Associations Between Treatment-Seeking Delay and Clinical Course of Patients with Suspected Acute Coronary Syndrome at Initial Emergency Department Encounter

by

Alexandra Tolassi

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This thesis was presented

by

Alexandra Tolassi

It was defended on

April 13, 2022

and approved by

Salah Al-Zaiti, PhD, RN, ANP-BC, FAHA, Associate Professor, University of Pittsburgh School of Nursing, Department of Acute and Tertiary Care

Paul Scott, PhD, Assistant Professor, University of Pittsburgh School of Nursing, Department of Health & Community Systems

Holli DeVon, PhD, RN, FAHA, FAAN, Professor & Associate Dean for Research, University of California Los Angeles School of Nursing

Thesis Advisor/Dissertation Director: Stephanie O. Frisch, PhD, RN, Postdoctoral Associate, University of Pittsburgh School of Medicine, Department of Biomedical Informatics

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Background: Acute coronary syndrome (ACS) is a high-risk clinical condition that requires reperfusion within 12 hours of symptom onset. Treatment-seeking delay prolongs ischemic time and may lead to adverse outcomes. Being aware of potential adverse events at triage may improve patient outcomes.

Purpose: We sought to determine the prevalence of delay greater than 12 hours in patients with suspected ACS and patient characteristics associated with delay. Then, we sought to determine if there was a link between delay and adverse clinical outcomes, as defined by major adverse cardiovascular events (MACE), hospital utilization, and 30-day readmissions.

Methods: This was a secondary analysis of a retrospective study of emergency department (ED) patients with suspected ACS. Descriptive statistics were used to investigate patient characteristics, including demographics, past medical history, vital signs, chief complaints, electrocardiogram results, and delay time, as measured from symptom onset to ED arrival or initial EMS contact. Clinical outcomes of interest include MACE, hospital utilization, and 30-day readmission. MACE was defined as the presence of confirmed ACS diagnosis, death, new onset/worsening heart failure, fatal ventricular dysrhythmia, or cardiogenic shock. Hospital utilization outcomes included: admission, ICU transfer, coronary revascularization, IABP insertion, CABG surgery, or pacemaker or ICD placement. Chi-square or Mann Whitney *U* tests were used to determine if there were differences in patient characteristics in early (< 12 hours) versus late (≥ 12 hours) presenters. Chi-square was used to find differences in early versus late delay groups for each outcome. Univariable and multivariable binary logistic regressions were used to determine patient factors associated with MACE and hospital utilization in early versus late presenters.

Results: The sample included 1201 patients. Over half (55%, n = 655) presented greater than 12 hours after symptom onset, and 546, (45%) presented before 12 hours. There was no difference in MACE or readmission between delay groups. Early presenters had higher rates of hospital utilization than late presenters.

Conclusion: Nurses should consider patient characteristics at initial ED presentation associated with increased MACE and hospital utilization to better risk stratify those patients. Maximizing reperfusion treatment for patients with delay should be initiated at initial ED assessment.

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1.0 Introduction

In 2021, there were approximately 130 million emergency department (ED) visits annually in the United States (US), of which over 5.5 million patients presented with symptoms suggestive of acute coronary syndrome (ACS) (*CDC*, 2021; Mirzaei et al., 2020). Patients with chest pain and other symptoms suggestive of ACS must be promptly evaluated for myocardial infarction (MI) to ensure timely administration of treatment. Short delay between symptom onset to ED arrival and from ED arrival to initiation of treatment is critical in minimizing myocardial ischemia (i.e., damage to the heart muscle). Treatment-seeking delay is comprised of three phases: 1) symptom onset to patient decision to present to the ED, 2) decision time to first medical contact (if the patient utilizes emergency medical services), and 3) transportation time (Moser et al., 2006). Approximately half of the 1.2 million individuals who have a confirmed MI annually die in the ED or before reaching the hospital because of this delay (Zègre-Hemsey et al., 2018). It is hypothesized that patients who delay seeking medical attention will have poorer clinical outcomes because of increased myocardial ischemic time.

ACS is a composite of three diagnoses in which there is evidence of myocardial ischemia or infarction: unstable angina (UA), ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI). UA is defined as the presence of chest pain at rest, without elevated cardiac biomarkers or electrocardiogram (ECG) changes (Reeder et al., 2021). STEMI and NSTEMI are defined by symptoms indicative of myocardial ischemia and elevated cardiac biomarkers, specifically troponin (Reeder et al., 2021). STEMI is differentiated from NSTEMI by the presence of ECG changes, notably ST-segment elevations or a new-onset left bundle branch block (O’Gara et al., 2013). Broadly, MI is diagnosed when there is an elevation in cardiac biomarkers, particularly troponin, with either ST-segment elevation, new onset bundle branch block, pathological Q waves, myocardial necrosis on imaging studies, or intracoronary thrombus (Jneid et al., 2017).

Most commonly, ACS is caused by the buildup and rupture of atherosclerotic plaque (Sweis & Jivan, 2020). This plaque rupture causes platelet aggregation and acute thrombus formation, limiting blood flow to the myocardium (Sweis & Jivan, 2020). Morbidity and mortality secondary to ACS is related to the duration of the occlusion, which determines the extent of myocardial ischemia and infarction. Myocardium begins to necrose within 30 minutes and total tissue necrosis is typically complete within 6 hours (Schömig et al., 2006). This infarcted myocardium is especially prone to arrhythmias (Yusuf et al., 1988). Treatment goals include limiting the extent of ischemia with reperfusion therapies and preventing fatal arrhythmias stemming from infarcted tissue (Ibanez et al., 2018; O'Gara et al., 2013; Yusuf et al., 1988).

The hallmark symptom of ACS is chest pain. This is also commonly described as a crushing, squeezing, pressure-like, or burning sensation that may radiate to the jaw, neck, back, shoulder, abdomen, or arm (Singh et al., 2022). Additionally, shortness of breath, weakness, lightheadedness, nausea, diaphoresis, and abdominal pain are common symptoms suggestive of an ACS episode (Singh et al., 2022). Women, older adults, and diabetics are more likely to report less frequent symptoms when evaluated for ACS (Moser et al., 2006). Because of this less frequent presentation, patients may be less likely to recognize the symptoms as cardiac in origin and seek prompt medical care, leading to delays in reperfusion therapy (DeVon et al., 2010). STEMI patients are more likely to present to the ED earlier than NSTEMI patients, as 23.5% of STEMI patients presented within 3 hours compared to 14.5% of NSTEMI patients in one study (Ibanez et al., 2018).

The phrase “time is muscle” is widely used in cardiology literature to describe the importance of prompt reperfusion therapy in ACS cases. As ischemia progresses, cardiac function is compromised, increasing morbidity and mortality. The American Heart Association (AHA) and European Society of Cardiology (ESC) urge individuals to present immediately to the ED for symptoms suggestive of an ACS episode for prompt reperfusion (Gulati et al., 2021; Ibanez et al., 2018; O’Gara et al., 2013). An ECG should be completed within 10 minutes of ED arrival to rule out STEMI and minimize time to treatment (Ibanez et al., 2018; O’Gara et al., 2013). Fibrinolytic medications or primary percutaneous coronary intervention (PCI) may be utilized to establish reperfusion. Fibrinolytic medications should be administered within 30 minutes of ED arrival (door-to-needle time), or primary PCI must be initiated within 90 minutes (door-to-balloon time) (O’Gara et al., 2013). Studies have shown that with increasing time to treatment, PCI and fibrinolytic therapy outcomes are poorer (Fibrinolytic Therapy Trialists’ (FTT) Collaborative Group, 1994; O’Gara et al., 2013). Infarction may be reversible if reperfusion to the affected vessel is attained within 30 minutes of symptom onset, and viable myocardium may be salvaged up to 6 hours from the onset of occlusion (Moser et al., 2006; Schömig et al., 2006). Treatment within the first hour after symptom onset is particularly effective at restoring blood flow, and mortality rates decline by up to 50% (Moser et al., 2006). The ISIS-2 (Second International Study of Infarct Survival) trial found a 37% mortality reduction if treatment was administered within 3 hours of symptom onset, 24% mortality reduction for treatment between 3-6 hours, and 17% reduction past 6 hours (Schömig et al., 2006). Mortality and morbidity reductions are seen in both reperfusion therapy options until 12 hours after symptom onset, although these associations are time dependent (Fibrinolytic Therapy Trialists’ (FTT) Collaborative Group, 1994; Hampton et al., 1993; O’Gara et al., 2013). Current AHA protocols dictate that reperfusion treatments are to be administered until 12 hours after symptom onset (O'Gara et al., 2013). The benefits of reperfusion therapy from 6 hours to 12 hours after symptom onset are due to improved infarct healing, electrical stabilization, and dysrhythmia prevention (Khowaja et al., 2021; Schömig et al., 2006). Beyond 12 hours from symptom onset, reperfusion benefits are quite limited (Schömig et al., 2006). Mortality reductions past 12 hours were not significant in the LATE study (Late Assessment of Thrombolytic Efficacy) (Hampton et al., 1993). More current literature suggests that there is some benefit to late reperfusion beyond 12 hours, but not as significant as reperfusion within 12 hours (Nepper-Christensen et al., 2018). A large proportion of patients who underwent late thrombolytic therapy from 12-72 hours after symptom onset received significant myocardial salvage (Nepper-Christensen et al., 2018). However, the myocardial salvage index was smaller in these late-presenting patients and final infarct size was larger than patients who underwent timely reperfusion therapy (Nepper-Christensen et al., 2018).

From 2003 to 2008, median door-to-balloon times in patients with STEMI decreased from 113 minutes to 76 minutes (Flynn et al., 2010). Menees et al., also found a significant decrease in median door-to-balloon time from 83 minutes in 2005-2006 to 67 minutes in 2008-2009 (2013). This indicates a significant reduction in system delay in treatment administration. A significant proportion of this decrease in time-to-treatment may be explained by the development and use of prehospital ECGs and early cardiac catheterization laboratory notification (Nam et al., 2014). EMS providers can rapidly identify STEMI patients by performing 12-lead ECGs during ambulance transport. The hospital may then be notified of the patient's ECG results and a copy of the 12-lead ECG is transmitted to the hospital prior to patient arrival, allowing for advanced activation of the cardiac catheterization laboratory. The use of prehospital ECGs is a class I recommendation from the AHA/American College of Cardiology (ACC) (O'Gara et al., 2013). Nam et al., found that prehospital ECGs were associated with a 21–78-minute reduction in medical contact to balloon time and a 39% reduction in mortality related to advanced cardiac catheterization laboratory notification (2014). Similarly, Morrison et al. found a 36.1-minute decrease in door-to-needle time in patients who received prehospital ECGs. The use of prehospital ECGs is also associated with increased use of in-hospital fibrinolytic drugs and percutaneous interventions (Morrison et al., 2006; Quinn et al., 2014).

