RESEARCH

Prehospital times in primary percutaneous coronary intervention: The new frontier for improvement

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Abstract

Background: Primary percutaneous coronary intervention (PPCI) remains the treatment of choice for patients presenting with ST-elevation myocardial infarction (STEMI). With STEMI, total ischemic time is an important predictor of myocardial injury and other short and long-term adverse events including mortality. Several studies have examined 'Door to Balloon' times, but few studies have examined pre-hospital and in hospital component times as individual pieces that make up total ischemic time. Methods: Total ischemic and component times for patients who received PPCI from 2012- 2015 in the Queen Elizabeth-II Halifax Infirmary were described. Median total ischemic times and component times were calculated and compared. Regression modeling was performed to identify which component times and component variables explained the most variation in total ischemic times. Results: 551 patients who had successful PPCI and complete component times were identified. Most were male (76%) with a median age of 59.2 years (IQR: 52.7-68.0 years). The longest component time was 'Symptom Onset to First Medical Contact' (Median: 61 min, IQR: 32-138 min). 'Symptom Onset to First Medical Contact' was found to account for most of the variation seen in total ischemic time (R2= 61%). Conclusions: We determined that most time in the component of receiving PPCI lies in the pre-hospital setting and that component variables including EHS use and pre-activation of the cardiac catheter lab reduce total ischemic time. More research needs to be devoted to reducing patient delay, as there appears to be little room for improvement in hospital component times.

Introduction

ST-Elevation Myocardial Infarction (STEMI) is a medical emergency that requires immediate intervention. Longer total ischemic time (time taken from symptom onset to provision of coronary reperfusion), is directly related to adverse outcomes in STEMI patients[1-4]. Coronary reperfusion can be achieved with either timely administration of fibrinolytic therapy or primary percutaneous coronary intervention (PPCI). Several studies have demonstrated that PPCI is superior to fibrinolytic therapy in reducing adverse outcomes if provided in a timely fashion. At the time of this study, guidelines stressed that the first medical contact to device time for STEMI should be less than 90-120 minutes depending on the site of presentation of the patient[5].

There is extensive literature on the outcomes following PPCI, but few studies have examined component times (the discrete times that make up the process starting from symptom onset to revascularization) in PPCI[6-9]. Of these, most examined the total ischemic and door to balloon times (time from arrival at hospital door to first balloon inflation in the coronary artery). At the time of this study, only a handful of studies had attempted to show the detailed components of PPCI from a patient perspective[10-12]. Total ischemic time for PPCI is made up of several component times that can each result in delays and contribute to variation in total ischemic time (Figure 1). For example, symptom onset to first medical contact time, first medical contact to diagnostic (ECG) time, diagnosis to cardiac catheter lab activation time, catheter lab activation to catheter lab arrival/ready time and catheter lab arrival/ready to device insertion time (balloon inflation or stent deployment or thrombectomy catheter).

The objective of this study was to determine, in a tertiary care centre in Halifax, Nova Scotia, Canada, which parts of the process of receiving PPCI for STEMI contribute most to total ischemic time and explain variation in total ischemic time. Secondary objectives were to assess the effect of Emergency Health Services (EHS) and pre-activation of cardiac catheter lab prior to patient arrival reduced total ischemic time.

Methods

Study Design

The study examined all patients (n=607) undergoing PPCI for STEMI during the period of January 1, 2012 to June 30, 2015. Patients who received fibrinolytic therapy or percutaneous coronary intervention (PCI) after fibrinolytic therapy (rescue PCI) were not included. The data were obtained from the Philips Cardiovascular Information System (CVIS)®. This database is used in the Queen Elizabeth II Health Sciences Centre in Halifax,

