Factors Affecting Symptom Onset to First-Medical-Contact in ST-Segment Elevation Myocardial Infarction Patients

Amira Balbaa[1]

Thesis Supervisor
Dr Jon-David Schwalm[2]
Thesis Committee Member
Dr. Madhu Natarajan[2]
External Committee Member
Dr. Ahmed ElGuindy[3]

[1]McMaster University/Faculty of Health Sciences /Department of Global Health, Hamilton, Ontario

[2]McMaster University/Hamilton Health Sciences/Population Health Research Institute, Hamilton, Ontario

[3]Aswan Heart Centre, Magdi Yacoub Foundation, Aswan, Egypt

A Thesis Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements for the M.Sc Degree in Global Health

SYNOPSIS

ST-segment elevation myocardial infarctions (STEMI) make up approximately 25% to 40% of total myocardial infarction (MI) presentations. The total occlusion of the coronary artery that results in a STEMI makes timeliness to reperfusion crucial. Previously, the focus has been on decreasing door-to-balloon time (D2B). Although D2B time plays an important role in achieving timely treatment, it is only one component of the route from symptom onset to reperfusion. It has been shown that total ischemic time is a better predictor of clinical outcomes, including mortality and infarct time. Delays between symptom onset to first-medical-contact (FMC) consume the majority of total ischemic time, and remains one of the main reasons that patients do not receive timely care. Factors affecting symptom onset to FMC for STEMI patients receiving primary PCI as a method of reperfusion at the Aswan Heart Center (AHC) in Egypt and the Hamilton General Hospital (HGH) in Canada were examined using the prospectively collected data held in the STEMI registries at these sites and a modified version of the Response to Systems Questionnaire applied in Egypt. Exploring factors linked to early and late presentation in STEMI patients showed that delays were associated with gender, smoking, cardiac history, cardiogenic shock and mortality rate. Furthermore, the type and number of symptoms, presence and actions of bystanders, emotional response and the actions of the patients, as well as transportation time was shown to be different among delay groups.

ACKNOWLEDGMENTS

I would like to express my sincere thanks to my supervisor, Dr. Jon-David Schwalm, for his support throughout this project. It is his continued mentorship and guidance that shaped my research interests and strengthened my skills over the past years. I would also like to extend my sincere gratitude to Dr. Ahmed ElGuindy, for his support throughout my research career, for always sharing his wealth of knowledge, and for the chance to work with him and his phenomenal team at the Aswan Heart Center. I would also like to thank Dr. Madhu Natarajan for his invaluable insight, input and support. I would like to thank Dr. Amparo Casanova for sharing her statistical expertise, and being a very patient teacher throughout the process. I would like acknowledge the work done by the team at the Aswan Heart center and Hamilton Health Sciences, particularly by Mohamed Elkhateb, Dr. Ahmad Samir, and Renu Syal to collect the data necessary for this study. I would also like to thank Dr. Tim O'shea for being the external examiner for the thesis defense, and Professor Michael Ladouceur for chairing the defense.

TABLE OF CONTENTS

Lists of Figures and Tables

ABBREVIATIONS

AHC: Aswan Heart Center
AM: Acute marginal branch
CABG: Coronary artery bypass graft
CAD: Coronary artery disease
CHD: Coronary heart disease
CNN: Hamilton General STEMI registry
CVD: Cardiovascular disease
Cx: Circumflex artery
D2B: Door-to-balloon
DIDO: Door-in-door-out
EMS: Emergency medical service
FAST-MI: French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction
HGH: Hamilton general hospital
HIC: High-income country
HHS: Hamilton Health Sciences
LAD: Left anterior descending artery
LCX: Left circumflex artery
LHIN IV: Hamilton Niagara Haldimand Brant Local Health Integration Network IV
LMIC: Low-middle income countries
LMT: Left main trunk
LPDA: Left posterior descending artery
LPL: Left posterolateral branch
MI: Myocardial infarction
NCD: Non-communicable disease
NSTEMI: Non-ST-segment-elevation myocardial infarction
OM: Obtuse marginal
PCI: Percutaneous coronary intervention
PDA: Posterior descending artery
RCA: Right coronary artery
RPDA: Right posterior descending artery
RPL: Right posterolateral branch
STEMI: ST-segment elevation myocardial infarction
STREAM: Strategic Reperfusion Early after Myocardial Infarction

Declaration of Academic Achievement

Conception of this idea was between Dr. J-D Schwalm, Dr. Ahmed ElGuindy and myself. The Aswan STEMI data base was developed by Dr. ElGuindy and his team, and I have previously worked with the Aswan Heart Center to collect data for this database over a three-month period. The Hamilton General Hospital database was shared by Dr. Madhu Natarajan and his team. With the supervision, guidance and mentorship of Dr. Schwalm, I conducted the literature review and developed the questionnaire for this study. The questionnaire was implemented in Aswan by Dr. ElGuindy and his team. This manuscript was written with the editorial guidance of Dr. Schwalm and Dr. Natarajan. Statistical analysis plan was outlined and reviewed by Dr. Amparo Casanova.

CHAPTER ONE

1.1 The Global burden of cardiovascular disease

Cardiovascular disease (CVD) is responsible for an estimated 17.5 million deaths, making it the leading cause of mortality worldwide (Okhovati, Zare, & Bazrafshan, 2015). This number is projected to increase to 22.2 million in 2030 (WHO, 2014). Figure 1 shows the proportions of total deaths for those under 70 years of age caused by CVD as compared to other causes. This burden is disproportionately placed on low-and-middle-income countries (LMIC), where 75% of these deaths occur (figure 2) (Okhovati, Zare, & Bazrafshan, 2015). While the rate of CVD has been decreasing in high-income countries (HIC) due to successful population-wide preventive strategies, effective primary and secondary preventive health care, and improved treatment for acute cardiovascular events, it has been concurrently increasing in LMIC (Schwalm, Huffman & Yusuf, 2016). Furthermore, these regions face a larger burden of disease due to the earlier age at which CVD occurs, with an estimated 50% of all CVD occurring before the age of 70 compared to 25% in HIC (Joshi, Jan, Wu & MacMahon, 2008).

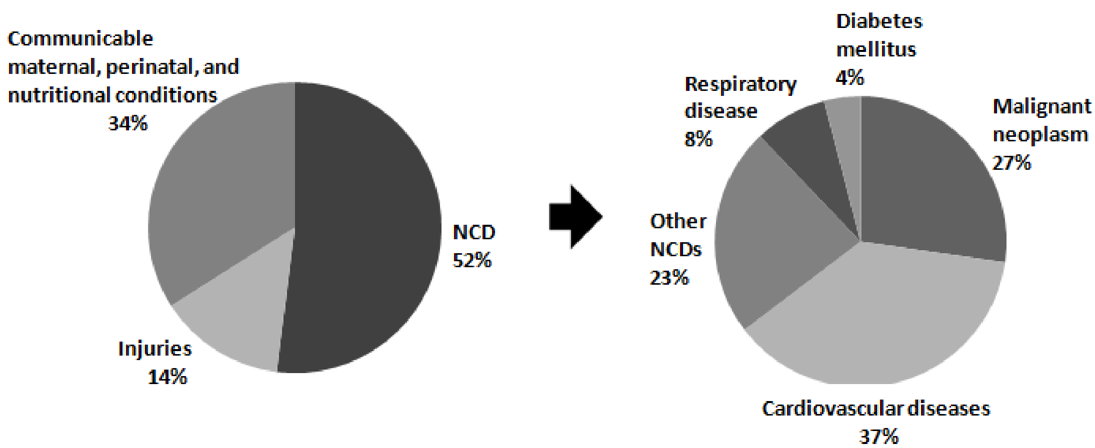

Figure 1. **Proportion of non-communicable diseases (NCD): NCD accounted for 52% of total deaths under the age of 70 in 2012. Of those deaths, CVD accounted for 37% (WHO, 2014).**

Figure 2. **The probability of dying from the four main NCD - CVD, diabetes, cancer, and respiratory disease- between the ages of 30 - 70 (WHO, 2014) Canada, a HIC, has a probability of 10.7% and Egypt, a lower middle-income country has a probability of 24.5%.**

This unequal burden is not only seen between countries, but also within each country at the patient level. Those with lower income and less education, experience increased mortality and prevalence of CVD. Furthermore, a person's subjective social status - an individual's perception of their position in the social and economic hierarchy- has also been shown to affect the risk of CVD (Tang, Rashid, Godley & Ghali, 2016).

1.2 ST-segment elevation myocardial infarction

Of the deaths caused by CVD, an estimated 7.4 million was due to coronary heart disease (CHD) (WHO, 2016), a number that is anticipated to double between 1990 and 2020 (Ôunpuu, Negassa & Yusuf, 2001). CHD can lead to acute coronary syndromes, which include conditions such as unstable angina, non-ST-segment-elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) (National Institute for Health and Care Excellence, 2010). STEMI make up approximately 25% to 40% of total myocardial infarction (MI) presentations (O'Gara et al., 2013).

The total occlusion of the coronary artery that results in a STEMI makes timeliness to reperfusion crucial. Within one hour of the coronary artery being occluded, half of potentially salvageable myocardium is lost, and by three hours, two-thirds (National Institute for Health and Care Excellence, 2010). The now well known phrase, 'time is myocardium' refers to the importance of this timely care in offsetting the damage caused by an MI. A strong correlation exists between longer door-to-balloon (D2B) time and clinical outcomes, including infarct size and mortality (Lambert et al., 2010; Martin et al., 2014). Mortality is estimated to increase by 10% for each hour delay (Sørensen & Mæng 2015).

In the 1990s, the method of choice for revascularization was fibrinolytic therapy. While this method of revascularization is still favourable in certain clinical situations, including rural geographic settings where delays to primary percutaneous coronary intervention (PCI) are expected, currently, best practice guidelines recommend primary PCI as the reperfusion method of choice when delivered in a timely manner (National Institute for Health and Care Excellence, 2010). Coronary angiography with primary PCI, if indicated, is to be delivered if presentation is less than 12 hours from symptoms onset (Level of Evidence: A) with an ideal first medical contact (FMC)-to-device time of 90 minutes (Level of Evidence: B). If patients present to non-PCI capable hospitals, transfer to a PCI center is recommended, with a door-in-door-out (DIDO) time of less than 30 minutes, if transfer time is less than 90-120 minutes. If this time is to be exceeded, a pharmacoinvasive strategy is recommended, with fibrinolytic therapy being administered within 30 minutes of hospital arrival and transfer to PCI between 3 to 24 hours following administration. In the event of failed reperfusion, urgent transfer for rescue PCI is required (O'Gara et al., 2013).