Despite a significant decrease in system delay via door-to-balloon time, there has not been a significant reciprocal decrease in in-hospital mortality rates (Flynn et al., 2010; Menees et al., 2013). Flynn et al., found a 4.10% mortality rate in 2003 and a 3.62% mortality rate in 2008 ($p=0.69$) (2010). Menees et al., found a 4.8% mortality rate in 2006 and a 4.7% mortality rate in 2009 ($p=0.43$) (2013). This indicates that a factor aside from door-to-balloon time is driving in-hospital mortality.

Door-to-balloon time hinges on the efficiency of the hospital system to accurately triage, diagnose, and treat patients with symptoms suggestive of ACS. Alternatively, total ischemic time considers the effect of treatment-seeking delay as well as door-to-balloon time (Flynn et al., 2010). One study found that infarct size and 30-day mortality were significantly associated with increasing ischemic times, but not with increasing door-to-balloon times (Solhpour et al., 2016). This suggests that total ischemic time is a better predictor of clinical outcomes than door-to-balloon time, and management goals should emphasize the reduction of patient delay and ischemic time, rather than solely door-to-balloon time (Solhpour et al., 2016).

Treatment-seeking delay is defined as the time it takes patients to recognize their symptoms, decide to seek treatment, and transportation time to the hospital (Mirzaei et al., 2019). Total ischemic time may be a more accurate approximation of the duration of vessel occlusion because measurement begins at symptom onset. The GUSTO-1 trial (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) demonstrated that morbidity increases as time from symptom onset increases (Newby et al., 1996). Khowaja et al. found that total ischemic time is an independent predictor of infarct size and mortality in STEMI patients, with the highest mortality rates occurring in the sample of patients with the greatest ischemic time (2021). Khowaja et al. also found that for every hour of treatment-seeking delay after symptom onset, the risk of mortality increased by 5%, and increased exponentially 5 hours after onset of chest pain (2021). As such, it is critical to reduce total ischemic time to salvage viable myocardium, prevent a large zone of infarction, thus leading to preservation of heart ejection fraction. Treatment-seeking delay time remains the greatest portion of total time to treatment (Cullen et al., 2016). Reducing patient treatment-seeking delay may be more effective than reducing door-to-balloon time to accomplish this goal. This proves to be a challenge, as less than 20% of patients present to the ED within 1 hour of symptom onset and 40% of patients with chest pain delay greater than 6 hours in seeking treatment (DeVon et al., 2010; Wu et al., 2011). Other studies found that between 26.2% and 49% of patients present within 2 hours of symptom onset, and approximately 38% of patients delay greater than 6 hours after symptom onset before presenting to the ED, representing a large proportion of individuals who may potentially miss the window of reperfusion (Cullen et al., 2016; DeVon et al., 2020; Frisch et al., 2019).

2.0 Background

Between 8% and 40% of STEMI patients delay seeking treatment in the ED for more than 12 hours after symptom onset (Nepper-Christensen et al., 2018). Median delay times in the United States range from 1.5 to 6 hours on average in patients with confirmed STEMI (Moser et al., 2006). In a 2020 study investigating predictors of delay in patients with symptoms suggestive of ACS, median delay was 6.68 hours (DeVon et al., 2020). The greatest portion of treatment-seeking delay time is explained by the time a patient takes to decide to seek care, followed by transportation time (DeVon et al., 2010; Rasmussen et al., 2003). As a result of this treatment-seeking delay, a large proportion of patients arrive at the ED outside of the timeframe to be eligible for reperfusion therapy. Despite public health and patient education programs, this delay figure has remained relatively stable for the past several decades (McKee et al., 2013). From 2001 to 2003, only 45.8% of patients arrived at the ED within 2 hours of symptom onset (Makam et al., 2016). From 2009 to 2011, this figure remained stable at 48.9% of patients arriving within 2 hours of symptom onset (Makam et al., 2016). The remaining proportion of individuals are at risk for missing the optimal window of reperfusion.

Treatment seeking delay in patients who may be having a coronary event is influenced by the interaction of several decision-making behaviors and social and demographic characteristics. The self-regulatory model has been cited in several studies to describe an indiviual's decision-making process when confronted with a health threat (Baxter & Allmark, 2013; Nymark et al., 2009). This model emphasizes the influence of both internal and external factors that contribute to a patient's problem-solving process and notes that people actively screen and control potential threats to their safety (Baxter & Allmark, 2013). There are three stages of decision-making in this model that culminate in the patient deciding to seek medical assistance (Figure 1) (Baxter & Allmark, 2013; Nymark et al., 2009).

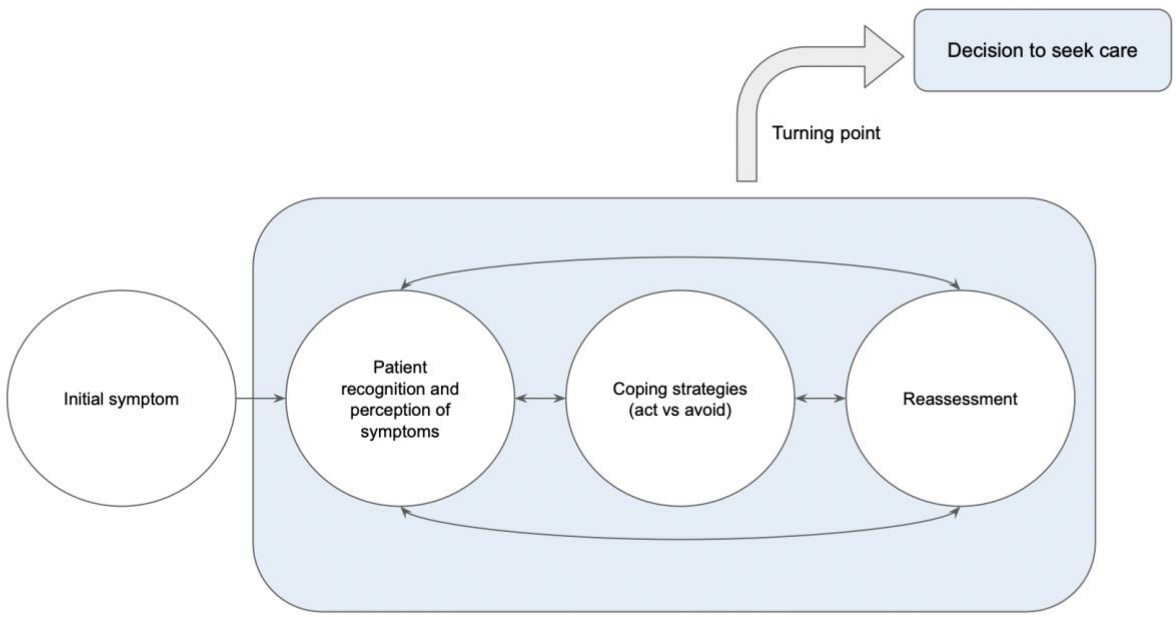

Figure 1: Self Regulatory Model of Decision to Seek Medical Treatment

The first stage deals with the patient's cognitive processes, including the recognition of their symptoms and the urgency of their condition (Baxter & Allmark, 2013). The patient's first step in deciding to seek treatment for a suspected ACS event is the recognition of abnormal symptoms, followed by the recognition that these symptoms can be attributed to a serious medical cause (Mumford et al., 1999). Chest pain and associated descriptors, like squeezing, burning, discomfort, and pressure sensations were the most commonly cited reason that patients elected to seek care (DeVon et al., 2010). Other symptoms, such as shortness of breath, diaphoresis, localized arm pain, dizziness, weakness, and nausea/vomiting that were severe or unrelenting also influenced a patient's decision to seek care (DeVon et al., 2010). Limited health literacy or knowledge of heart attack symptoms may preclude a patient from identifying the threat of these symptoms and presenting to the ED in a timely manner (Baxter & Allmark, 2013). Further, mismatch between expected and actual ACS symptoms may prevent a patient from recognizing the severity of their condition and increase treatment-seeking delay (Baxter & Allmark, 2013). Conversely, Mumford et al., found that patients who were able to identify MI symptoms in a survey did not necessarily present to the ED earlier, as they held misconceptions about their significance or did not recognize the urgency in their own presentation (1999). DeVon et al., found that patients were unsure when their symptoms were severe enough to label them as life-threatening (2010). In turn, this denial or uncertainty further increases delay.

The second phase of the self-regulatory model focuses on the patient's response to the health threat (Baxter & Allmark, 2013). After the patient recognizes the urgency of their symptoms, they must decide to seek medical care. This step of the decision-making process is frequently halted by a patient's attempt to control the situation themselves with coping behaviors (DeVon et al., 2010; Mumford et al., 1999; Baxter & Allmark, 2013; Nymark et al., 2009). These coping behaviors can be largely grouped into acting or avoiding behaviors (Nymark et al., 2009). Acting behaviors include self-care activities. Patients may initially engage in behaviors such as taking analgesics, antacids, nitrates, and carbonated drinks to relieve the pain, and only decide to seek care once these strategies fail (DeVon et al., 2010; Mumford et al., 1999). Some patients may act by consulting a friend, family member, primary care physician, or the ED for advice (Nymark et al., 2009). In general, the act of consulting others increased delay (Hartford et al., 1990; Mumford et al., 1999). Patients who utilized a private vehicle to travel to the ED also had prolonged treatment-seeking times (Hartford et al., 1990). Avoiding behaviors include denial and wishful thinking (Nymark et al., 2009) Patients commonly attribute the cause of their ACS symptoms to a less concerning source until they continue to progress, such as a musculoskeletal cause (Mumford et al., 1999, Nymark et al., 2009). Nymark et al. found that some patients believed the chest pain was harmless and would pass in time (2009).

The final stage of the self-regulatory model includes the patient's reassessment of their condition and their actions, and potentially a change in action (Baxter & Allmark, 2013; Nymark et al., 2009). Patients may continue to take nitroglycerin or pain medication if the pain does not subside. If the symptoms increase or remain, an individual may change their coping strategy (Nymark et al., 2009). When an individual feels they are no longer in control of the health threat, they decide to seek medical care, and this is referred to as the "turning point" (Nymark et al., 2009).