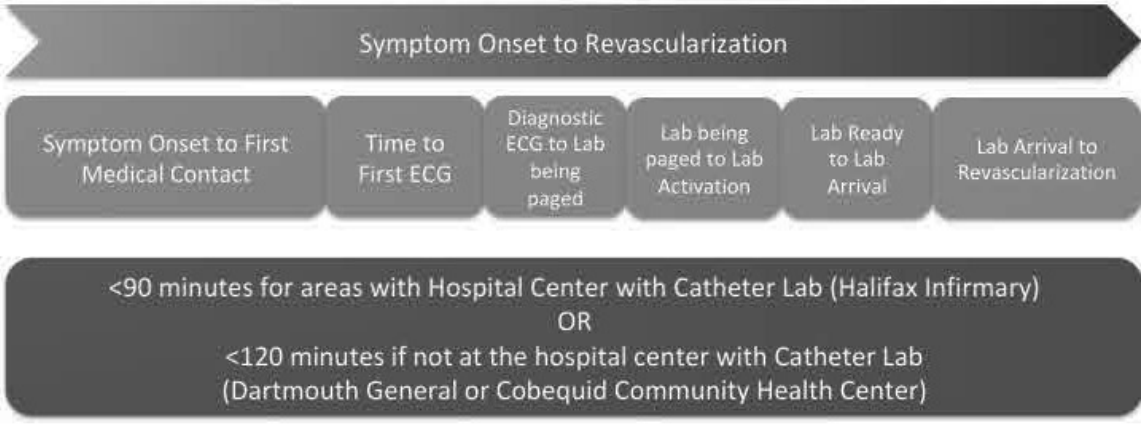

Figure 1. Total ischemic time and different points in the process of receiving PPCI. Total ischemic time measured as symptom onset to revascularization.

Nova Scotia to record patient data for those receiving cardiac catheterization, coronary angiography and percutaneous coronary intervention. The Nova Scotia Health Authority Research Ethics Board approved the study.

Study Cohort

This study was conducted in Nova Scotia, Canada. The province has a single, integrated health care system that serves a population of 940,000. PPCIs are exclusively performed in a single tertiary centre in Halifax, equipped with four cardiac catheterization laboratories. Approximately 400,000 people reside within 60 minutes of the total transport time to the cardiac catheter lab. Component times are routinely recorded as a quality assurance process in our centre. By describing the data for patients undergoing PPCI, we were able to disaggregate total ischemic time into its pre-hospital and hospital components, identify which components make the largest contribution to variation seen in total ischemic time. Patient demographics retrieved included age, sex, and available cardiac risk factors (diabetes, hypertension, dyslipidemia, and smoking history). Previous history of myocardial infarction (MI), coronary artery bypass graft (CABG), and percutaneous coronary intervention (PCI) were retrieved from our database.

STEMI was defined as presence of typical symptoms and >1mm ST-segment elevation on electrocardiogram (ECG) in at least two contiguous leads. All patients included presented with less than 12 hours of symptom duration. Five patients had PPCI for STEMI in hospital as inpatients and six patients had cardiac arrest prior to EHS arrival. These eleven patients were excluded from the study. Three other patients who received PPCI were from outside the catchment area (more than 60 minute driving distance) and were excluded. Forty-two patients had missing data and were removed. A total of 551 patients were included for final analysis.

Outcome Measures

The outcome variables were total ischemic time and each of the component times (which, when aggregated, equated to the total ischemic time). Total ischemic time was defined as symptom onset to device time. "Device" included intervention via balloon, thrombectomy device or stent. Symptom onset was defined by the patient as the onset of noticeable symptoms, and device time was the moment when revascularization was achieved. Component times were defined as symptom onset to first medical contact, first medical contact to first ECG, first diagnostic ECG to cardiac catheter lab activation (using a paging system for the PPCI on call team through the hospital telecommunication system), catheter lab activation to catheter lab ready, catheter lab ready to patient arrival in the catheter lab and catheter lab arrival to device time. Our centre also routinely collects door-to-balloon time for quality assurance and here we report our median time for consistency among the literature.