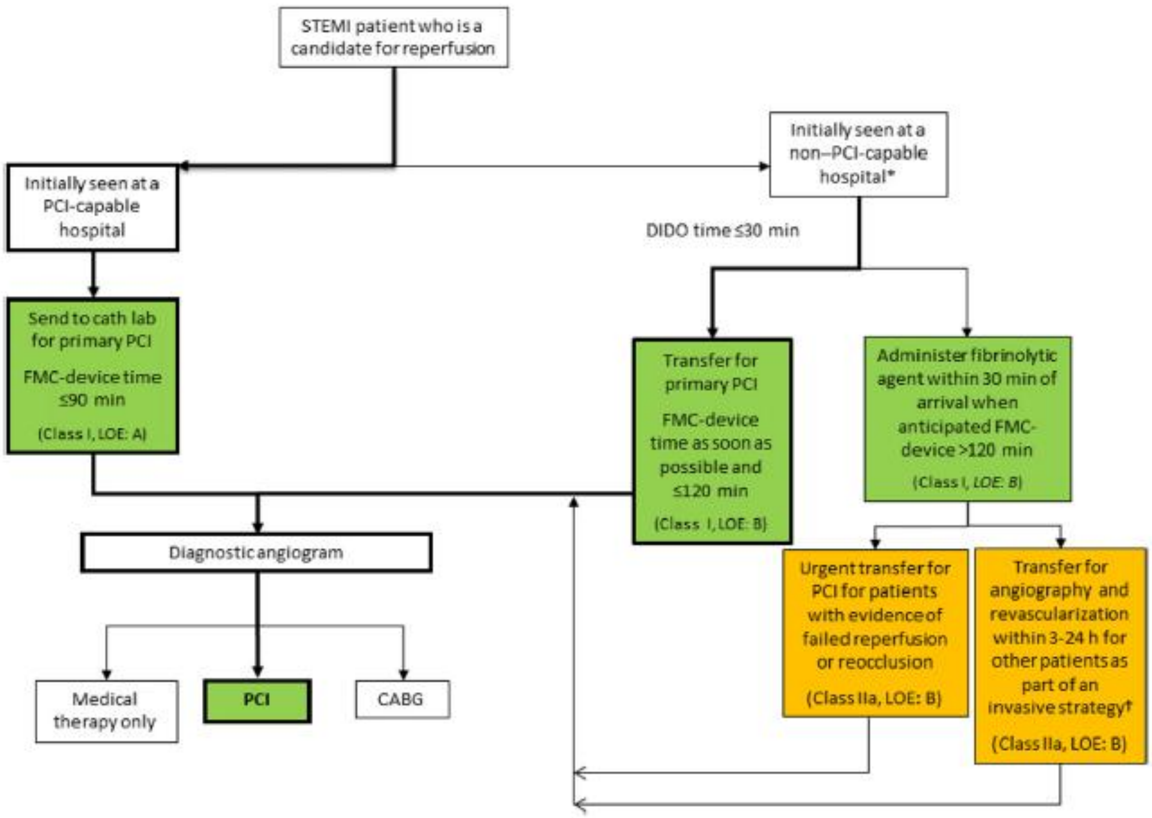

Figure 3. **Possible paths of care for STEMI, with the bold arrows representing preferred strategies. The class and level of evidence (LOE) is outlined with each recommendation (O'Gara et al., 2013)**

Although guidelines point to primary PCI as the gold standard, it is worth noting that this service cannot be universally implemented in a timely manner, and in some countries fibrinolytic therapy is the standard method of revascularization (Huber, Goldstein, Granger & Armstrong, 2014; Mercuri et al., 2015). This is not only the case in LMIC. In HIC, primary PCI may not be feasible for some patients due to population based-geographic distribution, comorbidities that a patient may have, and resource constraints (Mercuri et al., 2015). Notably, the Strategic Reperfusion Early after Myocardial Infarction (STREAM) and the French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) studies outlined the effect of primary PCI as compared to a pharmacoinvasive strategy on the clinical outcome of patients (Danchin et al., 2014; Sinnaeve et al., 2014). Comparing a pharmacoinvasive strategy in patients with FMC within three hours of symptom onset, and those with primary PCI performed beyond 60 minutes of initial diagnosis, it was found that there was no significant difference in clinical outcomes (death, reinfarction, shock and congestive heart failure) between the two group at 30 days and one year (Sinnaeve et al., 2014). It was further found that a pharmacoinvasive strategy provided results that were at least as good as those of primary PCI in patients who sought care in less than 12 hours from symptom onset, in terms of five year survival rates (Danchin et al., 2014). These finding support the notion that in areas where timely PCI is not feasible, a pharmacoinvasive strategy can be an effective alternative.

1.3 Effect of delay on effectiveness of fibrinolysis and PCI

Numerous studies have shown the association of early reperfusion in patients with STEMI, particularly within the first 12 hours of symptom onset, leading to increased myocardial salvage, preservation of left ventricular function, decreased mortality, and decreased injury to microcirculation (Prasad et al., 2015; Schömig et al., 2005). Early reperfusion trials comparing fibrinolysis to no treatment showed that those treated within 1 hour of symptom onset had a 51% reduction in mortality. The effect size dropped to 20% for those treated between 3 and 6 hours after symptom onset. Given the time-dependent nature of fibrinolysis therapy, studies have shown no benefit of fibrinolysis in STEMI patients who present after 12 hours of symptom onset (Cohen, Boiangiu & Abidi, 2010; O'Gara et al., 2013). Although one study has shown that viable salvageable myocardium exists after 12 hours of ischemia, and that PCI may be effective during this time window (Schömig et al., 2005), this benefit is not realized in patients presenting more than 12 hours after symptom onset (Bainey, Afzal, Rokoss, Velianou & Natarajan, 2010). Additionally, a study looking at mechanical reperfusion done 3 to 28 days after symptom onset showed no difference in mortality, reinfarction, or heart failure (Cohen, Boiangiu & Abidi, 2010). This is reflected in current guidelines, with a recommendation of either fibrinolysis or primary PCI to be delivered within 12 hours of symptoms onset (O'Gara et al., 2013). Guidelines also recommend that primary PCI should not be performed in asymptomatic patients more than 12 hours after onset of STEMI if they are hemodynamically and electrically stable (*Level of Evidence: C*) (O'Gara et al., 2013). However, it has been shown that although some patients may be asymptomatic, this may not necessarily reflect the absence of active ischemia. Intervention in patients with silent ischemia after 12 hours can have long term benefit, reducing infarct size, long-term rates of cardiac death, nonfatal MI, or symptom-driven revascularization, and improving functional capacity and left ventricular ejection fraction at 4 and 10 years (Cohen, Boiangiu & Abidi).

1.4 Programs of Care

The timely care required for a STEMI highlights the importance of an effective and well organized network of care. With the emphasis shifting from identifying the optimal mode of therapy, to a focus on how to ensure all patients receive the required therapy effectively and efficiently. This focus comes with a transition from standalone hospitals, to a network of systems that use a hub-spoke model. Each region tailors its system based on its own geography, availability of resources and infrastructure, the characteristics of healthcare systems, and patterns of reimbursement. Regardless of which model is the best fit, there are general principles that are essential for STEMI networks. This includes a focus on a pre-hospital diagnosis of STEMI, direct transfer to a primary PCI center, and 24/7 on-call services with activation times of no more than 30 minutes. Furthermore, a single telephone emergency number, and evaluation of pre-hospital ECGs allow for diagnosis before patient transfer (table 1) (Huber, Goldstein, Granger & Armstrong, 2014; Sørensen & Mæng 2015).

***Table 1.* General principles for STEMI networks (Huber, Goldstein, Granger & Armstrong, 2014)**

STEMI networks should include
Single telephone emergency number
Ambulance (vehicles, helicopters, planes), equipped with 12-lead ECGs and defibrillators, and staffed with physicians or well-trained paramedic, capable of basic and advanced life support
Occasionally automated ECG interpretation or ECG telemetry
Direct telephone access to the cath lab
Protocols for standardized care (diagnosis, therapy, and transfer)
Cardiologist or intensive care specialist as a network leader
Involvement of healthcare authorities
Public information campaigns
Regular meetings of involved parties
Prospective registry

Ideally, in the case of a tentative STEMI diagnosis, a primary PCI capable center is alerted. Patients are then taken directly to the catherization laboratory, bypassing the emergency department, intensive care unit and the coronary care unit. When transportation to a PCI capable center will result in a delay of more than 120 minute, patients are transported to the local hospital, after which they can be transferred to an interventional center. D2B time can be further reduced by the establishment of large volume centers, which ensure a sufficient number of physicians for the development of a 24/7 on-call system in which the catheterization laboratory can be ready within 20-30 minutes (Sørensen & Mæng 2015).

These STEMI networks have been adopted in many countries around the world, and adapt to work under the circumstances and resource availability of these different regions. In Vienna, the system is based on a rotational schedule, where primary PCI sites are all available during the morning, while only two are active during the night. Pre-hospital fibrinolysis is only given to patients with a transfer time greater than 90 minutes to a primary PCI center- this makes up only about 3% of STEMI patients. Primary PCI centers are also well distributed in Denmark, Netherlands, Germany, Poland, and Czech Republic.

In North America, networks are built to accommodate the large size of the regions. Currently, 79% of individuals in the USA are within a 60-minute drive from a PCI capable hospital, and the focus has shifted to improving rapid transport and decision making, as well as DIDO time. In Hamilton, Canada the regional STEMI network was established in 2010 with the goal of ensuring patients receive timely, optimal care, whether that be primary PCI, or fibrinolytics. The primary PCI program is located in a tertiary care center in an urban community, with additional tertiary care hospitals, community hospitals and urgent care centers feeding into it. This network also includes emergency medical services programs coordinated by 2 base hospitals and 4 dispatch centers (Mercuri et al., 2015). This allows for pre-hospital STEMI identification and for EMS to directly transfer patients to the PCI capable hospital, which has been shown to decrease D2B times (Le May et al., 2008). For those presenting at the emergency department, a standardized reperfusion algorithm is used by the staff. A single activation call alerting the STEMI team, rapid set up of the catheterization laboratory and oversight by a multidisciplinary team also followed the general principles for STEMI networks (Mercuri et al., 2015).

Systems of care are not unique to the west, and are now being developed in LMIC. In China, the ratio of primary PCI increased from 10.2% to 27.6%, while the ratio of fibrinolysis concurrently decreased from 45.0% to 27.4% from 2001 to 2010. In 2011, the STEMI PCI program was initiated, with a pilot study addressing steps to set up a local STEMI network that focused on pre-hospital alert by EMS, inter-hospital transfer, and bypassing of the emergency department in hospitals (Kaifoszova et al., 2014). In India, the STEMI India model adopts a hub and spoke model which forms clusters, and a dual approach which includes primary PCI and a pharmacoinvasive strategy (figure 4) (Kaifoszova et al., 2014). Each cluster is composed of class A and B hub hospitals, and class C and D spoke hospitals. Class A hospitals have 24 hour primary PCI capabilities. Class B hospitals have primary PCI capabilities during work hours, after which only fibrinolysis is available. Class C hospitals are located within 30 minutes of hub hospitals. Patients presenting to these locations will be transported to the hub hospitals after confirmation of a STEMI. Class D hospitals are locating more than 30 minutes from a hub hospital. Patients presenting to these locations will be provided thrombolytics then transported to a hub hospital within 3-5 hours for PCI (Alexander et al., 2015).

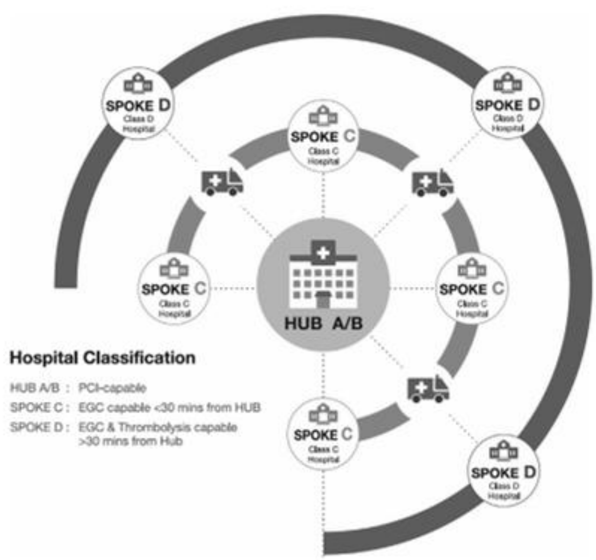

Figure 4. **The hub and spoke model in India. Each cluster contains class A and B hub hospitals, and class C and D spoke hospitals (Alexander et al., 2015).**

1.5 Total ischemic time

The programs and networks outlined focus primarily on decreasing D2B time. In the US, this time interval has seen a dramatic decrease in recent years (Huber, Goldstein, Granger & Armstrong, 2014). A study looking at 96,738 PCI for STEMI admissions found that there was a decrease in D2B time from 83 minutes in 2004-2005, to 67 minutes in 2008-2009 (Solhpour et al., 2015). Decreased D2B time is associated with decreased mortality, however the curve plateaus between D2B times of 60- 90 minutes (Fanari, Abraham, Hammami, & Doorey, 2015). Additionally, further reduction may lead to negative effects, such an increase of false positive STEMI (Fanari, Abraham, Hammami, & Doorey, 2015; Huber, Goldstein, Granger & Armstrong, 2014).

