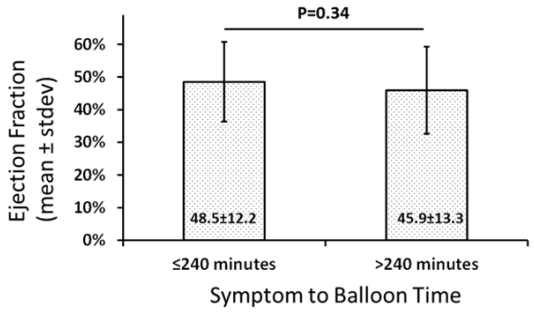

Figure 1. Ejection fraction at the time of admission in patients with Symptom to Balloon times of ≤240 minutes was not statistically different from ejection fraction in patients with longer times.

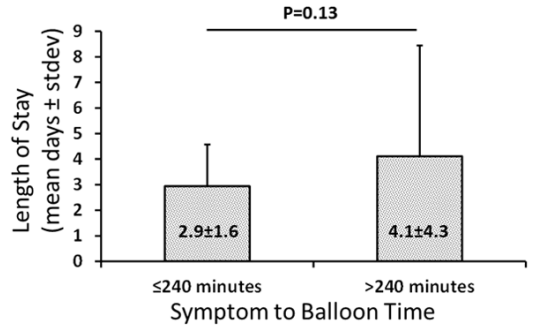

Figure 2. Length of stay for patients with Symptom to Balloon times of ≤240 minutes was not statistically different from length of stay for patients with longer times (Students T-test).

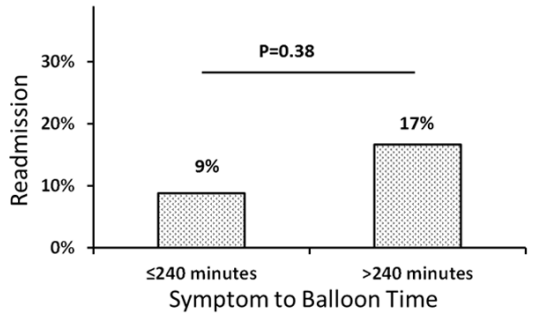

Figure 3. Readmissions for patients with Symptom to Balloon times of ≤240 minutes was not statistically different from readmissions for patients with longer times (Fishers Exact Test).

from symptom onset to treatment in patients with STEMI treated by thrombolysis [12-14], the effect of time delay on prognosis in patients undergoing PPCI has still not been clarified [2, 8, 9, 14]. The aim of our study is to evaluate the influence of symptom onset to balloon (S2B) time on presentation, outcomes and mortality

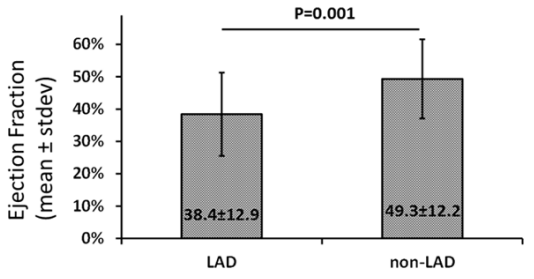

Figure 4. Ejection fraction at the time of admission in LAD patients with Symptom to Balloon times of >240 minutes was statistically lower than ejection fraction in non-LAD patients with similar times (Student's T-test).

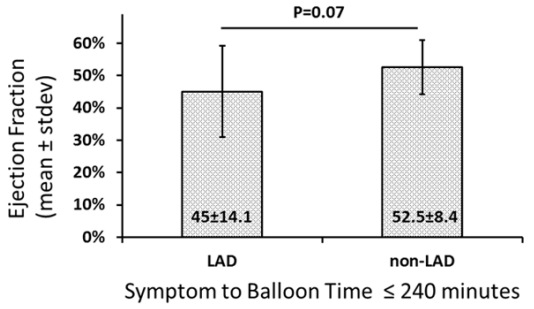

Figure 5. Ejection fraction at the time of admission in LAD patients with Symptom to Balloon times of ≤240 minutes was lower but not statistically significant compared to ejection fraction in non-LAD patients with similar times (Student's T-test).

in patients with STEMI treated by PPCI in a tertiary center.

Methods

Objective

We conducted this study to determine the effect of symptom-to-balloon (S2B) time on presentation and outcomes for patients presenting with acute STEMI at Providence Hospital and Medical Centers (PHMC)/Michigan State University at the Southfield and Novi campuses in Michigan.

Study design

This is an observational, retrospective study based on an electronic medical system review.

Null hypothesis

Symptom-to balloon time has no impact on presentation and outcomes for patients with STEMI.

Subjects

Our study population included all adult patients >18 years old who were diagnosed with an acute STEMI, had a documented S2B time and who underwent a PPCI at PHMC from the period of January 2014 until December 2014. S2B time was defined as the time interval beginning from the episode of chest pain that led the patient to present to the emergency department to the time of the first balloon inflation.