Additional process variables were included in the analysis, as they were hypothesized to influence variation in component times: use of EHS, pre-activation of the cardiac catheter lab, and activation after hours. "Use of EHS" refers to the patient calling 911 and being transported via ambulance. Paramedics in Nova Scotia are trained to recognize STEMI on ECGs and can activate the cardiac catheter lab prior to hospital arrival. "Pre-activation of the cardiac catheter lab" indicates that a diagnostic ECG was obtained prior to hospital arrival by paramedics and, through consultation with an emergency room physician, activation of the cardiac catheter lab occurred prior to hospital arrival. At our centre, the catheter lab is staffed during the week from 0800-17:00. On weekends, holidays, and outside the 08:00-17:00 window, the cardiac catheter lab staff

Table 1. Patient demographics and cardiac risk factors.

	N=551
Age (IQR)	59.2 (52.7-68.0)
Female Sex	129 (23.4%)
Hypertension	253 (45.9%)
Diabetes	94 (17.1%)
Dyslipidemia	223 (40.5%)
History of Smoking	275 (49.9%)
Previous PCI	56 (10.2%)
Previous MI	61 (11.1%)
Previous CABG	11 (2.0%)

are not in hospital and must be called in for PPCI. Therefore, cardiac catheter lab activation after hours is an important variable that could contribute to the total ischemic time.

Statistical Analysis

All statistical analyses were performed using STATA 13.1 statistics package[13]. Age is reported as a median with interquartile range (IQR). Frequencies were used to report sex, history of hypertension, diabetes, dyslipidemia, smoking, PCI, myocardial infarction (MI), and coronary artery bypass graft (CABG). Median times with interquartile ranges were calculated to describe total ischemic and component times. This allowed identification of component times that had the largest contribution to total ischemic time, and helped to determine which parts of the process were most amenable to intervention.

Total ischemic and component times were compared by process variables: use of EHS, pre-activation of the cardiac catheter lab, and activation after hours. Kolmogorov-Smirnoff tests were used to determine if the distribution of total ischemic and component times differed by process variables.

The proportion of variance in total ischemic time attributable to each component time was estimated via regression. Separate OLS regression models of each component time on total ischemic time were estimated. R-squared values for each regression measured the percent of variation in total ischemic time explained by each component time. As the distribution of the dependent variable total ischemic time was positively skewed, it was log transformed. Coefficients were estimated from OLS regressions of each process variable on the log of each measure of total ischemic time in order to identify which process variables were associated with reductions in total ischemic time.

Results

Among the 551 patients analyzed, most were male (76%) and the median age was 59.2 years (IQR: 52.7-68.0 years). A more detailed description of patient demographics and cardiac risk factors is shown in Table 1. Median door-to-balloon time was 81min (IQR: 55-103min) and the median first-medical contact to device time was 100min (IQR: 86-123). The median total ischemic time was 173min (IQR: 137- 257min). Quintiles for total ischemic times and component times are shown in Table 2. The longest component time was symptom onset to first medical contact (Median: 61min, IQR: 32-138min).

The majority of the variation in total ischemic time was accounted for by the earlier stages of receiving PPCI (Table 3). Symptom onset to first medical contact was found to account for most of the variation seen in symptom onset to device time (R2= 61%). All other component times were found to account for less than 10% of the variation in total ischemic time. Not all patients had a first ECG as diagnostic; 95 patients (17%) had a diagnostic ECG after their first ECG. The median was 39min (IQR: 18-72min) between first ECG and diagnostic ECG (R2 = 0.18).

The total ischemic time was significantly associated with the three process variables examined (Table 4). Most of our sample used EHS to transport to our centre (n= 296, 53.7%) and of those, 284 (96%) received a pre-hospital ECG. Both use of EHS and pre-activation of cardiac catheter lab were found to significantly reduce symptom onset to device time. Activation after hours of the cardiac catheter lab was associated with significantly longer symptom onset to device time (p=0.003). Specific component times were also significantly associated with process variables (Table 4).

Table 2. Quintiles of total ischemic and component times in minutes.