Although D2B time plays an important role in achieving timely reperfusion, it is only one component of the route from symptom onset to revascularization. It has been shown that total ischemic time is a better predictor of clinical outcomes, including mortality and infarction time (Figure 5) (Solhpour et al., 2015).

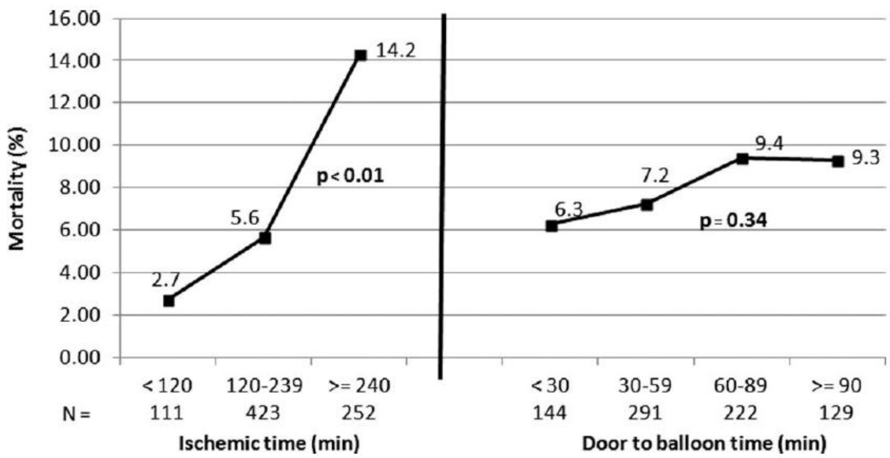

Figure 5. **30-day mortality rates by total ischemic time and D2B time (Solhpour et al., 2015)**

The total ischemic time involves symptom onset to FMC and D2B time (Solhpour et al., 2015). The former phase consumes the majority of total ischemic time, and remains one of the main reasons that patients do not receive timely care (Goldberg, Yarzebski, Lessard & Gore, 2000). Symptom onset to FMC delays can be further divided into patient related delays, systematic delays, and health care system delays. This includes decision time for patients to make the initial decision to seek medical attention, as well as transportation delays to hospital arrival (Khraim, Scherer, Dorn &Carey, 2009). *Reducing decision delays has now been recognized as the key factor to reducing pre-hospital delays, and current interventions aimed at increasing public knowledge have not been successful in doing so (Perkins-Porras, Whitehead, Strike & Steptoe, 2008).*

1.6 Problem

Symptom onset to FMC delay makes up the majority of total ischemic time. Given the importance of timely intervention in STEMI patients, these delays affect clinical outcomes and care received. With FMC to device time being effectively reduced in many parts of the world, the focus is shifting to reducing the time to patient presentation at a health care facility and better understanding the factors that affect these delays. The overarching goal of this study is to gain insight on these factors in order to reduce delays effectively, using targeted interventions.

1.7 Objectives and outcomes

Given the importance of:

1) Total ischemic time on the clinical outcome of patients

2) The large portion of time symptom onset to FMC makes up of total ischemic time

3) The lack of research in LMIC on this topic

This study aims to explore the factors that affect symptom onset to FMC delays for STEMI patients receiving primary PCI as a method of reperfusion at the Aswan Heart Center (AHC) in Egypt. Specifically, this will be done by exploring late and early presenters to the center, and identifying potential factors related to each group. A secondary outcome of this study is to further understand the overall demographics of STEMI patients in the region. This will also be compared with the overall demographics of STEMI patients presenting to Hamilton General Hospital (HGH), a center recognized for its primary PCI program in Canada. Chapter two will explore current knowledge of factors affecting symptom onset to FMC delays, drawing on literature pertaining to both HIC and LMIC. Chapter three will provide a brief overview of the locations of the study, and methods used to collect the data from the study population, including the theory used to develop the questionnaire and data base specification. Chapter four will outline the results found in the study population. Chapter five will discuss these results, highlighting the limitation of the study, as well as draw parallels to current knowledge and propose steps for future direction.

CHAPTER TWO

Patient delays account for about 80% of symptom onset to FMC, with the remaining 20% being taken up by transport time (Noureddine et al., 2006). The former delays occur as patients evaluate their symptoms and consider whether they are serious enough to seek medical attention (Finnegan et al., 2000). Both demographic and psychological factors may play a role in this decision making process (Finnegan et al., 2000).

2.1 Theoretical framework

These intertwining factors can be highlighted using Leventhal's commonsense model of illness representation. This model shows the progression from symptoms to behavioural response, and factors that affect this path. When a person experiences symptoms that are seen as a threat to their health, they construct illness representations in order to help them make sense of, and manage these symptoms. Many factors go into formulating these beliefs, including a person's social environment, cultural knowledge of the disease, current perceptions and previous experiences of the illness. These beliefs in turn affect a person's behaviour in response to these symptoms, including their physical, social and psychological functioning, coping and behavioural outcomes (Aujla et al., 2016). Beliefs are subdivided into two categories, emotional and cognitive, which are formed through a parallel process (Noureddine et al., 2006).

Emotional representations are the feelings that a person experiences as a result of the symptoms (anxiety, for example). Cognitive representations are further subdivided into five main domains:

(1) Identity: A person's belief about symptoms, which leads to targets for change (for example, eliminating symptoms)

(2) Timeline: A person's perception of the time frame of their symptoms and recovery (for example, acute versus chronic)

(3) Consequences: Beliefs about how serious the symptoms are and the impact they have on a person's daily routine

(4) Cure-control: A person's perception of the likelihood of the illness being cured, prevented or treated

(5) Causes: A person's perception of the possible cause of the symptoms (can be internal or external)

These factors combine to subsequently translate into a specific behavioural response (Aujla et al., 2016; Noureddine et al., 2006). In the context of this study, this behaviour is the decision to seek medical attention upon the experience of MI symptoms**.**

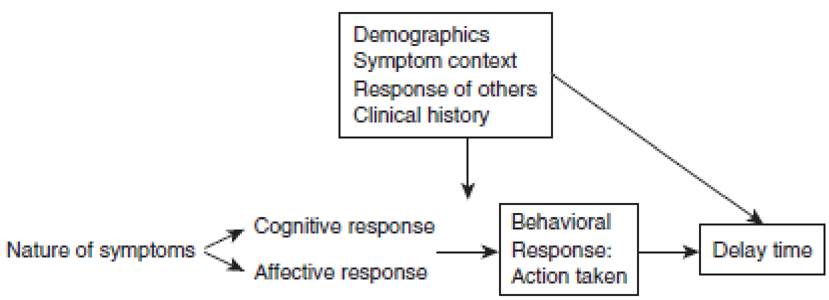

Figure 6. **Cognitive model of delay in seeking health care (Noureddine et al., 2006).**

2.2 Factors influencing symptom onset to FMC delay: A review of the literature

MEDLINE was used as the primary database, with the key words 'STEMI', 'delay' and 'symptom onset'. Articles included in this review were published between the years 2000 and 2014. Barriers were outlined from each paper, until no new barriers were found. Only papers published in English were included which may have limited this analysis. Understanding barriers previously outlined allows for a better understanding of the gaps present, and a more focused and effective collection and analysis of new data.

Sociodemographic Factors

Marital Status

Those who were married were shown to have shorter pre-hospital delay times (Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2008). This was also strongly associated with the presence of a bystander during symptom onset, another factor that led to shorter delays (Perkins-Porras, Whitehead, Strike & Steptoe, 2009).

Gender

There have been conflicting findings on the role gender plays in delayed presentation (Khraim, Scherer, Dorn &Carey, 2009). Although some studies have shown that there is no significant difference in time to presentation, others have found that men tend to present earlier than women (Goldberg et al., 2002; Goldberg, Yarzebski, Lessard & Gore, 2000; Peng et al., 2014). In a study exploring factors that may contribute to this difference in presentation, females were found to perceive themselves as lower risk to experiencing a heart attack. They were also more likely to initially contact family, friends or physicians as opposed to emergency medical service (EMS) (Finnegan et al., 2000).

Age

Younger patients tended to present earlier than older patients (Goldberg et al., 2002; Goldberg, Yarzebski, Lessard & Gore, 2000; Peng et al., 2014; Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2009). Older patients were more likely to attribute their symptoms to pre-existing conditions, prolonging their decision to seek medical treatment (Finnegan et al., 2000). This may also reflect more limited access to care, or negative previous experiences in a health care setting for older individuals (Goldberg, Yarzebski, Lessard & Gore, 2000).

Socioeconomic Factors

A lower education level was correlated with higher delay time (Noureddine et al., 2006). It has been speculated whether education level has a standalone relation to time delays, or whether it is a mirror of socioeconomic status, another factor tied to time delay. (Park et al., 2012; Peng et al., 2014).

Clinical Factors

(a) Previous cardiac history and risk factors

Patients with a history of an MI (Goldberg et al., 2002; Goldberg, Yarzebski, Lessard & Gore, 2000; Perkins-Porras, Whitehead, Strike & Steptoe, 2009), or coronary intervention are more likely to have shorter pre-hospital delay times (Goldberg et al., 2002; Perkins-Porras, Whitehead, Strike & Steptoe, 2009). This is hypothesized to be due to patients being familiar with these symptoms, and hence are able to make a more timely decision to seek care (Khraim, Scherer, Dorn &Carey, 2009).

Although data from the Worcester Heart Attack Study showed that those without a history of diabetes and angina have a longer delay time (Goldberg, Yarzebski, Lessard & Gore, 2000), more recent studies have found otherwise. Patients with hypertension, stroke, or heart failure have been shown to have shorter pre-hospital delay period (Goldberg et al., 2002), as well as those who smoke (Goldberg et al., 2002; Peng et al., 2014).

(b) Type of MI

Patients who presented with an STEMI, rather than an NSTEMI were more likely to have short pre-hopital delay times (Goldberg et al., 2002; Herlitz et al., 2010; Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2009).

(c) Symptoms

Patients experiencing a larger number of symptoms have an overall shorter pre-hospital delay time, as well as those who experience chest pain, diaphoresis (Goldberg et al., 2002), or syncope (Herlitz et al., 2010). Furthermore, those with 3 or more non-pain symptoms, for example dizziness, vomiting, or breathlessness (Goldberg et al., 2002; Perkins-Porras, Whitehead, Strike & Steptoe, 2009) were more likely to present earlier than those with only pain related symptoms (Perkins-Porras, Whitehead, Strike & Steptoe, 2009).

Pain appearing suddenly and reaching a maximum within minutes also resulted in shorter delay times. It is assumed that this type of symptom onset causes more alarm for patients, encouraging them to seek help (Herlitz et al., 2010; Khraim, Scherer, Dorn &Carey, 2009). Patients with symptoms described as gradual resulted in initially ignoring the symptoms, or self medicating, then re-evaluating over several hours. In the case that symptoms occurred at night, patients were found more likely to take a "wait and see" approach to symptoms (Finnegan et al., 2000). This was also seen with intermittent symptoms (Noureddine et al., 2006).