There is an extensive body of literature that has investigated patient-level characteristics associated with treatment-seeking delay. Patients who have symptoms suspicious of ACS and are female, persons of color, older adults, and have a low socioeconomic or education level are more likely to delay ED presentation (Moser et al., 2006, Devon et. al, 2010). Several behavioral and environmental factors are also related to prolonged treatment-seeking delay including: being at home at time of symptom onset, being alone at symptom onset, living in a rural environment far from a hospital, or low activity levels at symptom onset (Moser et al., 2006). When a patient's actual symptoms do not match their expectations of a heart attack, treatment-seeking delay increases (Moser et al., 2006). High levels of anxiety decrease delay, while higher levels of embarrassment increase delay (Moser et al., 2006). Interestingly, patients with a past medical history of prior MI, coronary artery disease, angina, diabetes mellitus, heart failure, hyperlipidemia, or hypertension are more likely to delay seeking care despite their cardiac risk factors (Dracup & Moser, 1991; Moser et al., 2006; Nguyen et al., 2010; Saczynski et al., 2008).

Patients who initially consult their primary care doctor or self-transport to the ED also face increased delay (Hartford et al., 1990, DeVon et. al, 2020). Shorter delay is associated with more severe chest pain, fast-onset acute symptoms, pain recognized as cardiac in origin, hemodynamic instability, and ambulance use (Dracup & Moser, 1991; O'Donnell et al., 2014). Patients with STEMI have shorter delay times than patients with UA, NSTEMI, or non-cardiac discharge diagnoses (Zègre-Hemsey et al., 2018).

There have been several intervention campaigns aimed at reducing treatment-seeking delay in patients who are suspected of having ACS or confirmed ACS. Most have been unsuccessful. The Rapid Early Action for Coronary Treatment (REACT) trial was a large randomized controlled trial that paired US cities based on baseline demographic characteristics and conducted a public education campaign in one city per pair to spread information about recognizing and appropriately responding to ACS symptoms (Luepker et al., 2000). The investigators found that treatment-seeking delay in intervention cities did not decrease after 18 months as hypothesized, although ambulance utilization increased (Luepker et al., 2000). Researchers in another randomized controlled clinical trial targeted individuals who were admitted to the ED with symptoms of ACS and provided individual education about ACS symptoms and prompt ED arrival for subsequent events (Dracup et al., 2009). There was no difference in treatment-seeking delay time between intervention and control groups during the two-year follow up (Dracup et al., 2009). Interventions aimed at decreasing treatment-seeking delay have thus far been largely ineffective. Patients continue to face exceedingly long delays before ED presentation.

These significant treatment-seeking delay times increase an individual's total ischemic time and may preclude them from receiving timely reperfusion therapy if they present after 12 hours of symptom onset. The aim of this study is to determine the clinical consequences of this delay in patients with suspected ACS by analyzing incidence of major adverse cardiovascular events (MACE), extent of hospital utilization, and readmission rates in the immediate inpatient period and at 30 days. The level of injury after a MI is predicted by the extent of infarction, so it is hypothesized that patients who delay seeking treatment greater than 12 hours will have higher rates of MACE complications, hospital utilization, and readmissions. The effect of treatment-seeking delay on short-term clinical outcomes in patients with confirmed ACS has previously been studied, and it was found that increased delay was associated with in-hospital complications (Wu et al., 2011). This study, however, will analyze the associations of delay on patients with any symptoms suggestive of ACS, not just those with a confirmed diagnosis. This is clinically relevant because patients must rapidly recognize their symptoms and decide to present to the hospital rapidly when they may be experiencing an ACS event, regardless of eventual discharge diagnosis.

3.0 Purpose and Specific Aims

The purpose of this study is to identify patient-level characteristics associated with treatment-seeking delay in individuals with suspected acute coronary syndrome and the association with in-hospital and 30-day clinical outcomes, as measured by MACE and hospital utilization, as well as 30-day readmission rates.

Specific Aim 1: Define the prevalence of delay in seeking care among patients presenting to the ED with symptoms suggestive of ACS and compare demographic and clinical characteristics between those who present early versus late.

- Aim 1a: Identify the prevalence of patients with suspected ACS who present early versus late based on a 12-hour cut-off in seeking emergency department care
- Aim 1b: Explore the association between treatment-seeking delay and patient-level characteristics at initial ED encounter in patients with suspected acute coronary syndrome who present to the ED early versus late

Specific Aim 2: Examine the association between early versus late presentation and patient outcomes, as measured by in-hospital and 30-day MACE, hospital utilization outcomes, and readmission to the hospital.

- Aim 2a: Link treatment-seeking delay time with MACE outcomes
- Aim 2b: Link treatment-seeking delay time with hospital utilization outcomes
- Aim 2c: Link treatment-seeking delay time to readmissions within 30 days

4.0 Methods, Design, and Setting

This study was a secondary analysis of data from Improving Emergency Department Nurse Triage via Big Data Analytics, which was a retrospective, correlational, descriptive cohort study of patients with suspected ACS at initial ED encounter (Frisch, 2020). Improving Emergency Department Nurse Triage via Big Data Analytics was approved by the Institutional Review Board at the University of Pittsburgh (STUDY18110026). Patients with symptoms suggestive of ACS presenting to any one of 17 different EDs within the University of Pittsburgh Medical Center (UPMC) system were recruited. These EDs represent a diversity of hospital settings, ranging from level 1 trauma and PCI centers to smaller community hospitals. From that cohort, 1201 patients were randomly selected. Data were manually extracted via electronic health record (EHR) chart review by reviewers blinded to study outcomes. All personal identifiers were removed from patient data before storage in a separate linkage list to protect confidentiality.

4.1 Study Population and Size

Individuals who presented to one of 17 EDs in the UPMC system in 2018 with symptoms suggestive of ACS at initial ED encounter and at least 20 years old were eligible for this study. Patients who presented to UPMC specialty hospitals, including UPMC Children’s Hospital and UPMC Western Psychiatric Hospital were excluded. Interfacility transfers from outside hospitals, as well as patients who arrived as a trauma or stroke alert were also excluded from this study. From this cohort, 1201 patients were randomly selected to comprise the study cohort. The Office of

Health Record Research Request provided a randomized cohort of patients who met the following criteria: 1) symptomology at ED presentation suggestive of ACS; 2) had a cardiac troponin (cTn) laboratory value > 0.1; or 3) had the presence of cardiac procedure codes (e.g., coronary angiogram, single- photon emission computerized tomography [SPECT] scan with an exercise stress test, and SPECT scan with drug-induced stress test). The cohort sample is comprised of an equal subset of patients diagnosed with ACS and patients with a non-ACS diagnosis. Figure 2 depicts the study population selection process.

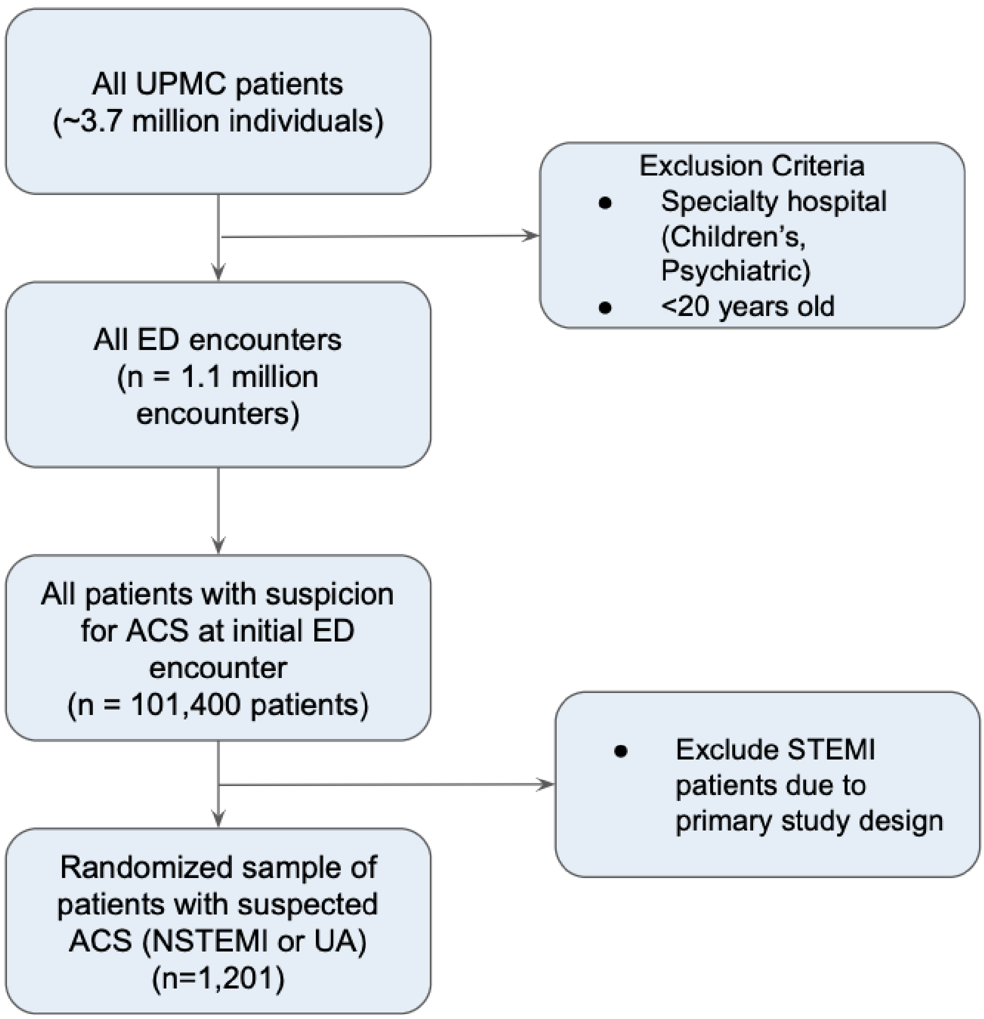

Figure 2: Study Population Selection Flow Chart

4.2 Variables and Data Collection

Data were collected via chart review by trained research assistants that were blinded to study outcomes. To ensure the reliability of data collection, the principal investigator trained and assisted all research assistants in data collection and verification. The principal investigator performed quality checks on every twentieth patient, and reference guides for data collection and management were available to research assistants throughout the entire data collection process. Data was de-identified and stored in REDCap, a HIPAA-compliant online database (Harris, et al., 2019).