Time (N=551)	10%	25%	50%	75%	90%
Total Ischemic Time					
Symptom Onset to Device Time	107	137	173	257	430
Component Times					
Symptom Onset to First Medical Contact	18	32	61	138	311
First Medical Contact to First ECG	0	5	8	13	21
Diagnostic ECG to Catheter Lab Activation	5	9	15	23	35
Catheter Lab Activation to Lab Ready	3	10	25	35	43
Catheter Lab Ready to Patient Arrival in the Lab	5	10	10	18	32
Catheter Lab Arrival to Device Time	20	26	32	40	48

Table 3. Percent of the variance in total ischemic time explained by each component time[a]

Time	Symptom Onset-First Device Time
Component Times	Percent
Symptom Onset to First Medical Contact	0.61
First Medical Contact to First ECG	0.07
Diagnostic ECG to Catheter Lab Activation	0.01
Catheter Lab Activation to Lab Ready	0.01
Catheter Lab Ready to Catheter Lab Arrival	0.02
Catheter Lab Arrival to Device Time	0.04

[a]Percent variation explained is estimated as the R-squared from OLS regressions of each component time on the log of each measure of total ischemic time.

Patients who contacted EHS had significantly shorter pre-hospital component times, while the catheter lab activation to catheter lab ready times were significantly longer during after hours activation ($p<0.001$ and $p=0.005$ respectively). When EHS was called, symptom onset to device time was reduced by 27% (Coefficient: -0.28, 95%CI: -0.37, -0.19). Pre-activation was also found to have a similar effect (Coefficient: -0.27, 95%CI: -0.36, -0.17).

Discussion

We have determined that the majority of total ischemic time occurs prior to hospital arrival, and that component times following arrival have far less of an impact on total ischemic time. We also found that the use of EHS and the pre-activation of the cardiac catheter lab at our centre resulted in significantly shorter total ischemic times.

At the time of this study, the majority of the literature had extensively examined door-to-balloon times as a performance measure to assess and reduce total ischemic time[10,14]. More recently, research has focused on total ischemic time from the perspective of first medical contact to device time[15]. In the Canadian context, recent guidelines have been updated to include a prehospital and component time focus for

Table 4. Median component times comparing use of EHS, pre-activation of cardiac catheter lab and after hours activation.

Time	Median Times (IQR) in minutes		
	Used EHS (n=296)	Self-Transport (n=255)	p-value[a]
Total Ischemic Time	155 (126.5-208)	201 (151-327)	<0.001
Symptom Onset to First Medical Contact	48 (26-87)	94 (48-208)	<0.001
First Medical Contact to First ECG	6 (3-10)	11 (7-16)	<0.001
Diagnostic ECG to Catheter Lab Activation	16 (9-25)	13 (8-19)	<0.001
Catheter Lab Activation to Catheter Lab Ready	25 (10-35)	25 (10-35)	0.86
Catheter Lab Ready to Catheter Lab Arrival	10 (10-15)	10 (10-20)	0.41
Catheter Lab Arrival to Device Time	31 (25-38)	33 (27-41)	0.11
	Pre-activation (n=209)	No Pre-activation (n=342)	p-value[a]
Total Ischemic Time	148 (122-196)	192.5 (148-295)	<0.001
Symptom Onset to First Medical Contact	50 (29-85)	74.5 (38-175)	<0.001
First Medical Contact to First ECG	6 (3-10)	10 (5-15)	<0.001
Diagnostic ECG to Catheter Lab Activation	15 (9-21)	14 (9-24)	0.5
Catheter Lab Activation to Catheter Lab Ready	27 (13-35)	25 (9-35)	0.11
Catheter Lab Ready to Catheter Lab Arrival	10 (8-15)	10 (10-20)	0.3
Catheter Lab Arrival to Device Time	31 (25-38)	32 (26-41)	0.15
	Regular Hours (n=366)	After Hours (n=185)	p-value[a]
Total Ischemic Time	169 (119-239)	177 (140-270)	0.003
Symptom Onset to First Medical Contact	61 (33-138)	60.5 (32-136)	0.98
First Medical Contact to First ECG	8 (5-13)	8 (4-13)	0.69
Diagnostic ECG to Catheter Lab Activation	13 (8-20)	15 (9-23)	0.08
Catheter Lab Activation to Catheter Lab Ready	6 (3-20)	30 (22-37)	<0.001
Catheter Lab Ready to Catheter Lab Arrival	10 (10-25)	10 (10-15)	0.006
Catheter Lab Arrival to First Device Time	32 (26-38)	31 (26-40)	0.83