It has been shown that there is a gap between the symptoms patients expect and the symptoms that the majority experience. A study done in 5 sites across the US showed that both patients and bystanders expected the symptoms of an MI to appear as they are portrayed in Hollywood movies- "a sharp crushing pain" (Herlitz et al., 2010). Those who experienced these symptoms were more likely to respond faster. Comparatively, 80% of patients experienced chest pain as "tightness" or "pressure", followed by non-specific symptoms including arm, neck, jaw, or back pain, extreme fatigue or lightheadedness. Patients who experienced back pain as a symptom were more likely to delay care, as compared to those who recognized symptoms as cardiac in origin (Herlitz et al., 2010).

Contextual factors

(a) Transportation

Patients using private transportation had a longer delay time than those presenting via EMS (Goldberg et al., 2002; Park et al., 2012; Peng et al., 2014). This may be a measure of underlying factors, such as a patient's perception of the urgency of the situation. Additionally, there was belief among some that EMS increases time to transport to the hospital (Finnegan et al., 2000). Presentation at a non-PCI capable hospital increased delay due to the additional transfer time to a PCI capable center required (Park et al., 2012).

(b) Time

The time of day of symptom onset has also been shown to affect time delays. Night time onset is correlated with longer time delays (Goldberg et al., 2002; Park et al., 2012), as well as those experiencing symptoms on the weekend (Goldberg, Yarzebski, Lessard & Gore, 2000).

(c) Location

The location of symptom onset affected time delays, with symptom onset outside of the home being correlated to shorter time delays. (Herlitz et al., 2010; Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2009). The presence of a bystander during symptom onset also reduced pre-hospital delays (Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2009). Conversely, it has been shown that bystanders tend to initially support patient's decisions to self-medicate and delay seeking medical care. However, they also tended to take action as the patient's symptoms worsened (Finnegan et al., 2000). Patients are likely to consult others as a coping strategy. In the case where symptoms occurred at work, co-workers were likely to encourage the patient to see a nurse or physician in the workplace. Some who were alone at the time of their symptom onset called family, friends, or a physician. Overall, it was seen that the majority of patients reported bystanders, as opposed to themselves, taking the action of seeking medical care (Finnegan et al., 2000).

Emotional Variables

Patients reported delays in seeking care due to embarrassment if symptoms were a false alarm (Finnegan et al., 2000; Khraim, Scherer, Dorn &Carey, 2009), and worrying about troubling others unless they are sure that symptoms were serious (Finnegan et al., 2000; Khraim, Scherer, Dorn &Carey, 2009; Moser, McKinley, Dracup & Chung, 2005).

Patients were more likely to have shorter delay times if they perceived the symptoms as frightening (Herlitz et al., 2010), or were anxious due to the continued symptom presentation (Khraim, Scherer, Dorn &Carey, 2009).

Cognitive Variables

A study done in the US showed that both patients and bystanders had little knowledge of the importance of timely reperfusion, or the role that EMS could play in the event of an MI (Finnegan et al., 2000). Conversely, those who did have this knowledge, as well as knowledge of fibrinolysis had shorter delay times (Herlitz et al., 2010; Khraim, Scherer, Dorn &Carey, 2009; Moser, McKinley, Dracup & Chung, 2005).

Furthermore, attribution of symptoms to those of an MI as opposed to another cause, (Løvlien , Schei & Hole, 2007; Perkins-Porras, Whitehead, Strike & Steptoe, 2008; Perkins-Porras, Whitehead, Strike & Steptoe, 2009) as well as recognizing symptoms as "coming from the heart" were correlated to shorter delay times (Perkins-Porras, Whitehead, Strike & Steptoe, 2009). Previous knowledge of the symptoms of an MI was also linked to shorter delays (Noureddine et al., 2006). However, a majority of patients interviewed said they had not talked to their physicians about the symptoms of a heart attack (Herlitz et al., 2010).

Delay to seek treatment was also caused by patient's decisions to wait and see if symptoms would go away, perceived symptom seriousness (Khraim, Scherer, Dorn &Carey, 2009), and self-medicating (Løvlien , Schei & Hole, 2007; Perkins-Porras, Whitehead, Strike & Steptoe, 2008). Additionally, patients who believed that their symptoms were caused by stress or emotional state were more likely to have a longer pre-hospital delay (Perkins-Porras, Whitehead, Strike & Steptoe, 2008).

Table 2. **A summary of factors linked with shorter symptom onset-FMC delay**

Demographics	Married Younger Men Higher level of education
Cardiac History and risk factors	History of an MI or coronary intervention Hypertension Stroke Heart failure
Clinical Factors	STEMI Larger number of symptoms Chest pain Diaphoresis Syncope Three or more non-pain symptoms Recognizing symptoms as cardiac in origin Pain appearing suddenly, reaching a maximum within minutes
Contextual Factors	EMS use Weekday onset Daytime onset Onset outside the home Onset in presence of bystanders
Emotional Variables	Perceiving symptoms as frightening Anxiety due to continued symptom presentation
Cognitive Variables	Knowledge of MI symptoms Knowledge of importance of timely reperfusion Perceiving symptoms as serious

Overall, it has been found STEMI patients who are male, younger, married, have a higher education, and a history of MI present earlier to hospital. The number and type of symptoms also affected delays, with a greater number of symptoms, and a less gradual progression of pain leading patients to more quickly seek care. Where the patient was during symptom onset, who they were with and the time that this occurred were shown to be important factors. Weekday, daytime onset in the presence of bystanders reduced delays. Those who used EMS rather than self transport also had shorter delay times. Patients who felt frightened or anxious due to their symptoms, and those that had previous knowledge of MI and importance of timely intervention showed shorter delays. With the majority of these studies being done in high income countries, it is worthwhile noting whether these parameters still hold true in LMIC and varying cultural settings.

CHAPTER THREE

3.1 Methodology

Egypt is a lower middle-income Country located in north Africa (WHO, 2014), with Aswan being its southernmost governorate. The governorate includes both urban and rural communities, as well a diverse population with a distinct Nubian culture. The Aswan Heart Center (AHC), a tertiary cardiac center established in 2009, provides free cardiac care for the 1,499,000 inhabitants in Aswan and those in the surrounding regions (Central Agency for Public Mobilization and Statistics). The center works with the aim of delivering state of the art facilities, resources, and research to underprivileged communities (Magdi Yacoub Heart Foundation, 2013). The sole catheterization laboratory in Aswan is located at the center. In January 2014, the lab's services expanded to include a 24/7 primary PCI program. Patients initially present to the emergency department at the Aswan Teaching Hospital, a government hospital located adjacent to the center. Upon confirmation of an MI, patients are transferred to AHC in the event that access to a catheterization laboratory is required (A. ElGuindy, personal communication , June 22, 2016) .

The Hamilton General Hospital (HGH) is a tertiary care center located in a large urban community, in the Hamilton Niagara Haldimand Brant Local Health Integration Network IV (LHIN IV), which covers an area greater than 7000 km^2, and a population of over 1.4 million. With a mixture of both urban and rural regions, this network includes 3 tertiary care hospitals, 9 community hospitals, 4 urgent care centres, and 7 emergency medical services programs coordinated by 2 base hospitals and 4 dispatch centres (Mercuri et al., 2015). With the largest Heart Investigation Unit in Ontario, HGH's established primary PCI program is considered as one of the leaders in Canada (Hamilton Health Sciences, 2016).

The AHC has developed their STEMI database in the past year in order to track and evaluate the new primary PCI program and pinpoint areas for improvement. Given the long pre-hospital delays previously identified at the center, this database provides opportunity to explore contextual barriers in symptom onset to FMC delays in a LMIC. This can be further compared to HGH's established primary PCI program to draw parallels, and highlight differences, between these two settings.

3.1.1 Database Criteria

Database methodology

A review of the AHC STEMI registry in Egypt, and the HGH STEMI registry (LHIN IV) in Canada was conducted. Clinical data was collected at both centers for all STEMI patients as part of ongoing prospective registries by physicians and catheterization laboratory staff. The data were divided into six main categories: demographics (sex and age), risk factors (hypertension, diabetes and smoking), cardiac history (history of CABG or primary PCI), MI specification (type and location of MI, cardiogenic shock), procedural and in hospital mortality, and time factors (symptom onset to FMC). FMC was defined as the time that the patient first presented at the hospital.

Inclusion

All patients from the registry who have undergone a primary PCI from January 2015 to February 2016 were included in this study. Patients with a symptom onset to FMC delay of more than 48 hours were excluded as outliers. Patients who received fibrinolysis as part of a pharmacoinvasive strategy, or prior rescue PCI were included.

3.1.2 Questionnaire

Background

The Response to Systems Questionnaire (RSQ) was first developed in 1995 by Burnett and colleagues. This questionnaire focused on six domains that contributed to patient delays in seeking health care (Eshah, 2013):

1) The context in which the MI symptoms first appeared (i.e. where patient was when symptoms began, day of week, time of day, whom patient was with

2) The antecedents of symptom onset (i.e. what patient was doing when symptoms occurred, how expected to anticipate the symptoms were, the level of emotional stress the patient was under)

3) Behavioral responses to the symptoms (i.e. first thing the patient did when symptoms were noticed, ease in reaching the doctor, get difficulty in transportation to the hospital)

4) Emotional response to the symptoms (i.e. how anxious or upset the patient felt, comfort in seeking medical assistance, severity of pain)

5) Cognitive responses to the symptoms (i.e. symptoms attribution, perceived seriousness of the symptoms, perception of ability to control over the symptoms)

6) The response of others to patient symptoms (e.g. behavioral, emotional responses of others)

Questionnaire development

A modified version of the RSQ that captured these six domains and basic demographic data was developed and reviewed by a panel of experts (interventional cardiologists and knowledge translation researcher) from both AHC and HHS. The questionnaire was then tested for readability in a sample of 10 patients, and changes were made based on responses received. This pilot of 10 patients was not included in the results of the final study. The instrument was translated into Arabic for use at AHC.

This questionnaire contained a total of 27 questions (Appendix A). Of those, 17 were multiple choice questions, with the possibility of "other" as an answer in order to capture choices not outlined in the survey. The remaining 10 questions were based on a 7-point likert scale. Demographic Variables measured included age, gender, educational level, occupation, and marital status. Cardiac history and risk factors included questions pertaining to history of MI, angina or any known coronary artery disease (CAD). Questions pertaining to clinical factors outlined the number, type and intensity of symptoms. Contextual factors were observed by questions highlighting mode of transportation to the hospital, presence and reaction of bystanders as well as day, time, and location of symptom onset. Possible systematic factors were highlighted through the location where patient first presented, as well as transport time. Emotional variables were outlined by questions exploring factors such as anxiety, embarrassment, fear of consequences, comfort in seeking medical care, and reluctance to trouble others. Questions highlighting cognitive variables explored the actions of the patient upon symptom onset, knowledge of symptoms of MI and importance of timely reperfusion, attribution of symptoms to MI as serious, and perceived control over symptoms.

Patient Interviews

Semi-structured questionnaires were carried out at the AHC by the health care team retrospectively for a convenience sample of 80 patients from the STEMI registry. Patients were stratified by early (≤180 mins) and late (>180 mins) presentation to FMC. Previous studies have used 2-3 hours from symptom onset as an indicator for early presentation (Goldberg, Yarzebski, Lessard & Gore, 2000;Park et al., 2012; Peng et al., 2014; Perkins-Porras, Whitehead, Strike & Steptoe, 2009). In the STREAM study looking at the effectiveness of primary PCI versus a pharmacoinvasive approach, early presentation was defined as those presenting within 3 hours (180 minutes) of symptom onset (Gershlick et al., 2010). This timeline was adopted from the ACCF/AHA guidelines for the Management of STEMI (2013), where presentation "very early after symptom onset" is < 2 to 3 hours (O'Gara et al., 2013).