4.2.1 Specific Aim 1 Variables

An a priori list of independent variables to be extracted from the EHR were compiled based on the information that would be available to an ED nurse at initial patient triage, as recommended by the ACC (Amsterdam et al., 2014). These patient factors include demographics (e.g., age, sex, race, ethnicity), past medical and surgical history, vital signs, home medications, and chief complaints. The AHA and ACC recommend an initial ECG within 10 minutes of ED arrival, so the automatic ECG interpretation is also available at initial patient encounter (Amsterdam et al., 2014; Gulati et al., 2021; O'Gara et al., 2013). The following variables were extracted from the EHR for Specific Aim 1: 1) demographics; 2) past medical and surgical history per patient report and chart review; 3) initial ED vital signs; 4) chief complaints (e.g., chest pain, shortness of breath, nausea/vomiting, diaphoresis, etc.); 5) initial automatic ECG interpretation; and 6) treatment-seeking delay as measured by time from patient reported onset of symptoms to ED presentation.

For patients reporting chronic or long-term symptoms, any acute onset or change in condition was considered the onset of symptoms for data collection.

4.2.2 Specific Aim 2 Variables

Clinical outcomes were extracted from the EHR during the patient's initial ED encounter and associated hospital stay and again at 30 days after discharge. Charts were reviewed for the occurrence of several clinical composite endpoints, including MACE, hospital utilization, and 30-day readmission. Treatment-seeking delay, as defined by patient self-report and chart review was collected.

The composite endpoint of MACE has traditionally been defined as the occurrence of acute MI, stroke, or cardiovascular death (Bosco et al., 2021). However, the definition of MACE varies widely between observational studies, and may also include outcomes such as stroke, heart failure, and unstable angina (Bosco et al., 2021). For the purposes of this study, MACE is defined as the composite endpoint consisting of confirmed ACS diagnosis, new onset/worsening heart failure, fatal ventricular dysrhythmia, cardiogenic shock, re-infarction, and all-cause mortality.

The hospital utilization endpoint serves to evaluate the level of care an individual requires after initial ED encounter. The hospital utilization composite endpoint consists of the following outcomes: hospital admission (yes/no), unexpected transfer to the ICU, coronary revascularization, intra-aortic balloon pump (IABP) insertion, coronary artery bypass graft (CABG) surgery, and pacemaker/ICD insertion. Coronary revascularization is defined as a repeat PCI after the initial procedure due to restenosis of the target vessel or a similar complication. The incidence of outcomes during the initial hospital stay and within the immediate 30-day period after discharge were collected to evaluate the immediate and short-term clinical consequences of treatment-seeking delay. Thirty-day hospital readmission rates were also collected. Thirty-day readmission is a significant clinical outcome to assess because a readmission may indicate a deterioration in patient condition, or that the original condition was not properly treated. Additionally, the Center for Medicare and Medicaid Services adjusts a hospital's payment based on their excess unplanned readmissions (*Hospital Readmission Reduction Program (HRRP)*, 2021).

4.3 Statistical Analysis

Statistical analysis was performed using SPSS® Statistics software version 25 of International Business Machines (IBM) Corporation in Armonk, New York. Descriptive statistics of the study population and variables under investigation were performed. Continuous variables were presented as either means and standard deviations, or medians and inter-quartile ranges to account for skew and tested with a Mann-Whitney *U* test. Categorical variables were presented as percentages and associations among categorical variables were assessed with Chi-squared Tests of Independence to determine the prevalence of certain characteristics and if there are differences between treatment-seeking delay groups. Graphical techniques were used to detect outliers in treatment-seeking delay time.

In Specific Aim 1, a descriptive analysis of treatment-seeking delay time was performed. Because delay time is positively skewed, we present the median and inter-quartile range. Descriptive statistics for patient demographics, past medical history, vital signs, chief complaints, and initial ECG results are presented in Tables 2, 3, and 4, respectively. The prevalence of each characteristic in the study population, and in the late and early presentation cohorts were calculated. Chi-square tests of independence were conducted on each variable to determine if there was a difference between early and late presenters. An a priori alpha level of 0.05 was set to determine statistical significance.

In Specific Aims 2a, 2b, and 2c, descriptive analyses for the outcomes of MACE, hospital utilization, and 30-day readmissions were performed to determine the prevalence of early and late presenters with each clinical outcome. A chi-square test of independence was performed for each aim to determine if there were differences between early versus late presentation for the outcomes of MACE, hospital utilization, and 30-day readmissions, respectively. An a priori alpha level of 0.05 was set to determine statistical significance.

Subgroup analyses were then performed to determine the patient characteristics that were associated with early and late presentation for the outcomes of MACE and hospital utilization. Data were separated into two groups, one for early presenters (e.g., < 12 hours; n= 546) and one for late presenters (≥ 12 hours; n= 655). Patient level characteristics that are present at first ED assessment (e.g., triage) were entered into a binary logistic regression for each outcome of interest. Predictors of MACE and hospital utilization in early and late presenter models with a p value of $\leq .1$ in univariable binary logistic regression were entered in multivariable binary logistic regression models with backward selection (Hosmer, Lemeshow, & Sturdivant, 2013). The cut-off value in backward selection in the final binary logistic regression was a p value of $\leq .05$. The significance level was set at < .05 for two-sided hypothesis testing. Adjusted odd-ratios with 95% confidence intervals and p-values for identified predictors are reported for the final models. For 30-day readmission, treatment-seeking delay was used as a continuous variable based on duration of symptoms and a Mann Whitney *U* test was performed to determine if there was a difference in readmissions among those who presented early versus late to the ED.

5.0 RESULTS

5.1 SPECIFIC AIM 1

5.1.1 SPECIFIC AIM 1a RESULTS

Specific aim 1a identified the prevalence of patients with suspected ACS who presented early versus late to the emergency department. The cutoff for early versus late presentation was 12 hours after symptom onset, as reperfusion therapy may be administered until 12 hours after the beginning of ACS symptoms according to the 2013 AHA/American College of Cardiology Foundation (ACCF) STEMI guidelines (O'Gara et al., 2013). The sample included 1201 patients, of whom 546 (45%) presented within 12 hours and 655 (55%) presented at or after 12 hours. Treatment-seeking delay was measured as time from symptom onset to emergency medical services (EMS) arrival or arrival to ED per patient report and chart review. The shortest treatment-seeking delay was 0.1 hours, or 6 minutes. The longest treatment-seeking delay was 4032 hours, or about 6 months, per patient report of symptom duration. The distribution of delay times was positively skewed with significant outliers, so median delay time was analyzed. The median treatment-seeking delay time was 14.97 hours, with an interquartile range of 70 hours. Eighty-seven patients reported exceedingly long delay times, spanning from 192 to 4032 hours, which constituted outliers in the dataset. These patients typically noted that their symptoms had been chronic, and they were finally deciding to seek care after several weeks or months. Treatment-seeking delay outliers were excluded from the histogram in Figure 3 to depict the distribution of treatment-seeking delay times.

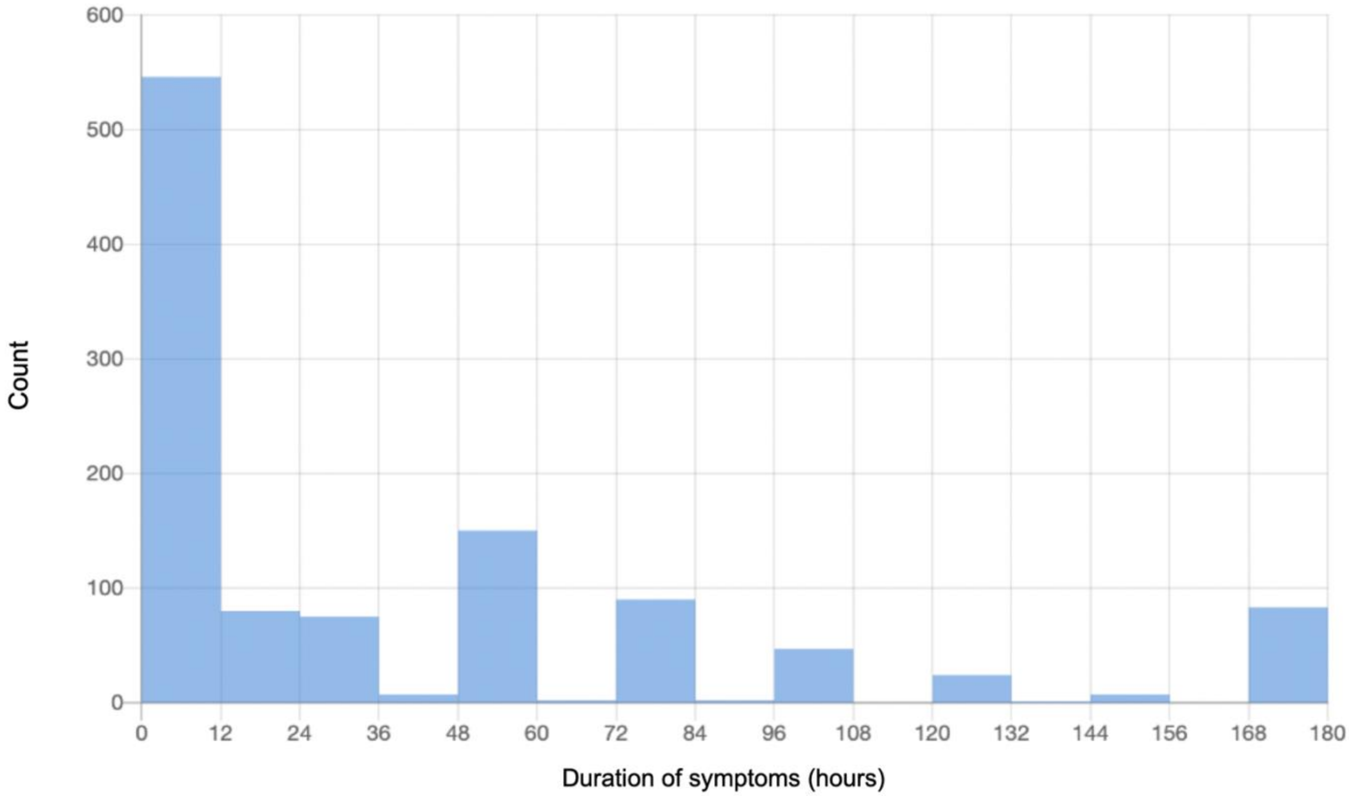

Figure 2: Distribution of Treatment-Seeking Delay Times

5.1.2 SPECIFIC AIM 1b RESULTS

Specific aim 1b identified the patient-level characteristics that were associated with early and late ED presentation among patients with suspected ACS. Table 1 reports the descriptive statistics and p-values testing differences between early versus late ED presenters across demographics and other patient level characteristics between early versus late presenters. In our sample, a greater proportion of people of color were more likely to present late (≥ 12 hours) to the ED. There was also a greater proportion of patients who presented late to the ED who transported themselves via private vehicle; those patients who were transported via EMS had a greater proportion of being early presenters to the ED.