Statistical analysis

Statistical analysis included Student's t-test for comparing two groups of continuous variables such as the mean age of LAD versus non-LAD patients. One way analysis of variance was used to compare more than three groups of continuous variables. Chi Square and Fisher's Exact tests were used to compare groups of discrete variables. A *P*-value of <0.05 was considered statistically significant. IMB SPSS version 23 was used with Microsoft Excel for data analysis.

Results

The total number of patients that met our inclusion criteria was 106 patients. We categorized our patients into two main groups based on S2B time duration. The first group included patients with a S2B of 240 minutes or less while the second group included S2B time of more than 240 minutes. Each group was further subdivided into 2 subgroups depending on the site of the culprit lesion whether it was a left anterior descending (LAD) or a non-LAD lesion.

Overall, there was no difference between the two main groups in regard to the left ventricular ejection fraction (EF) on presentation, length of stay, and readmission with heart failure or chest pain (**Figures 1**-**3**). **Figure 1** shows that the average EF on presentation is 48.5% when S2B time is equal or less than 240 min and 45.9% when S2B time is more than 240 min (P=0.34).

However, taking into account the culprit vessel and when S2B time was greater than 240 min, there was a statistically significant difference in EF between a LAD and non-LAD culprit lesion with a mean of 38.4% and 49.3% respectively (P=0.01) (**Figure 4**). For S2B time of less than 240 min on the other hand, the LAD culprit lesion did not seem to impact EF significantly with a mean EF value of 48.5% in LAD culprit and 45.9% in a non-LAD culprit lesions (P=0.07) as shown in **Figure 5**. Furthermore, there was no relationship between S2B time and gender or age.

Discussion

The American College of Cardiology (ACC), American Heart Association (AHA) and the European Society of Cardiology have all recommended a door to balloon (D2B) time of 120 minutes from the first medical contact or 90 minutes from the patient presentation to the first balloon inflation [2, 4]. This is mainly driven by the large US National registry of Myocardial Infarction. The registry showed a decrease in in-hospital mortality when D2B time is less than 90 minutes [1, 8].

However, in a study by Menees et al, comparing data from July 2005 to June 2006 with a median D2B time of 83 minutes, with data from July 2008 to June 2009 with a median D2B time of 67 minutes showed no difference in hospital mortality. The study concluded that other factors contributing to overall outcomes were present [15].

Ischemia starts at the time of symptoms and precedes patient presentation to medical contact. The earlier the ischemia is treated, the better the outcomes. However the time lapse between symptom onset and patient arrival to medical facilities (symptom to door) and hence acute intervention (S2B) can be variable and is affected by multiple factors including patient awareness of symptoms, socioeconomic variables, family support and geographical availability of medical facilities.

Previous studies have shown inconsistent results regarding the effect of S2B time compared with door to balloon times on clinical outcomes in patients with STEMI undergoing PCI [1, 3, 8, 9]. Various small studies suggest a positive correlation between short symptom onset to balloon time and decreased overall mortality [3, 9]. However, a large study that included 20,000 patients found that in-hospital mortality did not increase with longer S2B time [1]. On the other hand, short D2B time was

associated with lower in-hospital mortality regardless of time from symptom onset to presentation in the same study [1]. However, several other registries have reported the benefit of short D2B times to be limited to patients who present early [9-11]. In a study from Italy, 790 patients who had STEMI and treated with PCI were divided according to their symptoms onset time and delay in reperfusion to >180, 120-180 and <120 minutes. There was lower mortality at 1, 3, 5, 7 years of follow up in patient presenting <120 minutes vs. <180 minutes vs. >180 minutes [16].

The Japanese CREDO-Kyoto study in 2005-2007 enrolled 3391 patients from 26 tertiary hospitals who suffered from an acute STEMI. Shoimo et al found that, compared with an onset to balloon time greater than 3 hours, a time of less than 3 hours was associated with a lower incidence of a composite of death and congestive heart failure [17].

Our retrospective study analyzed 106 patients with STEMI in the year of 2014. The patients were divided in two main categories based on symptoms to balloon (S2B) presentation of 240 minutes or less, and more than 240 minutes. There was no difference in EF between the two groups in the overall cohort, however, when S2B time was more than 240 minutes, there was a significant difference in EF when categorized as LAD culprit vs. non-LAD culprit lesion (mean of 38% vs. 49% respectively, P=0.01). LAD culprit lesion seemed to have more impact on overall left ventricular function. In other words, in patients with LAD culprit lesion, longer S2B time (>240 minutes) significantly affected overall left ventricular systolic function. Whether this effect on LV systolic function can be extrapolated to hard outcomes of death, MI or congestive heart failure remains to be determined.

Limitations: this study was limited by its retrospective design, being conducted in a single center with two campuses and limited by recall bias of the patients. However, our patients were unselected and are from an area of mixed ethnic origin and social status. The physicians treating those patients were not aware that we would be examining patient's outcomes.

Further studies are warranted especially with a larger patient population, in order to further elucidate the role of S2B on EF and overall prognosis.

Disclosure of conflict of interest

None.

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