The most recently presenting 40 patients in each category were interviewed. Following verbal consent, the questionnaire was administered over the phone by a health care provider within the patient's circle of care.

Inclusion criteria

Patients were contacted a total of three times on separate days, after which they were considered non-responders. Non-survivors at the time of the call were not included in this section of the study, as all information was captured directly from the patient.

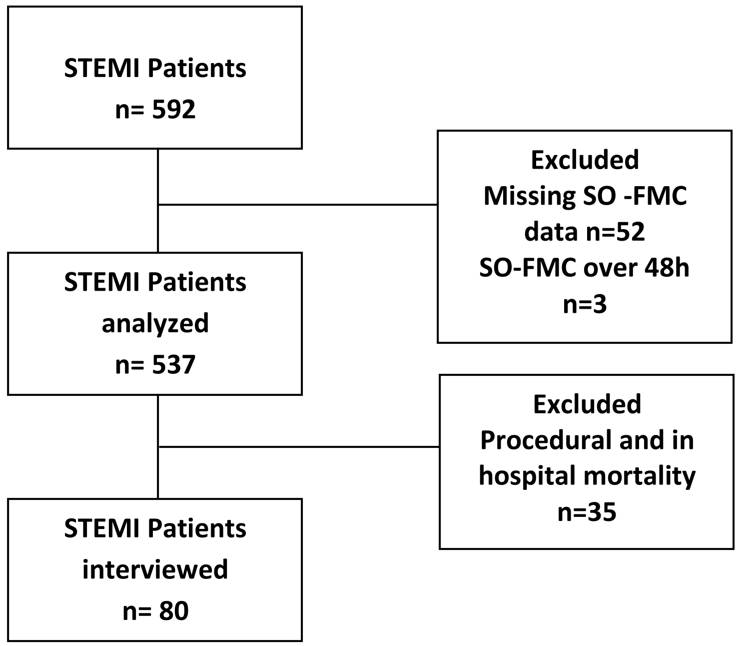

***Figure 7*. Patient flow diagram of study population at AHC and exclusion criteria**

3.1.3 Ethics

Research ethics board (REB) approval was obtained from both HHS and the AHC (REB-02-245, project number 1223). For database access, requirements needed to waive express consent were met as outlined by Personal Health Information Protection Act" (PHIPA). Given the low risk of this study, verbal consent was approved by REB. Patients were only contacted by a health care professional within their circle of care.

3.1.4 Data analysis

Time factors were measured overall as well as for late and early presentation by mean, standard deviation, median, interquartile range, minimum and maximum. Patient characteristics (demographics, risk factors, cardiac history), MI specification, health outcomes, and potential factors affecting time from symptom onset to FMC were described overall and for early and late presenters, and compared between the two groups using standard methods. Categorical variables were described by number and percentages, and compared with chi-square test. Numerical variables (age) were described by mean, standard deviation, median, interquartile range, minimum and maximum, and compared with Student-t test. These measures were further compared between AHC and HHS using qualitative methods.

Potential factors affecting symptom onset to FMC derived from the questionnaire were described using this same approach. Ordinal variables (e.g. pain intensity, perception questions) were described by median, interquartile range, minimum and maximum, and compared with a non-parametric test. Categorical variables were compared with chi-squared test. Statistical significance was fixed at 0.05.

CHAPTER 4

Using the databases and questionnaire, baseline demographics and data pertaining to the six domains outlined by Burnette et al. were collected. This chapter outlines the analyzed results from the AHC and HGH. Results from the Aswan STEMI registry and the HGH STEMI registry were compared and parallels drawn between participant baseline characteristics. The questionnaire was carried out at the AHC and provided insight into patient characteristics that had not been initially captured in the database in this region.

4.1 Aswan STEMI registry

The Aswan STEMI database included a total of 592 patients, of which 52 were excluded due to no documented symptom onset to FMC time, and 3 due to symptom onset to FMC time greater than 48 hours. Data on the remaining 537 patients was analyzed. Mean symptom onset to FMC times was 323 minutes (SD 570.9) and median 180 minutes, with the minimum being 5 minutes, and maximum 7200 minutes. Overall age of those presenting had a mean of 57 years old (SD 12.3), with a minimum of 25 and maximum of 87 years old.

Baseline characteristics for the early and late groups are shown in table 3. There was no significant difference in age between the two groups, with the mean in the early group being 56.6 and late group 57.4 (P=0.411). Overall, more men than women presented to the center (78.2%), with a significantly larger number of men presenting in the early group (83% versus 72.4% in the late group; P= 0.003). Smoking was the sole risk factor that showed a significant difference between the two groups. In the early group, 69.3% of patients were smokers, compared to 55% in the late group (P=0.001). There were no significant differences between the other risk factors explored, including diabetes mellitus, and hypertension. There was no significant difference between those with a history of PCI/ CABG between the two groups (5.5% in the early group compared to 8% in the late group; P=0.258).

A significantly larger number of patients in the late group suffered from cardiogenic shock (18.1% compared to 11.4% in the short delay group; P=0.028). Furthermore, in-hospital mortality was significantly higher in the late group (9.6% compared to 4.8% in early group; P=0.034).

The majority of patients presented with an anterior MI (60.8%), followed by inferior MI (38.3%), lateral MI (8.8%) and posterior MI (8.1%). There were no significant differences between early and late presenters based on the type of STEMI. The majority of occlusions were found in the proximal left anterior descending artery (LAD) (36.4%), followed by the mid, distal LAD or mid diagonal (29%), the right coronary artery (RCA), acute marginal branch (AM), (RPL), or right posterior descending artery (RPDA) (28.1), the left circumflex artery (LCX), obtuse marginal (OM), left posterior descending artery (LPL), or left posterior descending artery (LPDA) (12%), the left main trunk (LMT) (1.5%) and the Ramus (0.4%). There was no significant differences between early and late presenters based the location of the coronary occlusion.

***Table 3.* Baseline characteristics of early and late presenting STEMI patients presenting at the Aswan Heart Center. Overall, those in the late presentation group were more likely to be male, smokers, have cardiogenic shock and a higher mortality rate**

Characteristic		≤ 180 mins (%)	>180 mins (%)	Overall (%)	p value
Gender (Male)		83.0	72.4	78.2	0.003
	n=	294	243	537	
DM		39.8	47.7	43.4	0.065
	n=	294	243	537	
HT		39.1	36.6	38.0	0.554
	n=	294	243	537	
Smoking		69.3	55.0	62.9	0.001
	n=	293	240	533	
Prev PCI/CABG		5.5	7.9	6.6	0.258
	n=	291	239	530	
Ant MI		59.0	63.1	60.8	0.335
	n=	290	241	531	
Inf MI		39.7	36.6	38.3	0.466
	n=	290	238	528	
Lat MI		9.3	8.1	8.8	0.603
	n=	289	236	525	
Post MI		8.1	8.1	8.1	0.993
	n=	209	148	357	
LMT		1.7	1.3	1.5	0.662
	n=	288	237	525	
Px LAD		35.9	37.1	36.4	0.763
	n=	290	237	527	
Mid/Distal Lad/ Mid Diag		27.2	31.1	29.0	0.325
	n=	287	238	525	
LCX/OM/LPL/LPDA		12.3	11.7	12.0	0.843
	n=	285	239	524	
RCA/AM/RPL/RPDA		28.5	27.8	28.2	0.874
	n=	288	237	525	
Ramus		0.3	0.4	0.4	0.889
	n=	286	235	521	
Cardiogenic Shock		11.4	18.1	14.4	0.028
	n=	290	243	533	
Total Mortality		4.8	9.6	7.0	0.035
	n=	272	229	501	

4.2 Hamilton General Hospital STEMI registry

The Hamilton General Hospital STEMI registry included a total of 715 patients, none of which were excluded for analysis. Mean symptom onset to FMC times was 248 minutes (SD 377.5) and median 92 minutes, with the minimum being 3 minutes, and maximum 1440 minutes. Symptom onset to FMC were shorter than those seen at the AHC, with a difference in mean delays of 74.8 minutes and median difference of 88 minutes (P=0.005) (figure 8).

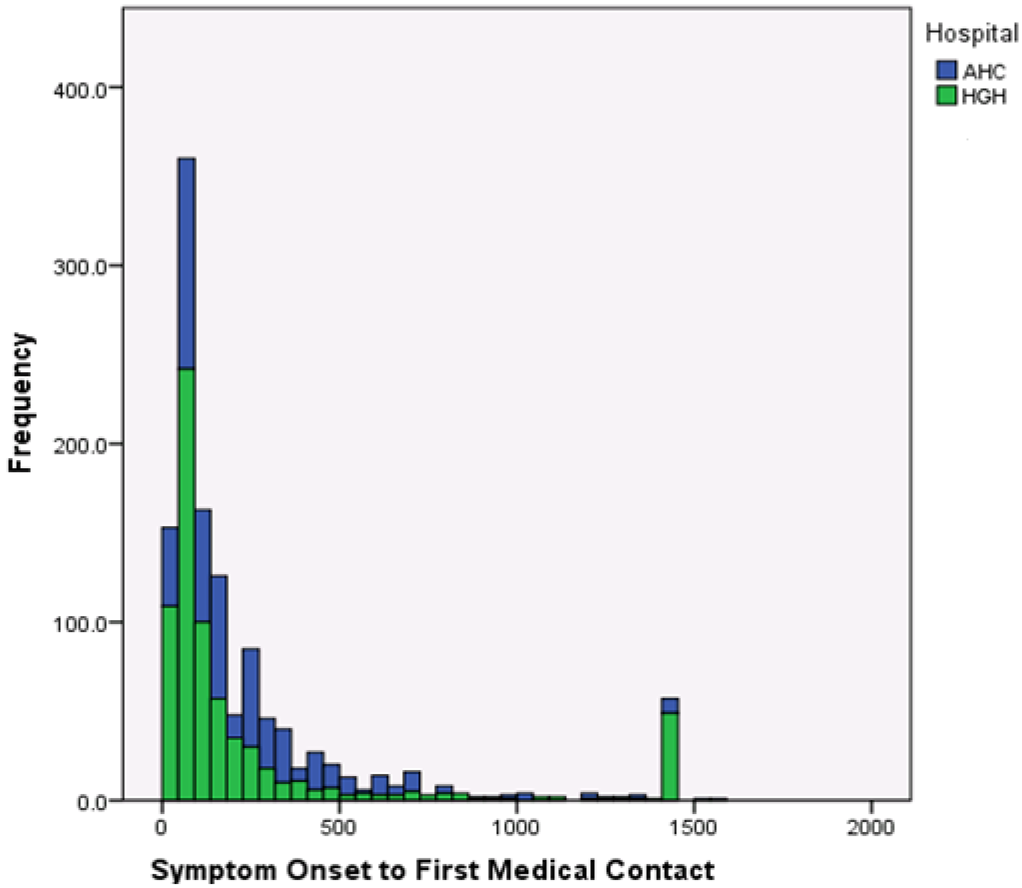

Figure 8. **Symptom onset to FMC delays in AHC and HGH**

Baseline characteristics for the early and late groups are shown in table 4, and comparative data between the two centers in table 5. Overall patients were older than those presenting at the AHC, with a mean of 63 (SD 12.6), a minimum of 31 and maximum of 97. There was no significant difference in mean age between the early (63 years) and late (65 years) delay groups (P=0.056). As seen at the AHC, more men than women presented to the center (72.3%), but there was no significant differences in gender between the delay groups (73% of early presenters versus 70.5% of late presenters; P= 0.438).

Risk factors explored were smoking, diabetes mellitus, and hypertension, none of which showed a statistically significant difference between the delay groups. The majority of patients presenting overall had a history of hypertension (53.3%), were non-smokers (59.2%) and did not have a history of diabetes (79.3%). This is compared to 38% of patients with hypertension, 37.1% non-smokers and 56.6% presenting without a history of diabetes the AHC.