Table 1: Summary of Demographics of Early and Late Presenters

		Treatment-Seeking Delay		
Patient Characteristic	**All Patients (N=1201) [N (%)]**	**Early Presenters (<12hrs) (n=546, 45%) [n (%)]**	**Late Presenters (≥12hrs) (n=655, 55%) [n (%)]**	***p***
Demographics				
Age (years, mean ± standard deviation)	65 ± 14	64 ± 15	65 ± 14	.07
Sex (male)	654 (54%)	306 (54%)	343 (52%)	.18
Body Mass Index (BMI)	30.9 ± 7.5	31.0 ± 7.3	30.8 ± 7.7	.31
Ethnicity [n (%)]				
Hispanic	15 (1%)	5 (1%)	10 (2%)	.34
Race [n (%)]				.05
White	1069 (89%)	499 (91%)	570 (87%)	
Black/African American	115 (10%)	40 (7%)	75 (11%)	
Other	17 (1%)	7 (1%)	10 (2%)	
Mode of Transportation				<0.001
Emergency medical services	412 (34%)	243 (45%)	169 (26%)	
Private vehicle	759 (63%)	293 (54%)	466 (71%)	
Wheel chair van	30 (2%)	10 (2%)	20 (3%)	

Table 2 shows the prevalence of past medical history and surgical history for the study cohort. Patients who have a past medical history of dysrhythmia (e.g., atrial fibrillation or atrial flutter) had a greater proportion of late presenters. Patients who have a past medical history of prior MI, PCI, or stent placement had a greater proportion of being early presenters to the ED.

Table 2: Past Medical History Among Early and Late Presenters

Past Medical History	All Patients (N=1201) [N (%)]	Early Presenters (<12hrs) (n=546, 45%) [n (%)]	Late presenters (≥12hrs) (n=655, 55%) [n (%)]	*p*
Hypertension	876 (73%)	396 (72%)	480 (73%)	.77
Type II diabetes mellitus	413 (34%)	183 (33%)	230 (35%)	.24
Gastroesophageal reflux disease	516 (43%)	227 (41%)	289 (44%)	.38
Past/current smoking	645 (54%)	278 (51%)	367 (56%)	.22
Congestive heart failure	192 (16%)	78 (14%)	114 (17%)	.14
Dysrhythmia (Atrial fibrillation/Atrial flutter)	235 (20%)	92 (17%)	143 (22%)	.03
Dyslipidemia	647 (54%)	308 (56%)	339 (52%)	.11
Coronary artery disease	410 (34%)	186 (34%)	224 (34%)	.96
Angina	110 (9%)	59 (11%)	51 (8%)	.07
Previous myocardial infarction	266 (22%)	141 (26%)	125 (19%)	.01
Previous percutaneous coronary intervention	328 (27%)	166 (30%)	162 (25%)	.03
Prior myocardial stent placement	182 (15%)	96 (18%)	86 (13%)	.03
Prior open heart surgery or coronary artery bypass graft	130 (11%)	65 (12%)	65 (10%)	.27
Pacemaker or implantable cardioverter defibrillator	88 (7%)	39 (7%)	49 (7%)	.82
Peripheral artery disease	34 (3%)	18 (3%)	16 (2%)	.37
Stroke	112 (10%)	53 (10%)	59 (9%)	.68
Chronic obstructive pulmonary disease (COPD)	225 (19%)	101 (18%)	124 (19%)	.85
Other chronic lung disease	206 (17%)	88 (16%)	118 (18%)	.39
Past illicit drug abuse	53 (4%)	26 (5%)	27 (4%)	.59
Current drug abuse	34 (3%)	17 (3%)	17 (3%)	.59
Peripheral vascular disease	167 (14%)	70 (13%)	97 (15%)	.32
Chronic renal disease	137 (11%)	56 (10%)	81 (12%)	.25
Sleep apnea	93 (8%)	46 (8%)	47 (7%)	.42
Cancer	163 (14%)	73 (13%)	90 (14%)	.85
Hypothyroidism	141 (12%)	65 (12%)	76 (12%)	.87
Arthritis	223 (19%)	90 (16%)	133 (20%)	.09
Pulmonary embolism	38 (3%)	17 (3%)	21 (3%)	.93
Anxiety	183 (15%)	72 (13%)	111 (17%)	.07
Depression	178 (15%)	76 (14%)	102 (16%)	.42
Back pain	127 (11%)	46 (8%)	81 (12%)	.88
Cardiomyopathy	45 (4%)	18 (3%)	27 (4%)	.45
Anemia	84 (7%)	41 (8%)	43 (7%)	.52

Table 3 describes the mean initial vital signs upon ED presentation among early and late presenters. There was no significant difference in initial ED vital signs between early and late presenters.

Table 3: Initial Emergency Department Vital Signs Among Early and Late Presenters

Initial Vital Signs	All Patients (N=1201) [N (%)]	Early Presenters (<12hrs) (n=546, 45%) [n (%)]	Late presenters (≥12hrs) (n=655, 55%) [n (%)]	*p*
Heart rate	86 ± 23	86 ± 24	86 ± 22	.62
Systolic blood pressure (mmHg)	146 ± 29	146 ± 29	146 ± 28	.72
Diastolic blood pressure (mmHg)	82 ± 17	82 ± 17	83 ± 18	.47
Temperature	36.6 ± 0.5	36.7 ± 0.4	36.8 ± 0.5	.92
Respiratory rate (breaths per minute)	19 ± 4	19 ± 4	19 ± 4	.90
Oxygen saturation (%)	96 ± 4	96 ± 4	96 ± 4	.28
Pain rating	4 ± 3	4 ± 3	4 ± 3	.38

Table 4 reports the prevalence of chief complaints suggestive of ACS among early and late presenters upon initial ED evaluation. There were a greater proportion of patients who presented early to the ED with the following symptoms: chest pain, radiating pain, chest pressure, diaphoresis, dizziness/syncope, and arm pain. Late presenters had a greater proportion of the following chief complaints: shortness of breath, cough, fatigue, generalized weakness, and abdominal pain.

Table 4: Initial ED Chief Complaints Among Early and Late Presenters

Initial Chief Complaints	All Patients (N=1201) [N (%)]	Early Presenters (<12hrs) (n=546, 45%) [n (%)]	Late presenters (≥12hrs) (n=655, 55%) [n (%)]	*p*
Chest pain	684 (57%)	348 (64%)	336 (51%)	<0.001
Radiating pain	323 (27%)	171 (31%)	152 (23%)	.002
Chest tightness	142 (12%)	64 (12%)	78 (12%)	.92
Chest pressure	241 (20%)	130 (24%)	111 (17%)	.003
Chest heaviness	100 (8%)	52 (10%)	48 (7%)	.17
Shortness of breath	652 (54%)	256 (47%)	396 (60%)	<0.001
Palpitations	129 (11%)	65 (12%)	64 (10%)	.23
Cough	206 (17%)	51 (9%)	155 (24%)	<0.001
Sweating/diaphoresis	211 (18%)	121 (22%)	90 (14%)	<0.001
Dizziness/syncope	288 (24%)	164 (30%)	124 (19%)	<0.001
Anxiety	46 (4%)	21 (4%)	25 (4%)	.98
Indigestion	110 (9%)	44 (8%)	66 (10%)	.23
ONLY nausea	196 (16%)	100 (18%)	96 (15%)	.09
ONLY vomiting	16 (1%)	4 (1%)	12 (2%)	.10
Nausea AND vomiting	97 (8%)	47 (9%)	50 (8%)	.54
Fatigue	119 (10%)	32 (6%)	87 (13%)	<0.001
Generalized weakness	172 (14%)	64 (12%)	108 (16%)	.02
Abdominal pain	119 (10%)	40 (7%)	79 (12%)	.01
Arm pain	163 (14%)	90 (16%)	73 (11%)	.01
Back pain	128 (11%)	59 (11%)	69 (11%)	.88
Shoulder pain	69 (6%)	30 (5%)	39 (6%)	.73
Jaw pain	54 (4%)	26 (5%)	28 (4%)	.69

Initial ECG interpretation variables are displayed in Table 5. Patients with sinus arrhythmia were more likely to be early presenters to the ED.

Table 5: Inital ED Automatic Electrocardgiogram Interpretations Among Early and Late Presenters

Initial Emergency Department Automatic Electrocardiogram Interpretation	All Patients (N=1201) [N (%)]	Early Presenters (<12hrs) (n=546, 45%) [n (%)]	Late presenters (≥12hrs) (n=655, 55%) [n (%)]	*p*
Normal sinus rhythm	774 (64%)	353 (65%)	421 (64%)	.89
Sinus tachycardia	144 (12%)	60 (11%)	84 (13%)	.70
Sinus bradycardia	86 (7%)	43 (8%)	43 (7%)	.38
Sinus arrythmia	18 (1%)	13 (2%)	5 (1%)	.02
Right bundle branch block (RBBB)	110 (9%)	49 (9%)	61 (9%)	.84
Left bundle branch block (LBBB)	51 (4%)	21 (4%)	30 (5%)	.53
Paced	48 (4%)	22 (4%)	26 (4%)	.96
Atrial fibrillation / Atrial flutter	81 (7%)	36 (7%)	45 (7%)	.85
Atrial flutter	15 (1%)	8 (1%)	7 (1%)	.54
1st-degree heart block	63 (5%)	30 (5%)	33 (5%)	.72
Premature ventricular contraction (PVC)	84 (7%)	39 (7%)	45 (7%)	.85
T wave inversion	42 (3%)	19 (3%)	23 (4%)	.98
Q waves present	2 (<1%)	1 (<1%)	1 (<1%)	.90
T wave abnormality	183 (15%)	75 (14%)	108 (16%)	.19
ST-segment abnormality	152 (13%)	73 (13%)	79 (12%)	.50
ST-segment elevation or depression	26 (2%)	14 (3%)	12 (2%)	.39

5.2 SPECIFIC AIM 2

A chi-squared test of independence investigated differences between early and late presenters amongst the outcomes of MACE, hospital utilization, and 30-day readmission. The proportion of patients with each outcome, as well as p values for each chi-square analysis are presented in Table 6. Hospital utilization was the only clinical outcome that had a statistically significant difference between early and late presenters. Early presenters were more likely to have hospital utilization than late presenters.