[a]Percent variation explained is estimated as the R-squared from OLS regressions of each component time on the log of each measure of total ischemic time.

the acute management of STEMI with a target of first medical contact to device time being <120min where possible[15]. Over the past decade, improved pre-hospital assessment and pre-activation systems have reduced total ischemic times[16,17]. However, in our centre, as in many others[18], there is limited potential for further reductions in component times within hospital. The real potential for reduced total ischemic time is much earlier in the process, before contact with health care has even occurred. Considering this, total ischemic time is more related to patient factors than hospital system issues.

The new frontier in reducing total ischemic time must be at the level of the patient. Identifying high-risk patients, educating them on signs and symptoms of acute myocardial infarction and stressing the importance of seeking care as soon as possible are all ways that pre-hospital component times could be reduced. Thanks to studies using the Framingham Heart Study data, health care providers are well aware of what factors predict the risk of myocardial infarction[19-21]. Although physicians may be aware of which patients are most at risk for STEMI, they may not always communicate this effectively to patients themselves. It is crucial that these high-risk patients know the signs and symptoms of STEMI and when to seek care. It is crucial to communicate to patients that using EHS, and not self-transporting to hospital, may lead to improved outcomes. That said, pre-hospital patient delay might be explained through reluctance to receive medical evaluation. Reluctance to seek care is not a new phenomenon, and patients may not benefit from education programs in symptom recognition[22,23]. At the community level, these interventions have not had high levels of retention[24,25]. A more targeted approach to high-risk patients (as opposed to general media campaigns) has been thought to have a higher rate of uptake among patients who are likely to have PPCI for STEMI, but unfortunately this has also been unsuccessful[26]. Despite this, more effort in a personalized approach to reduce patient delay is warranted to improve short and long term outcomes in patients who have STEMI.

Study Limitations

This study has certain limitations. This study was performed before more recent Canadian Guidelines regarding optimizing management of STEMI were published, and thus our findings may not be entirely reflective of current practice[15]. In addition, the symptom onset time was derived from patient history. Recall bias aside, these patients are in a critical state when seeking medical care and may not be able to provide an accurate time of when their symptoms started. Another limitation of this study is that only patients who received PPCI were included in analysis. Those that died on the way to hospital, in-hospital prior to PPCI, arrested prior to EHS arrival, or died during PPCI were excluded. Although these were very few in number, these patients did not have the full process of receiving PPCI and their exclusion may have subsequently biased the results. It is possible that these are the patients who had the longest delay. For the purpose of this study, we wanted to examine the majority of patients who went through the entire process of PPCI in order to have a clear picture of where delays occur on average.

Conclusion

Studies have indicated cannabis may have the potential In conclusion, this study identified where most of the total ischemic time occurs in the process of receiving PPCI for STEMI, and that EHS and pre-activation of the cardiac catheter lab reduce total ischemic time. The analysis in this study indicated that the majority of delay occurs in the earlier stages of total ischemic time, prior to first medical contact. This would suggest that to improve total ischemic time new strategies that focus on targeting high-risk patients at the individual level need to be evaluated. Comparing our findings with more current data would be beneficial to determine whether the updated Canadian Guidelines have had an impact on delivering care for those who receive PPCI for STEMI. Further investigation into patient perspectives of acute coronary syndrome and patient delay in seeking medical care is warranted. Overall, however, it appears that the length of component times in receiving PPCI for STEMI are short from first medical contact onward and that system delays are low at our PPCI centre in Halifax, Nova Scotia.

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