Previous CABG was the only cardiac history category that showed a significant difference between the two delay groups. In the early group, 5.1% of patients had a history of CABG, compared to 1.4% in the late group (P=0.024). Although not a significant difference, more patients at the HGH had a history of PCI/ CABG (15.7% overall) as compared to the AHC (6.6%). There were similar overall proportions of patients with cardiogenic shock at both centers (14.3% at the HGH and 14.4% at the AHC). However, unlike the AHC, there was no significant difference in cardiogenic shock between the two delay groups at HGH. There was also no significant difference for in-hospital mortality (2.8% in the early group compared to 5.3% in the late group; P=0.091).

Following the breakdown seen at the AHC, the majority of patients presented with an anterior MI (60.8%), followed by inferior MI (54.5%), lateral MI (32.6%) and posterior MI (2.5%). There was a significant difference between early and late presenters in those with a lateral MI (35.4% in the early group compared to 25.6% in the late group; P=0.012). The majority of occlusions were found in the proximal RCA and posterior descending artery (PDA) (72.2%), followed by other LAD (57.1%), the circumflex artery (Cx), OM, or Ramus (52.2%), the proximal LAD (32.3%), and the LMT (7.3%). There was a significant difference between early and late presenters in those with occlusion in the RCA or posterior descending artery (PDA) (69.7% in the early group compared to 78.3% in the late group; P=0.02).

***Table 4.*Baseline characteristics of early and late presenting STEMI patients presenting at the Hamilton General Hospital. Overall, those in the late presentation group were more likely have a history of CABG, and a lateral MI, with an occlusion in the RCA/PDA.**

Characteristic		≤ 180 mins (n=508) (%)	>180 mins (n=207) (%)	Overall (n=715) (%)	p value
Gender (Male)	M	73.0	70.5	72.3	0.498
DM	Y	19.7	23.2	20.7	0.294
HT	Y	51.2	58.5	53.3	0.077
Smoking	Y	40.4	42.0	40.8	0.679
Prev PCI	Y	13.2	13.0	13.1	0.958
Prev CABG	Y	5.1	1.4	4.1	0.024
Prev MI	Y	16.7	15.9	16.5	0.796
History of CAD	Y	23.0	24.2	23.4	0.748
Ant MI	Y	39.4	36.2	60.8	0.434
Inf MI	Y	53.5	57.0	54.5	0.399
Lat MI	Y	35.4	25.6	32.6	0.012
Post MI	Y	2.2	3.4	2.5	0.346
LMT	Y	7.9	5.8	7.3	0.332
Px LAD	Y	34.8	26.1	32.3	0.023
Other LAD	Y	54.9	62.3	57.1	0.070
Cx/OM/Ramus	Y	50.4	56.5	52.2	0.137
RCA/ PDA	Y	69.7	78.3	72.2	0.020
Cardiogenic Shock	Y	15.4	11.6	14.3	0.192

***Table 5.* Baseline characteristics of early and late presenting STEMI patients presenting at the Aswan Heart Center compared to Hamilton General Hospital.**

	≤ 180 mins			> 180 mins			Overall		
Charactersitic	AHC	HGH	P	AHC	HGH	P	AHC	HGH	P
Age (Mean, SD)	56.6, 11.8	63, 12.3	<0.001	57.4, 12.8	65, 13.2	<0.001	56.9, 12.3	63, 12.6	<0.001
Gender (Male) (%)	83	73	0.0013	72.4	70.5	0.657	78.2	72.3	0.0172
DM (%)	39.8	19.7	<0.001	47.7	23.1	<0.001	43.4	20.7	<0.001
HT (%)	39.1	51.2	0.001	36.6	58.5	<0.001	38.0	53.2	<0.001
Smoking (%)	69.3	40.4	<0.001	55.0	42	0.006	62.9	40.8	<0.001
In-Hospital Mortality (%)	4.8	2.8	0.141	9.6	5.3	0.091	7	3.5	0.006

4.3 Aswan Heart center questionnaire results

The questionnaire included 80 patients in total, 40 of which were in the early group, and 40 in the late group. The majority of the patients presenting at the AHC had completed secondary education (41.3%), were either unemployed or retired (36.25% and 17.5% retired respectively) and married (77.5% overall) with no significant difference between the two groups in these categories. Overall, 72.5% of patients had no previous cardiac history.

Symptom onset for the majority of patients occurred at home (87.5% overall). A non-significant difference was found in day and time of onset. A statistical significance was found in the presence of bystanders between the two groups. In the early group, patients were alone in only 2.5% of the cases, with a family member present in 87.5%, and a co-worker in 10%. In the late group, patients were alone in 7.5% of the cases, and a family member was present in 75%, a co-worker in 2.5% and other bystanders in 15% (P=0.027).

Chest discomfort was present in almost all the cases (92.5%), with no significant difference between the two groups. In the early group 20% of patients experienced diaphoresis compared to 47.5% in the late group (P=0.009). Light headedness was experienced by 12.5% of patients in the early group, and 37.5% of patients in the late group (P=0.01). There was no significant difference found in other symptoms between the two groups. Shortness of breath was a symptom experienced by a large number of patients overall (45%), followed by vomiting (43.8%), nausea (21.3%), discomfort in the jaw and arms (17.5%), palpitations (11.3%), and back pain (11.25%). A majority of patients did not attribute their symptoms to an MI, with a total of 72.5% of patients in the early group, and 87.5% in the late group (P=0.935).

There was a significant difference seen in the number of symptoms between the two groups. In the early group, 2.5% of patients presented with more than 5 symptoms, compared to 17.5% in the late group (P=0.025). No patients in either group described their pain level as '0 to 3' when at its worst. In the early group, 5% experienced pain at '4 to 6' and 95% at '7 to 10', compared to the late group with 25% pain at '4 to 6' and 75% at '7 to 10' (P=0.012).

The response of both patients and bystanders was significantly different between the two groups. In the early group, the majority of patients called/went to a physician (37.5%), while the majority of patients in the late group self -medicated/tried to self-help (42.5%)(P=0.01). Almost all bystanders in the early group called EMS (74.4%) compared to only 20% in the late group (P= 0.00008).

Transportation method and location of FMC were similar between the two groups. In both groups, the majority of patients used a taxi as a method of transportation (67.5% in the early group and 87.5% in the late group; P=0.203). Overall, 90% of patients presented at the Aswan Teaching Hospital. A significant difference was seen in transportation time between early and late presenters. In the early group, 12.5% of patients arrived in less than 20 minutes, 27.5% in 20 to 40 minutes, and 60% in over 40 minutes. This is comparable to 100% of patients in the late group with a transport time of over 40 minutes (P=0.00004). A summary of these results are found in table 6.

Knowledge of the importance of rapid intervention during an MI also showed a significant difference between the two groups, with a mean rank of 45.98 in the early group compared to 35.03 on the late group (P=0.031). Patients in the early group were also more likely to have feelings of anxiety due to their symptoms (mean rank 46.01 compared to 34.99 in the late group; P=0.01). Furthermore, significantly more patients in the late group were embarrassed to seek help, with a mean rank of 47.56 compared to 33.44 in the early group (P=0.003). Those in the late group also tended to initially underestimate their symptoms compared to the early group (mean rank 47.16 and 33.84 respectively; P=0.009). Late presenters were also more likely to delay seeking care due to not wanting to trouble others (mean rank 50.15 compared to 30.85 in early presenters; P=0), feeling in control over their symptoms (mean rank 55.56 compared to

30.44 in early presenters; P=0), and feeling afraid of the consequences of seeking help (mean rank 43.06 compared to 37.94 in early presenters; P=0.044). Non-significant differences were found between knowledge of MI symptoms, waiting to ensure symptoms were those of an MI, and comfort in seeking medical assistance. A summary of these results are found in table 7.

Table 6. **Responses to the modified Response to Systems Questionnaire in early and late presenters at the Aswan Heart Center**

Characteristic	≤ 180 mins (n=40) (%)	>180 mins (n=40) (%)	Overall	p value
Education level				
None	20	50	35	
Primary	12.5	5	8.75	0.064
Secondary	52.5	30	41.25	
University/ college	15	15	15	
Occupation				
Unemployed	30	42.5	36.25	
Employed	50	42.5	46.25	0.499
Retired	20	15	17.5	
Marital Status				
Married	80	75	77.5	0.592
Cardiac History				
Yes	32.5	22.5	27.5	0.317
Location of symptom onset				
Home	90	85	87.5	0.499
Outside Home	10	15	12.5	
Bystanders				
None	2.5	7.5	5	
Family	87.5	75	81.25	0.027
Co-worker	10	2.5	6.25	
Other	0	15	7.5	
Symptoms present				
Chest discomfort	92.5	92.5	92.5	1
Sweat	20	47.5	33.75	0.009
Nausea	22.5	20	21.3	0.785
Light headedness	12.5	37.5	25	0.01
Shortness of breath	47.5	42.5	45	0.653
Palpations	12.5	10	11.3	0.723
Discomfort to Jaw/arms	22.5	12.5	17.5	0.239
Back pain	7.5	15	11.25	0.288
Vomiting	40	47.5	43.8	0.499
Number of symptoms				
1	2.5	2.5	2.5	
2	37.5	27.5	32.5	
3	37.5	30	33.75	0.239
4	20	22.5	21.25	
5+	2.5	17.5	10	
Pain intensity				0.012
1 to 3	0	0	0	

4 to 6	5	25	15	
7 to 10	95	75	85	
Symptom attribution to MI				
Yes	27.5	12.5	20	0.935
Response of Bystander				
Called EMS	74.4	20	46.8	
Did nothing	0	5	2.5	
Suggested getting help	12.8	22.5	17.7	0.00008
Suggested rest/medication	12.8	5	24.1	
Told you not to worry	0	15	7.6	
Tried to comfort you	0	2.5	1.3	
Patient's first response				
Called EMS	35	12.5	23.8	
Called/went to physician	37.5	35	36.25	
Pretended nothing was wrong	5	2.5	3.75	0.01
Told someone	0	5	2.5	
Self treatment/help	12.5	42.5	27.5	
Tried to relax	10	2.5	6.25	
Day of Symptom onset				
Weekday	87.5	97.5	92.5	0.09
Weekend	12.5	2.5	7.5	
Time of Symptom onset				
12 am -8 am	35	32.5	33.75	
9 am - 5 pm	45	32.5	38.75	0.289
6 pm -11 pm	20	35	27.5	
Location of FMC				
Aswan teaching hospital	87.5	92.5	90	0.456
Other	12.5	7.5	10	
Transportation Method				
Driven to Hospital	2.5	0	1.25	
EMS	10	7.5	8.75	
Public transit	17.5	5	11.25	0.203
Self transport	2.5	0	1.25	
Taxi	67.5	87.5	77.5	
Transportation Time				
<20 min	12.5	0	6.25	
20-40 min	27.5	0	13.75	0.00004
>40 min	60	100	80	

Table 7. **Likert scale responses to the modified Response to Systems Questionnaire in early and late presenters at the Aswan Heart Center**

Characteristic	Mean Rank ≤ 180 mins (n=40)	Mean Rank >180 mins (n=40)	p value
Knowledge of importance of rapid intervention during an MI	45.98	35.03	0.031
Embarrassment to seek help	33.44	47.56	0.003
Awareness of symptoms of MI	36.6	44.4	0.128
Initially underestimating Symptoms	33.84	47.16	0.009
Delaying seeking care due to not wanting to trouble other	30.85	50.15	<0.001
Wanting to ensure symptoms were those of MI before seeking care	40.94	40.06	0.861
Feeling anxious due to symptoms	46.01	34.99	0.01
Feeling of control over symptoms	30.44	50.56	<0.001
Feeling comfortable in seeking medical assistance	38.96	42.04	0.158
Feeling afraid of the consequences of seeking help	37.94	43.06	0.044

CHAPTER 5

In this study, factors affecting delays from symptom onset to FMC were explored. The STEMI databases from the AHC and HGH were analyzed to highlight and compare patient demographics in the early and late groups. A convenience sample of 80 patients was selected from the AHC to further explore barriers and facilitators to seeking medical contact. With the majority of research focusing on high income countries, this study explores contextual factors that may be more specifically related to LMIC. Furthermore, exploring the setting around a newly established primary PCI program, and comparing it with an established system allows for future interventions that are specifically tailored to this population.