Table 6: Chi-Square Analysis of Treatment-Seeking Delay Time and Clinical Outcomes

Clinical outcome	All Patients (N=1201) [N (%)]	Early Presenters (<12hrs) (n=546, 45%) [n (%)]	Late presenters (≥12hrs) (n=655, 55%) [n (%)]	*p*
MACE	544 (45%)	248 (45%)	296 (45%)	.94
Hospital utilization	1003 (84%)	469 (86%)	534 (82%)	.04
Readmission	167 (14%)	76 (14%)	91 (14%)	.99

5.2.1 SPECIFIC AIM 2a RESULTS

Specific aim 2a examined the relationship between treatment-seeking delay and MACE outcomes. Of all patients with suspected ACS, 544 (45%) patients developed a MACE outcome during the indexed hospitalization or within 30 days after discharge. Of the 546 early presenters, 248 (45%) patients developed MACE during the indexed hospitalization or within 30 days. Of the 655 late presenters, 296 (45%) patients developed MACE during the indexed hospitalization or within 30 days (Table 6). A chi-square analysis showed that there was not a statistically significant difference between early and late presenters who develop MACE, X^2 (1, N=1201) = .006, p = .936 (Table 6).

5.2.1.1 Multivariable binary logistic regression analysis for predictors of MACE in early presenters

A subgroup analysis of patient level characteristics that were available at initial ED triage was conducted using binary logistic regression for the outcome of MACE in those patients who presented early (<12 hours) to the ED. Table 7 displays the multivariable model of patient characteristics in early presenters predictive for the outcome of MACE. Amongst early presenters, those who transport themselves to the hospital via EMS, have a past medical history of hypertension, have prior PCI, and have a chief complaint of shoulder pain or arm pain are more likely to develop MACE. Patients with T wave abnormalities, and ST elevation or depression on initial ECG are also more likely to develop MACE. Patients who have a normal sinus rhythm on initial ECG or who are female sex were less likely to develop MACE.

Table 7: Multivariable binary logistic regression analysis for predictors of MACE in early presenters

Patient Characteristic	Odds Ratio (95% Confidence Interval)	*p*
Transportation via EMS	1.54 (1.04, 2.29)	0.03
Hypertension	1.75 (1.10, 2.76)	0.02
Prior percutaneous coronary intervention	1.65 (1.09, 2.51)	0.02
Shoulder pain	3.93 (1.62, 9.57)	0.003
Arm pain	1.97 (1.19, 3.28)	0.01
T wave abnormalities	2.17 (1.26, 3.76)	0.01
ST-segment elevation or depression	5.68 (1.46, 22.07)	0.01
Age	1.02 (1.00, 1.03)	0.03
Normal sinus rhythm	0.65 (0.44, 0.96)	0.03
Sex (female)	0.61 (0.41, 0.90)	0.01

5.2.1.2 Multivariable binary logistic regression analysis for predictors of MACE in late presenters

A subgroup analysis of patient level characteristics that were available at initial ED triage was conducted using binary logistic regression for the outcome of MACE in those patients who presented late (≥ 12 hours) to the ED. Table 8 displays the multivariable model of patient characteristics of late presenters for the outcome of MACE. Late presenters who develop MACE were more likely to have type 2 diabetes, dyslipidemia, prior CABG, shortness of breath, elevated heart rate, T wave abnormalities, and ST-segment elevation or ST depression on initial ED ECG. Also, increasing age is associated with a higher likelihood of MACE. A past medical history of GERD or chronic lung disease, normal sinus rhythm on initial ECG, and female sex were all associated with a lower likelihood of MACE.

Table 8: Multivariate binary logistic regression analysis for predictors of MACE in late presenters

Patient Characteristic	Odds Ratio (95% Confidence Interval)	*p*
Type 2 Diabetes	1.67 (1.10, 2.52)	0.016
Dyslipidemia	1.69 (1.12, 2.55)	0.012
Prior CABG	2.26 (1.15, 4.46)	0.018
Shortness of breath	2.13 (1.42, 3.18)	<0.001
Heart rate	1.02 (1.01, 1.03)	0.001
T wave abnormalities	2.35 (1.42, 3.91)	0.001
ST-segment elevation or depression	8.45 (1.74, 41.08)	0.008
Age	1.03 (1.01, 1.05)	<0.001
Gastroesophageal reflux disease	0.56 (0.38, 0.83)	0.004
Chronic lung disease	0.36 (0.21, 0.64)	<0.001
Normal sinus rhythm	0.59 (0.39, 0.90)	0.013
Sex (female)	0.65 (0.44, 0.96)	0.031

5.2.2 SPECIFIC AIM 2b RESULTS

Specific aim 2b examined the relationship between treatment-seeking delay and hospital utilization. Overall, 1003 (84%) patients had hospital utilization during the indexed hospitalization or within 30 days. Of the early presenters, 469 (86%) had hospital utilization. Of the late presenters, 534 (82%) had hospital utilization (Table 6).

A chi square test of independence was conducted to assess group differences in hospital utilization; there was a statistically significant difference between early and late presenters for the outcome of hospital utilization, X^2 (1, N=1201) = 4.132, p = .042. Those with treatment-seeking delay less than 12 hours had a greater proportion of patients for the outcome of hospital utilization.

5.2.2.1 Multivariable binary logistic regression analysis for predictors of hospital utilization in early presenters

A subgroup analysis of patient level characteristics that were available at initial ED triage was conducted using binary logistic regression for the outcome of hospital utilization in those patients who presented early (< 12 hours) to the ED. Table 9 displays the final model for the outcome of hospital utilization. Patients with chest pain, chest pressure, shortness of breath, diaphoresis, ST-segment elevations or depressions on initial ED ECG, ST-segment abnormalities on initial ED ECG, and a medical history of coronary artery disease had a higher likelihood for hospital utilization. Increasing age is also associated with a higher likelihood of hospital utilization. Patients presenting with a chief complaint of anxiety or those who are female were less likely to have hospital utilization.

Table 9: Multivariable binary logistic regression model for predictors of hospital utilization in early presenters

Patient Characteristic	Odds Ratio (95% Confidence Interval)	*p*
Age	1.04 (1.02, 1.06)	<0.001
Coronary artery disease	3.05 (1.25, 7.45)	0.01
Chest pain	2.27 (1.23, 4.19)	0.01
Chest pressure	6.40 (1.76, 23.26)	0.01
Shortness of breath	3.42 (1.74, 6.73)	<0.001
Diaphoresis	3.27 (1.19, 8.95)	0.02
ST-segment elevation or depression	3.20 (1.01, 10.16)	0.05
ST-segment abnormalities	3.64 (1.17, 11.35)	0.03
Anxiety	0.13 (0.04, 0.46)	<0.001
Sex (female)	0.54 (0.30, 0.96)	0.04

5.2.2.1 Multivariate binary logistic regression model for predictors of hospital utilization in late presenters

A subgroup analysis of patient level characteristics that were available at initial ED triage was conducted using binary logistic regression for the outcome of hospital utilization in those patients who presented late (≥ 12 hours) to the ED. Patients with a past medical history of hypertension, renal disease, chief complaint of chest pressure, or diaphoresis had a higher likelihood of hospital utilization (Table 10). Also, patients who arrived at the ED via EMS, had ST-segment abnormalities on the initial ED ECG, were more likely to have hospital utilization. Late-presenting females were less likely to have hospital utilization.

Table 10: Multivariable binary logistic regression model for predictors of hospital utilization in late presenters

Patient Characteristic	Odds Ratio (95% Confidence Interval)	Sig.
Hypertension	2.08 (1.24, 3.50)	0.01
Transportation via EMS	4.17 (2.04, 8.52)	<0.001
Chronic renal disease	4.16 (1.38, 12.60)	0.01
Chest pain	1.76 (1.02, 3.02)	0.04
Radiating pain	2.02 (1.03, 3.96)	0.04
Chest pressure	3.80 (1.74, 8.33)	<0.001
Diaphoresis	2.45 (1.06, 5.63)	0.04
ST-segment abnormalities	4.68 (1.73, 12.65)	0.002
Age	1.03 (1.01, 1.05	<0.001
Sex (female)	0.50 (0.30, 0.80)	0.004

5.2.3 SPECIFIC AIM 2c RESULTS

Specific aim 2c examined the relationship between treatment-seeking delay and 30-day readmissions. One hundred and sixty-seven (14%) of patients were readmitted within 30 days after discharge from the indexed hospital visit. Of the early presenters, 76 (14%) patients were readmitted within 30 days. Of the late presenters, 91 (14%) were readmitted within 30 days after discharge (Table 6). Chi square analysis did not find a statistically significant difference between early and late presenters for the outcome of 30-day readmission. A Mann Whitney *U* test was done to assess for group differences in 30-day readmission between early and late presenters with time delay as a continuous variable. There was no significant difference in delay time between early and late presenters with suspected ACS, Mann Whitney *U* (N=1201) = 86755, p = .920.

6.0 Discussion

The purpose of this study was to examine the relationship between treatment-seeking delay and the clinical characteristics and outcomes of patients with suspected ACS. By examining patients with and without a confirmed diagnosis of ACS and having symptoms suspicious of ACS, this analysis gives a comprehensive overview of the clinical course of patients with suspected ACS who delay seeking medical care for the outcomes of MACE, hospital utilization, and 30-day readmission.

The sample consisted of 1201 patients, with a mean age of 65 years, 54% male, and 89% white. Five hundred and forty-six patients (45%) presented within 12 hours, and 655 (55%) patients presented 12 hours or later. Additionally, the median delay time was 15 hours, which is outside of the reperfusion window according to AHA/ACCF guidelines for reperfusion intervention (O'Gara et al., 2013).

Overall, 544 (45%) of patients in both the early and late presentation groups developed MACE outcomes during the indexed hospitalization or within 30 days after discharge. There was not a statistically significant between early and late delayed presentation groups and MACE outcomes. Eighty-four percent of all patients had at least one hospital utilization outcome, including 86% of early presenters and 82% of late presenters. There was a statistically significant difference between these groups, with early presenters having a greater likelihood of hospital utilization. Lastly, 168 (14%) of all patients were readmitted to the hospital within 30 days. There was not a statistically significant difference in readmissions among early and late presenters.

6.1 Importance of minimizing treatment-seeking delay

Because the level of infarction and injury depends on total ischemic time, extensive literature has shown that prolonged treatment-seeking delay is associated with poorer cardiac function, clinical outcomes, and mortality (O'Gara et al., 2013). The cutoff for initiation of reperfusion therapy is 12 hours, after which myocardium is largely unsalvageable (Schömig et al., 2006). Reperfusion therapy is most effective the sooner it is administered; in those with reperfusion within one hour, the 30-day mortality rate was 1.0% (Wu et al., 2011). The mortality rate increased by a factor of 1.6 for every 15 minute delay (Wu et al., 2011). As such, it is critical for patients to be able to recognize the symptoms of ACS and respond quickly and appropriately to be eligible for reperfusion therapy and protect cardiac function.

In our study, 655 (55%) of patients presented outside the window for reperfusion, limiting salvageable myocardium. Although some patients were not ultimately diagnosed with ACS, but it is critical to present to the ED within 12 hours of symptom onset for prompt evaluation and treatment if a patient has symptomology concerning for a coronary event.

6.2 Patient-level characteristics and treatment-seeking delay

Existing literature report median delay times for those with confirmed acute MI ranging from 1.5-6 hours (Moser et al., 2006). DeVon et. al found a median delay time of 6.68 hours in patients with suspected ACS (2020). However, our study population also included several extreme outliers that few other studies report, which may explain our larger median delay time. In a study comparing racial disparities in patients with suspected ACS, DeVon et. al studied a population of patients with delay ranging from minutes to weeks, similar to our data set (2014). Sixty percent of the study population presented within 12 hours, and the median treatment-seeking delay by group ranged from 2.67-6.5 hours (DeVon et al., 2014). DeVon et al. (2014) reports a median delay time shorter than our median delay time of 15 hours. The difference in median delay could be due to our patient population including patients with and without a confirmed diagnosis of ACS compared to the DeVon et al. research that examined patients with a confirmed diagnosis of ACS.

Eighty-two patients waited several days to weeks before seeking medical care, constituting outliers to our dataset. Outlier delay times ranged from 192 hours to 4,032 hours. To our knowledge, there are no known studies that mentioned outliers in delay times similar to our findings. Future work could entail examining patient characteristics in those with extended symptom delay time who have suspicion of an ACS event. A subgroup analysis would be useful in future studies to determine the characteristics and outcomes of these patients specifically to target them for intervention and delay reduction.

In our study population, early presenters had a higher prevalence of EMS transportation, a prior MI, prior PCI, prior stent placement, sinus arrhythmia on initial ECG, and chief complaints of chest pain, radiating pain, chest pressure, diaphoresis, dizziness/syncope, and arm pain. Late presenters had a higher prevalence of older age, Black/African American race, past medical history of atrial fibrillation, and chief complaints of shortness of breath, fatigue, generalized weakness, and abdominal pain.

Our patient demographics were similar to other studies (Cox et al., 1997; McNair et al., 2019). There is an extensive body of literature on predictors of treatment-seeking delay in ACS patients. Cox et al. studied treatment-seeking delay in patients who present up to 6 hours after symptom onset (1997). Cox et al., found that there was a higher prevalence of males in the <2-

hour presentation delay group, and a higher prevalence of females in the > 4-to-6-hour delay group (1997). McNair et al. found that there was a higher prevalence of women in the >12-hour delay group (2019). Although not statistically significant, we found was a higher percentage of males in the early presentation group than in the late delay group. Generally, older patients, females, and Black/African American race are associated with longer delay (Moser, 2006). There was a higher prevalence of patients with a history of diabetes mellitus, and previous CABG in the later delay group (Cox et al., 1997; McNair et al., 2019). This is similar to the demographics of our study cohort. McNair et al. found that early presenters (<12 hours) were more likely to have chest pain than late presenters (≥ 12 hours) (2019). We also found that a higher number of patients with a chief complaint of chest pain presented within 12 hours.

In this study, presentation delay was not significantly associated with the development of MACE outcomes or 30-day readmissions. There was a statistically significant association between delay time and hospital utilization. Early presenters had higher rates of hospital utilization, as compared to late presenters.

6.2.1 Treatment-seeking delay and MACE outcomes

Because of the effect of total ischemic time on myocardial damage, it is hypothesized that longer delay is associated with MACE outcomes during the immediate and short-term clinical period. In our study, we did not find a statistically significant association between treatment-seeking delay and MACE. Our data do not support a relationship between prolonged treatment-seeking delay greater than 12 hours and increased MACE outcomes. There is conflicting literature regarding delay and the development of MACE, so it is unclear if a relationship between these two variables actually exists.

Wu et al. investigated the impact of treatment-seeking delay on short-term in-hospital complications in patients with acute MI (2011). Their definition of in-hospital complications was similar to our operational definition of MACE and included the outcomes of recurrent ischemia, reinfarction, sustained ventricular tachycardia, ventricular fibrillation, and cardiac death. Over 25% of the patients in their study experienced at least one in-hospital complication, compared to our study which showed a higher rate of MACE of 45% (544 patients; Wu et al., 2011). Wu and colleagues reported that treatment-seeking delay was statistically significant to predict in-hospital complications (Wu et al., 2011). This contradicts the results of our study, as we did not find the same association. However, Wu and colleagues only looked at in-hospital complications, and our study examined in-hospital and 30-day follow-up for complications. Additionally, Wu et al. only analyzed those with confirmed MI and used 6 hours as the late presentation cutoff (2011). These differences in study design may explain why Wu et al. found an association between delay and MACE and we did not. Cox et al. found that treatment-seeking delay between 4 to 6 hours significantly predicted adverse outcomes, including in-hospital death, 30-day death, and nonfatal cardiac events like shock and ventricular dysrhythmias (Cox et al., 1997). Alternatively, there have been studies with similar findings to our study that do not report an association of treatment-seeking delay with the outcome of MACE (Caldwell et al., 2000; Elbarouni et al., 2008) Caldwell et al. also used a 6-hour cutoff to distinguish between early and late presentation in patients with confirmed MI and did not find a statistically significant difference in cardiovascular outcomes between groups (2000). Elbarouni et al. also did not find a statistically significant difference between early (<6 hours) and late presenters (>6 hours) for the outcome of MACE (2008). Because reperfusion benefits from 6 hours to 12 hours are mostly related to thrombus dissolution and electrical stabilization as opposed to true myocardial salvage, it may be worthwhile to investigate in future studies if 6 hours is a more appropriate cutoff time to determine the impact of treatment-seeking delay on cardiovascular outcomes (Khowaja et al., 2021).

Multivariate logistic regression models of all patient characteristics upon initial ED presentation showed group differences between early and late presenters for the outcome of MACE. We examined early presenting patients (< 12 hours, n=546) for the outcome of MACE. The clinical variables with the greatest association with MACE in early presenters were ST-segment elevation or ST-segment depression, shoulder pain, and T wave abnormalities

In a separate logistic regression analysis of late presenters, (>12 hours, n = 655) we examined patient-level factors present at ED initial triage assessment for the outcome of MACE. The clinical variables most strongly associated with MACE in late presenters are ST-segment elevation or ST-segment depression, T wave abnormalities, and shortness of breath.

To our knowledge, this is the only study to assess the patient-level characteristics of early and late presenters for the outcome of MACE. Other studies have investigated patient characteristics that are predictive of MACE but have not examined the influence of delay time on MACE outcome development. Cox et al. performed a multivariable logistic regression model to determine patient characteristics that predicted adverse outcomes (1997). In their analysis, treatment-seeking delay was entered into the model as a univariate predictor variable. According to Cox et al., delay between 4 to 6 hours, increases in systolic blood pressure of 10mmHg, increases in initial ED heart rate of 10 beats per, bradycardia, age greater than 80 years, and congestive heart failure and pulmonary edema were predictive of nonfatal adverse cardiac events (1997). Our study also found that patients who present earlier than 12 hours with an increased initial heart rate had a high likelihood of developing MACE.

Esposito et al. conducted a logistic regression to investigate patient-level predictors of 30-day cardiovascular events in patients with prior PCI or CABG revascularization who presented to the ED with symptoms suggestive of ACS (2011). Cardiovascular events were defined as death, MI, and revascularization (Esposito et al., 2011). The following patient characteristics were associated with the development of 30-day cardiovascular events in patients with prior PCI or CABG: male sex, nonblack race, having a family history of coronary artery disease, having a past medical history of dyslipidemia, prior MI, abnormal initial ECG, and a positive initial troponin (Esposito et al., 2011). Similarly, patients with a history of dyslipidemia, several abnormal ECG findings (T wave abnormalities, and ST elevation or depression) were more likely to develop MACE in our study.

6.2.2 Treatment-seeking delay and hospital utilization outcomes

The hospital utilization endpoint included the following outcomes: hospital admission, unexpected transfer to the intensive care unit, coronary revascularization, IABP insertion, CABG surgery, and pacemaker/implanted cardioverter defibrillator insertion. It was originally hypothesized that late presenters would have a larger extent of myocardial injury and thus require a greater amount of medical support, as indicated by hospital utilization. However, we found the opposite case to be true. There was a higher prevalence of hospital utilization among early presenters. Overall, 1003 (84%) patients had hospital utilization, including 469 (86%) of early presenters and 534 (82%) of late presenters. The association between early presentation and increased hospital utilization may possibly be attributed to several factors that would require a follow-up analysis. It is possible that patients who present sooner have a more serious clinical condition, can recognize, and respond to their condition because of a heavier symptom burden, and ultimately require a greater level of care after initial ED encounter, as evidenced by hospital utilization. It is also possible that early presenters have higher rates of hospital utilization because they present within the window for reperfusion and have access to a greater range of treatment modalities. Few studies have examined the effect of treatment-seeking delay on inpatient and 30-day resource utilization, and further research is needed to corroborate or challenge the association identified in this study (Caldwell et al., 2000; Elbarouni et al., 2008)

Caldwell et al. analyzed resource utilization as a function of healthcare costs related to treatment-seeking delay (2000). The investigators defined resource utilization as additional cardiac diagnostic and treatment procedures, like echocardiogram, stress test, heart catheterization, CABG, IABP, stent placement, pacemaker, and revascularization. This definition is similar to ours but lacks the ICU transfer and admission variables. Caldwell et al. did not find a statistically significant association between treatment-seeking delay (> 6 hours) and overall resource utilization (2000). However, the study found that it was statistically significant that early presenters had a higher likelihood of cardiac stress testing and CABG procedures (Caldwell et al., 2000). While overall resource utilization was not significantly associated with delay, specific additional cardiovascular procedures were associated with early ED presentation, which is comparable to the results in our study (Caldwell et al., 2000). This indicates a need for further studies to examine the reasons early presenters use hospital resources more frequently than late presenters. Elbarouni et al. also found a statistically significant relationship between stress testing and those who present earlier than 6 hours (2008). This reflects the findings of increased hospital utilization among early presenters in the Caldwell study and in this study. Conversely, Elbarouni et al. found that those who present later than 6 hours had higher rates of coronary angiography, although they did not have increased PCI or CABG procedures (2008).