5.1 Database

Overall, time delays in Aswan were found to be longer than those in Hamilton, with a mean of 323 minutes and median of 180 minutes, compared to a mean of 248 minutes and median of 92 minutes respectively (P=0.005). Both patient and system delays may have played a role in this difference between the two sites, given the unique setting and cultural context of each location.

Although there were no significant differences between the time of presentation of men and women in Hamilton, women were more likely to have a longer symptom onset to FMC delay in Egypt. Previously, this time difference has been attributed to the type of symptoms that women experience during an MI. Unlike the 'classic' symptoms that have been shown to decrease delay times, women tend to experience vaguer, non-cardiac symptoms such as neck, back and jaw pain (Goldberg et al., 1998). This can be further affected by the perception of heart attacks as a condition more likely to be experienced by men. Additionally, this delay may also be due to women being more likely to spend time consulting others before seeking care (Finnegan et al., 2000). A study done in Jordan brought cultural insight to this delay, highlighting that married women in the Arab culture assume a large responsibility over the household and family, and may initially ignore or devalue their symptoms (Khraim, Scherer, Dorn & Carey, 2009). Furthermore, depending on location, women may be dependent on others for transportation (Noureddine et al., 2006). It is also worth noting that although women experienced a greater delay, the majority of patients presenting, in both locations, were men, and as such should be included in the focus of future interventions.

The sole risk factor found to be significantly different between the two delay groups was smoking. Patients in Aswan, who were smokers, were more likely to present earlier than non-smokers. This may be due to these patients perceiving themselves as higher risk for adverse events, and thus more likely to quickly respond to symptoms (Peng et al., 2014). Overall, the majority of patients presenting in Aswan were smokers (62.9%) compared to 40.8% in Hamilton ($P<0.001$). Furthermore, the percentage of patients presenting with diabetes mellitus was about two times higher than that in Hamilton (43.4% compared to 20.7%; $P<0.001$). Conversely, in Hamilton more than half of patients presenting had a history of hypertension, compared to 38% in Aswan ($P<0.001$). This reinforces the importance of targeted interventions for patients at high risk for cardiac conditions.

At both locations, those with a cardiac history were more likely to have shorter delays. In Hamilton, those who have had a previous CABG were more likely to be in the early group. Patients with a history of both CABG and PCI were more likely to be early presenters in Aswan. This is hypothesized to be due to patients having previous experience with cardiac symptoms, and thus a better understanding of what to expect and the course of action required.

In Aswan, patients in the late delay group were more likely to have cardiogenic shock. Although the cause-effect relationship cannot be determined for certain, it can be hypothesized that cardiogenic shock occurred due to the late delay. Those in the late group in Aswan were also more likely to experience higher in-hospital mortality, which may also be a result of the delay in seeking care.

5.2 Questionnaire

As would be expected, the majority patients in the early group took health care seeking action by contacting a physician/EMS as compared to those in the late group, who first attempted self-help methods. The majority of patients were in the presence of others during symptom onset, while only 5% were alone. Particularly, 81.3% of all patients were with their family. The action taken by bystander showed a link to time delays, with 74.4% of bystander calling EMS for patients presenting early, compared to only 20% of bystanders calling EMS for patients presenting late. Furthermore, a significant difference was found in patients delaying seeking care in order to avoid troubling those around them. These factors combined, highlight the importance of including patients' families in education programs, along with the general public, and takes into account the inclusion of family in health care decisions found in the Arab culture (Noureddine et al., 2006).

The type and intensity of symptoms proved another important factor in time delays. Diaphoresis and light headedness were significantly related to longer delays. Although patients experiencing diaphoresis have been shown to present earlier (Goldberg et al., 2002), symptoms that are non-cardiac in origin have been generally linked to longer delays (Herlitz et al., 2010). These unspecific symptoms may prove harder for patients to interpret the underlying cause and in-turn lead to the undermining of the seriousness of the situation. The number of symptoms experienced by patients may further add to this confusion. Patients experiencing 5 or more symptoms were more likely to have longer delays. This is contrary to current findings, with greater numbers of symptoms being linked to shorter delay times (Goldberg et al., 2002). Higher pain intensity was also linked to shorter delays, and is likely due to patients evaluating their symptoms as more serious. This is reinforced by the finding that those presenting later were more likely to initially underestimate their symptoms as compared to early presenters.

Overall, 92.5% of patients experienced chest pain, yet 80% of patients did not attribute their symptoms to an MI. This may contribute to the overall delay found in this setting as compared to Hamilton, and brings attention to the potential lack of patient awareness of MI symptoms. The importance of knowledge is further highlighted in the difference found between early and late presenters in the understating of the importance of rapid intervention during an MI. As would be expected, patients with this knowledge were less likely to delay seeking care.

Another important contribution to delay is the time taken to reach FMC after an individual has made the decision to seek care. It was found that all patients in the late delay group had a transport time of over 40 minutes, while early presenters were more likely to have a transport time of less than 40 minutes. However it is important to note that the majority of patient in both groups faced this delay. This may be attributed to long distances to a hospital, or due to self transportation. The majority of patients used a taxi to reach care, followed by public transport. A study evaluating EMS use in STEMI patients in Canada found that patients who did not use EMS were more likely to have the perception that EMS is a slower means of transportation, as well as concerns about misusing health care resources, and being a burden on the health care system (Connolly, Dmetrichuk, Natarajan, Schwalm, 2014). However, the lack of use of EMS in Aswan is likely secondary to a gap in the infrastructure of the system in providing timely transportation to hospitals in the region, as compared to patient beliefs. This is highlighted by the discrepancy in the number of people who contacted EMS, compared to the number of patients that used the service to reach the hospital. It can be hypothesized that EMS either cannot be successfully contacted over the phone, or that they cannot provide their service in a timely manner, leading patients to utilize alternative methods of transportation.

Emotional factors also showed a significant difference between the early and late groups. Those in the late group were more likely to have had feelings of control over symptoms, felt embarrassment in seeking help, and fear of the consequences of seeking help. These emotions may have resulted in patients devaluing their symptoms, or balancing their concern over their symptoms with this embarrassment and fear. Those in the early group were more likely to feel anxiety due to their symptoms, and thus may have been less likely to delay care due to their increased concern.

5.3 Limitations

There are several limitations in this study that should be taken into consideration. First, the survey used was not validated, but rather a modified version of a widely used questionnaire. Furthermore, due to the retrospective nature of the data collection for the questionnaire, there may have been recall bias, especially as patients were asked about a particularly stressful event. However, the database was used to supplement the information provided by the patients and only larger themes were drawn from the survey. Response bias may have also played a role in specific questions concerning comfort with the health care system, especially given that interviews were conducted by health care workers.

Due to the inability to interview non-survivors, and the further link between mortality and long delays, barriers affecting this population may not have been effectively captured.

Furthermore, the use of existing databases from two different locations, with different definitions and groupings of parameters at each site, resulted in the inability to compare some factors between the two. Completion of these databases did not prove to be a concern, as no more than 10% of the data was missing for each parameter, with the exception of posterior MI. However, this diagnosis requires a 15 lead ECG and is not done as part of routine practice in every patient. It is also recognized that this study was conducted at two specific locations, and this must be kept in mind before generalizing these results to all HIC and LMIC.

5.4 Future direction

This study can provide direction for further research, and guide the development of future interventions. The modified RSQ can be applied to the patient population in Hamilton to supplement results found from the database, and provide an extended platform for comparison with Aswan. Furthermore, it may also prove worthwhile to carry out further research that divides symptom onset to FMC delays. Exploring the delays from symptom onset to the decision to seek care, independently from the delay between the decision to seek care and FMC can shed light onto the different patient, and systematic factors at play. This study grouped together this timeframe, which did not clarify the length of time or factors attributed to each.

Additionally, further understanding factors that have been outlined in this study as affecting delay can lead to better informed interventions. For example, the long transportation times found in Aswan may be due to several factors, ranging from long distances to hospitals to lacking EMS infrastructures. Pinpointing the underlying causes may allow for more effective solutions. Furthermore, given the link between bystanders and delay time, applying a similar questionnaire to gain the perspective of the bystanders, and exploring reasons behind actions taken can provide insight for future interventions targeted at the public.

Finally, this study has outlined factors that are linked to patient delays in Aswan. Developing tailored intervention at the Aswan Heart Center to these specific factors can target the long patient delays found in the region. Education programs aimed at patients and the general public that raise awareness of MI symptoms, highlight the different presentation in men and women, as well as the importance of rapid intervention can target gaps in public knowledge. Patients counseling for those with risk factors, and the inclusion of the family in this knowledge sharing when possible, as well as making patients cognizant of their potential emotional response to symptoms and how it may affect their decision to seek care can be adopted by physicians.

5.5 Conclusion

The importance of timely reperfusion during a STEMI, combined with the large portion of total ischemic time that symptom onset to FMC time comprises, and the lack of research done exploring barriers that affect these delays in LMIC makes this an important area of study. Exploring factors linked to early and late presentation in STEMI patients showed that delays were associated with gender, smoking, cardiac history, cardiogenic shock and mortality rate. Furthermore, the type and number of symptoms, presence and actions of bystanders, emotional response and the actions of the patients, as well as transportation time was shown to be different among delay groups. Further research is needed in different regions in Egypt, as well as other LMIC in order to shed light on contextual barriers unique to each culture and location.

References

Alexander, T., Mullasari, A. S., Kaifoszova, Z., Khot, U. N., Nallamothu, B., Ramana, R. G., ... & Chand, K. (2015). Framework for a National STEMI Program: Consensus document developed by STEMI INDIA, Cardiological Society of India and Association Physicians of India. *Indian heart journal*,*67*(5), 497-502.cite

Armstrong, P. W., Gershlick, A., Goldstein, P., Wilcox, R., Danays, T., Bluhmki, E., ... & STREAM Steering Committee. (2010). The strategic reperfusion early after myocardial infarction (STREAM) study. *American heart journal*, *160*(1), 30-35.

Aujla, N., Walker, M., Sprigg, N., Abrams, K., Massey, A., & Vedhara, K. (2016). Can illness beliefs, from the common-sense model, prospectively predict adherence to self-management behaviours? A systematic review and meta-analysis. *Psychology & health*, 1-28.

Bainey, K., Afzal, R., Rokoss, M., Velianou, J., Natarajan, M. (2010) Reperfusion Therapy in STEMI: Do Late Presentation Patients (> 12 hours) Derive Clinical Benefit? Unpublished manuscript.

Cardiovascular diseases (CVDs). (2016). *World Health Organization*. Retrieved from http://www.who.int/mediacentre/factsheets/fs317/en/

Central Agency for Public Mobilization and Statistics. (2015) Retrieved from http://www.capmas.gov.eg/?lang=2.

Cohen, M., Boiangiu, C., & Abidi, M. (2010). Therapy for ST-segment elevation myocardial infarction patients who present late or are ineligible for reperfusion therapy. *Journal of the American College of Cardiology*, *55*(18), 1895-1906.

Connolly, K., Dmetrichuk K., Natarajan, M., & Schwalm S. (2014) Barriers to the use of Emergency Medical Services in ST-Elevation Myocardial Infarction. Unpublished manuscript

Danchin, N., Puymirat, E., Steg, P. G., Goldstein, P., Schiele, F., Belle, L., ... & Ferrières, J. (2014). Five-year survival in patients with ST-segment elevation myocardial infarction according to modalities of reperfusion therapy: the French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) 2005 cohort. *Circulation*, CIRCULATIONAHA-113.

Early management guidance and guidelines. *National Institute for Health and Care Excellence* (2010). Retrieved from https://www.nice.org.uk/guidance/cg167

Fanari, Z., Abraham, N., Hammami, S., & Doorey, A. J. (2015). Aggressive Measures to Decrease Door to Balloon Time May Increase the Incidence of Unnecessary Cardiac Catheterization and Delay Appropriate Care. *Delaware medical journal*, *87*(9), 276-279.

Finnegan, J. R., Meischke, H., Zapka, J. G., Leviton, L., Meshack, A., Benjamin-Garner, R., ... & Weitzman, E. R. (2000). Patient delay in seeking care for heart attack symptoms: findings from focus groups conducted in five US regions. *Preventive medicine*, *31*(3), 205-213.

Goldberg, R. J., O'Donnell, C., Yarzebski, J., Bigelow, C., Savageau, J., & Gore, J. M. (1998). Sex differences in symptom presentation associated with acute myocardial infarction: a population-based perspective. American heart journal, 136(2), 189-195.

Goldberg, R. J., Yarzebski, J., Lessard, D., & Gore, J. M. (2000). Decade-long trends and factors associated with time to hospital presentation in patients with acute myocardial infarction: the Worcester Heart Attack study.*Archives of internal medicine*, *160*(21), 3217-3223.

Goldberg, R. J., Steg, P. G., Sadiq, I., Granger, C. B., Jackson, E. A., Budaj, A., ... & Goodman, S. (2002). Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). *The American journal of cardiology*, *89*(7), 791-796.

Global status report on noncommunicable diseases 2014 http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=1

Hamilton Health Sciences. *Heart Investigation Unit (HIU).* (2016). Retrieved from http://www.hamiltonhealthsciences.ca/body.cfm?id=2401

Herlitz, J., Thuresson, M., Svensson, L., Lindqvist, J., Lindahl, B., Zedigh, C., & Jarlöv, M. (2010). Factors of importance for patients' decision time in acute coronary syndrome. *International journal of cardiology*, *141*(3), 236-242.

Huber, K., Gersh, B. J., Goldstein, P., Granger, C. B., & Armstrong, P. W. (2014). The organization, function, and outcomes of ST-elevation myocardial infarction networks worldwide: current state, unmet needs and future directions. *European heart journal*, *35*(23), 1526-1532.

Joshi, R., Jan, S., Wu, Y., & MacMahon, S. (2008). Global inequalities in access to cardiovascular health care: our greatest challenge. *Journal of the American College of Cardiology*, *52*(23), 1817-1825.

Kaifoszova, Z., Kala, P., Alexander, T., Zhang, Y., Huo, Y., Snyders, A., ... & Gavidia, L. M. (2014). Stent for Life Initiative: leading example in building STEMI systems of care in emerging countries. *EuroIntervention*, *10*(suppl T), T87-T95.

Khraim, F. M., Scherer, Y. K., Dorn, J. M., & Carey, M. G. (2009). Predictors of decision delay to seeking health care among Jordanians with acute myocardial infarction. *Journal of Nursing Scholarship*, *41*(3), 260-267.

Lambert, L., Brown, K., Segal, E., Brophy, J., Rodes-Cabau, J., & Bogaty, P. (2010). Association between timeliness of reperfusion therapy and clinical outcomes in ST-elevation myocardial infarction. *JAMA*, *303*(21), 2148-2155.

Løvlien, M., Schei, B., & Hole, T. (2007). Prehospital delay, contributing aspects and responses to symptoms among Norwegian women and men with first time acute myocardial infarction. *European Journal of Cardiovascular Nursing*, *6*(4), 308-313.

Martin, L., Murphy, M., Scanlon, A., Naismith, C., Clark, D., & Farouque, O. (2014). Timely treatment for acute myocardial infarction and health outcomes: An integrative review of the literature. *Australian Critical Care*,*27*(3), 111-118.

Mercuri, M., Welsford, M., Schwalm, J. D., Mehta, S. R., Rao-Melacini, P., Sheth, T., ... & Natarajan, M. K. (2015). Providing optimal regional care for ST-segment elevation myocardial infarction: a prospective cohort study of patients in the Hamilton Niagara Haldimand Brant Local Health Integration Network. *CMAJ open*, *3*(1), E1.

Moser, D. K., McKinley, S., Dracup, K., & Chung, M. L. (2005). Gender differences in reasons patients delay in seeking treatment for acute myocardial infarction symptoms. *Patient education and counseling*, *56*(1), 45-54.

Noureddine, S., Adra, M., Arevian, M., Dumit, N. Y., Puzantian, H., Shehab, D., & Abchee, A. (2006). Delay in seeking health care for acute coronary syndromes in a Lebanese sample. *Journal of Transcultural Nursing*, *17*(4), 341-348.

O'Gara, P. T., Kushner, F. G., Ascheim, D. D., Casey, D. E., Chung, M. K., De Lemos, J. A., ... & Granger, C. B. (2013). 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*, *61*(4), e78-e140.

Okhovati, M., Zare, M., & Bazrafshan, A. (2015). Variations in Ischemic Heart Disease Research by Country, Income, Development and Burden of Disease: A Scientometric Approach. *Journal of cardiovascular and thoracic research*, *7*(4), 164.

Ôunpuu, S., Negassa, A., & Yusuf, S. (2001). INTER-HEART: A global study of risk factors for acute myocardial infarction. *American heart journal*, *141*(5), 711-721.

Prasad, A., Gersh, B. J., Mehran, R., Brodie, B. R., Brener, S. J., Dizon, J. M., ... & Dudek, D. (2015). Effect of ischemia duration and door-to-balloon time on myocardial perfusion in ST-segment elevation myocardial infarction: an analysis from HORIZONS-AMI Trial (harmonizing outcomes with revascularization and stents in acute myocardial infarction). *JACC: Cardiovascular Interventions*, *8*(15), 1966-1974.

Park, Y. H., Kang, G. H., Song, B. G., Chun, W. J., Lee, J. H., Hwang, S. Y., ... & Kim, Y. D. (2012). Factors related to prehospital time delay in acute ST-segment elevation myocardial infarction. *Journal of Korean medical science*,*27*(8), 864-869.Cite 2

Peng, Y. G., Feng, J. J., Guo, L. F., Li, N., Liu, W. H., Li, G. J., ... & Zu, X. L. (2014). Factors associated with prehospital delay in patients with ST-segment elevation acute myocardial infarction in China. *The American journal of emergency medicine*, *32*(4), 349-355.

Perkins-Porras, L., Whitehead, D. L., Strike, P. C., & Steptoe, A. (2008). Causal beliefs, cardiac denial and pre-hospital delays following the onset of acute coronary syndromes. *Journal of behavioral medicine*, *31*(6), 498-505.

Perkins-Porras, L., Whitehead, D. L., Strike, P. C., & Steptoe, A. (2009). Pre-hospital delay in patients with acute coronary syndrome: factors associated with patient decision time and home-to-hospital delay. *European Journal of Cardiovascular Nursing*, *8*(1), 26-33.

Schwalm, J. D., McKee, M., Huffman, M. D., & Yusuf, S. (2016). Resource effective strategies to prevent and treat cardiovascular disease. *Circulation*,*133*(8), 742-755.

Sinnaeve, P. R., Armstrong, P. W., Gershlick, A. H., Goldstein, P., Wilcox, R., Lambert, Y., ... & Vandenberghe, K. (2014). ST–Segment-Elevation Myocardial Infarction Patients Randomized to a Pharmaco-Invasive Strategy or Primary Percutaneous Coronary Intervention Strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-Year Mortality Follow-Up.*Circulation*, *130*(14), 1139-1145.

Solhpour, A., Chang, K. W., Arain, S. A., Balan, P., Loghin, C., McCarthy, J. J., ... & Smalling, R. W. (2015). Ischemic time is a better predictor than door-to-balloon time for mortality and infarct size in ST-elevation myocardial infarction. *Catheterization and Cardiovascular Interventions*.

Sørensen, J. T., & Mæng, M. (2015). Regional systems-of-care for primary percutaneous coronary intervention in ST-elevation myocardial infarction.*Coronary artery disease*, *26*(8), 713-722.

Tang, K. L., Rashid, R., Godley, J., & Ghali, W. A. (2016). Association between subjective social status and cardiovascular disease and cardiovascular risk factors: a systematic review and meta-analysis. *BMJ open*, *6*(3), e010137.

Appendix 1: Questionnaire

Study ID:

Educational level: ☐Non ☐primary ☐Secondary school ☐University ☐College

Occupation:

Marital status: ☐Single ☐Married ☐Widowed ☐Divorced

Cardiac History: ☐Previous MI ☐Previous Angina ☐Any known coronary artery Disease

---

What time did your symptoms start?

Where were you when your symptoms started? ☐Home ☐Work ☐Other: ___________

Was there a bystander present when your symptoms started? ☐Alone ☐Family ☐Friends ☐Co-workers ☐Other: _____________

Symptoms: ☐ Chest discomfort ☐Sweaty ☐Nausea ☐Light headedness ☐Shortness of breath ☐Palpations ☐Discomfort to Jaw/arms (☐Back pain, ☐Vomiting?)

When your pain was at its worst, how would you rate its intensity?

0 1 2 3 4 5 6 7 8 9 10
No pain Worst pain

When your symptoms were at their worst, did you attribute them to a heart attack? ☐Yes ☐No

---

How did those around you respond to your symptoms: ☐N/A ☐Did nothing ☐Told you not to worry ☐Got upset ☐Tried to comfort you ☐Suggested rest/medication ☐Suggested getting help ☐Called EMS/took you to emergency department

What was your first response to your symptoms: ☐Waited for symptoms to resolve ☐Tried to relax ☐Pretended nothing was wrong ☐Told someone ☐Took medication/other self help remedies ☐Called/went to physician ☐Called EMS/went to emergency department

---

What day did you seek medical attention? ☐Weekend ☐Weekday

Time of day: ☐9:00 am -5:00 pm ☐ 6:00 pm - 11:00 pm ☐12:00 am -8:00 am

Where did you first go when seeking medical care? ☐Aswan Teaching Hospital ☐Aswan Heart Center ☐Hamilton General Hospital ☐Other hospital ☐Physician's office ☐Other: _______

How did you get there? ☐EMS ☐ Taxi ☐Public transit ☐Self transportation ☐Driven to hospital ☐Other: _________

How long did it take you to get there? ☐ > 20 mins ☐ 20-40 mins ☐< 40 mins

I think rapid intervention during a heart attack is crucial:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I was embarrassed to seek help:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I am aware of the symptoms of a heart attack:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I initially underestimated the symptoms of my heart attack:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I delayed seeking help because I did not want to trouble others:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I wanted to ensure the symptoms were those of a heart attack before seeking help:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

My symptoms made me anxious:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I felt that I had control over my symptoms:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I was comfortable seeking medical assistance:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

I was afraid of the consequences of seeking help:

Strongly Agree ○ ○ ○ ○ ○ ○ ○ **Strongly Disagree**

Appendix 2: Classification of recommendations and level of evidence

(O'Gara et al., 20131)

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *No Benefit* or **CLASS III** *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines
do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is
useful or effective.
*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior
myocardial infarction, history of heart failure, and prior aspirin use.
†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.