There was a very high rate of hospital utilization in our data set because admission was considered part of the composite outcome, and a large proportion of patients were admitted to observation status or to an inpatient unit. Further analysis could exclude admissions to determine if there is a difference between more adverse hospital utilization outcomes, like transfer to the intensive care unit and CABG surgery.

A logistic regression was performed in SPSS for early presenters for the outcome of hospital utilization. This analysis showed that early presenters who had hospital utilization outcomes were more likely to be male, older, and initially present to the ED with chest pain, chest pressure, shortness of breath, diaphoresis, ST-segment elevations or depressions, ST-segment abnormalities, and a medical history of coronary artery disease.

Another logistic regression was completed on patients who had reported delay in seeking medical care greater to or equal to 12 hours. Late presenters who had an increased likelihood for the outcome of hospital utilization were more likely to be male, had a history of hypertension or renal disease, had a chief complaint of chest pain, radiating pain, chest pressure, diaphoresis, ST abnormalities on initial ECG, or arrive to the ED via private vehicle. Individuals with these characteristics represent a patient population that may benefit from increased observation and vigilance because of their predisposition to require supportive hospital care.

McNair et al. analyzed the clinical outcomes of STEMI patients with a delay cutoff of 12 hours (2019). Patients who presented at or after 12 hours of symptom onset were more likely to be women, have prior CABG, and have diabetes (McNair et al., 2019). Similar to the results of our study, late presenters had lower levels of hospital utilization, as they were less likely to undergo coronary angiography and percutaneous intervention (McNair et al., 2019). These lower levels of hospital utilization may be related to the AHA/ACCF recommendations to defer reperfusion therapy in late-presenting patients unless there is ongoing evidence of ischemia (O'Gara et al., 2013).

6.2.3 Treatment-seeking delay and rehospitalizations

It was hypothesized that late presenters would have higher 30-day readmission rates as a result of increased total ischemic time and resultant cardiac dysfunction. Overall, 168 (14%) of patients were readmitted within 30 days, distributed equally between early and late presenters. The Mann-Whitney *U* test examined time as a continuous variable for the outcome of 30-day readmission. There was no difference in 30-day readmission among early and late presenters. ACS typically causes high rates of admission and readmission, related to the level of cardiac dysfunction after the coronary event (Wu et al., 2011). However, our study analyzed outcomes for all patients with suspected ACS, regardless of discharge diagnosis, which may explain the lack of statistically significant differences between early versus late presenting patients for the outcome of hospital readmission. Cullen et al. found that patients who delayed seeking medical care had higher readmission rates up to 12 months after initial ED encounter (2000). Conversely, Alsamara et al. investigated the effect of symptom onset to balloon time on rehospitalization rates in STEMI patients (2018). Early presenters were those who presented to the ED within 4 hours, and late presenters were those with delay greater than 4 hours. Alsamara et al. did not find a statistically significant difference in rehospitalization rates in STEMI patients who present with 4 hours versus patients who present later than 4 hours after symptom onset (2018). However, this study had a narrower focus than our study, as it only investigated the role of delay in STEMI patients and had an early versus late delay cutoff of 4 hours. Nonetheless, further research is needed to determine if a significant association between readmission and treatment-seeking delay exists among patients who have suspicion for a coronary event.

6.3 Strengths and Limitations

This study has several strengths. First, the study population was collected from 17 different EDs in a large healthcare system with over a million ED visits annually. This allowed us to sample patients with diverse clinical presentations and clinical outcomes. However, due to the location of the healthcare system, the population was lacking in racial and ethnic diversity. The inclusion of patients with suspicion of an ACS diagnosis rather than a confirmed diagnosis of ACS is reflective of a real-world clinical scenario in the ED. Analyses of a cohort of undifferentiated patients who present to the ED with symptoms suspicious of ACS may provide insight into clinical characteristics and future interventions to improve delay in seeking medical treatment for a possible coronary event.

The patient's clinical presentation, in-hospital and 30-day outcomes, and a variety of other clinical factors were available because data was collected via chart review. However, information that was not in the EHR was not available to collect for this study. Treatment-seeking delay, based on patient report of symptom duration, may be biased by the patient's recall. This data was gathered by ensuring concordance between patient report of delay time and the symptom duration listed in the EHR. If a patient had an acute-on-chronic complaint, the acute symptom duration was included as the treatment-seeking delay time. Lastly, there were few research assistants who collected data. Each research assistant was trained by the principal investigator and data collection quality was checked to ensure consistency. Although these steps were taken to minimize data collection variability, there is a chance for data collection variability.

6.4 Clinical Implications

This study helped to determine the extent of patient delay in those with suspected ACS, identify the characteristics of patients who delay seeking ED treatment, and determine the clinical consequences of delayed ACS treatment. It is important for ED nurses to be able to recognize the extent of patient delay and the characteristics and consequences associated with delay in patients with suspected ACS at triage to avoid further delay in time-sensitive reperfusion and promote positive clinical outcomes. By investigating the clinical predictors associated with MACE, hospital utilization outcomes, and ED 30-day readmission and early (< 12 hours) and late (≥ 12hours) treatment-seeking delay, further understanding of those at increased risk could lead to ED protocols to avoid negative patient outcomes. These data could be translated into a clinical decision support tool that is implemented at ED triage to help nurses identify those patients at increased risk for an adverse event. Further, ED nursing practice councils should encourage updating evidence-based practice to reflect current research in treatment-seeking delay in patients who have suspicion for a coronary event. Overall, this analysis will allow nurses to be more aware of clinical variables to assess for in patients with suspected ACS at initial ED encounter that may predispose individuals to negative clinical outcomes.

Our study found that 55% (655) of patients with suspected acute coronary syndrome delayed greater than 12 hours before presenting to the ED, and delay times ranging from a few minutes to several months. In our study, several patient-level characteristics made individuals more or less likely to be early versus late presenters. It is important for the ED triage nurse to be able to recognize these patient-level characteristics to accurately investigate patient delay time and determine an individual's eligibility for reperfusion therapy.

Education may be prioritized for those patients who are more likely to delay greater than 12 hours in an effort to reduce delay time. Several mass-media campaigns targeted at disseminating information about ACS signs and symptoms and the importance of seeking care urgently have been performed, with most reporting no difference in delay time before and after the intervention (Luepker et al., 2000; Mooney et al., 2012). Other authors recommend that interventions to reduce treatment-seeking delay should include the factors that predispose patients to increased delay and consist of individualized education to those at greatest risk for ACS (Mooney et al., 2012).

Although there was not a statistically significant difference between early and late presenters for the development of MACE, several clinical variables were identified that are associated with a higher likelihood for MACE in early versus late presenters. Nurses should be aware of these patient-level characteristics to better risk stratify ED patients with suspected ACS based on their initial ED presentation.

These significant patient characteristics associated with adverse outcomes are clinically relevant because triage nurses may be able to recognize these clinical characteristics and determine that a patient is at increased risk of developing MACE and respond appropriately; for example, the nurse may consider this when assigning an Emergency Severity Index (ESI) level, put the patient on a continuous cardiac monitor, increase observation and vital signs monitoring, or institute serial ECGs. The Emergency Severity Index implementation manual recommends that triage nurses assign patients with suspected acute coronary syndrome a level 2 ESI score, indicating an urgent need for medical attention (Gilboy et al., 2020). The ESI manual also notes that nurses may initiate intravenous access, obtain an ECG, initiate continuous cardiac monitoring, and administer oxygen in level 2 acuity patients before a physician orders these interventions due to risk of a declining clinical condition (Gilboy et al., 2020). Amsterdam et al. recommend serial ECGs in 5-to-10-minute increments to observe for ischemic changes in patients with suspected ACS with chest pain, especially if the initial ECG is negative (2010). There is a Class I Recommendation from the AHA to place all patients in the early phase of ACS on a continuous cardiac monitor upon ED arrival (Drew et al., 2004). Patients with UA or a "rule-out" infarction should be placed on a continuous cardiac monitor until the patient has been free of ischemic signs and symptoms for 24 hours (Drew et al., 2004).

The HEART score is a clinical decision tool that assists in risk stratification of patients with chest pain based on their history, ECG, age, risk factors, and troponin, and predicts the patient's the risk of developing MACE (Brady & de Souza, 2018). However, the HEART score does not take the effect of treatment-seeking delay into account, unlike our study. The current HEART score algorithm recommends several clinical pathways for patients based on their risk stratification (Brady & de Souza, 2018). Low-risk patients, as determined by a low HEART score, may be considered for early discharge (Brady & de Souza, 2018). High-risk patients with a negative repeat troponin are recommended to be admitted to an observation unit for further assessment (Brady & de Souza, 2018). High-risk patients with positive repeat troponins should be admitted, have cardiology consultation, and further diagnostic testing (Brady & de Souza, 2018). The findings from our study link individual patient-level characteristics to the development of MACE in early and late presenters and may be incorporated into this existing clinical decision support tool to effectively determine a patient's risk of developing MACE and provide treatment recommendations.

Hospital utilization was significantly associated with treatment-seeking delay time, indicating a need for a higher greater degree of hospital care and resources. Dhaliwal et al. developed an electronic clinical pathway (ePATH) for patients with chest pain in the ED that described the recommended ED workflow for patients with suspected ACS (2020). Recommendations for initial assessment, ECG, laboratory biomarker testing, stress testing, medication orders, and criteria for admission were outlined (Dhaliwal et al., 2020). The implementation of this clinical pathway resulted in statistically significant decreases in admission rates, stress testing, and hospital length of stay without a resultant increase in rates of MACE (Dhaliwal et al., 2020). Bhatti et al. found that the implementation of high-sensitivity troponin sampling led to a reduction in inappropriate admissions to the hospital for suspected ACS patients ultimately diagnosed with non-cardiac chest pain (2019). ED nurses may recognize that early presenters as a whole and those with certain patient-level characteristics were at increased risk of hospital utilization and implement a standardized clinical pathway and collect serial high-sensitivity troponin levels to reduce the likelihood of hospital utilization outcomes, such as admission (Bhatti et al., 2019; Dhaliwal et al., 2020).

Lastly, there was no significant difference between early and late presenters for the outcome of 30-day readmission. However, 14% (168) of our study cohort was ultimately readmitted within 30 days. This represents a significant subset of the cohort, and efforts should be made to reduce readmission rates. In existing literature, the following characteristics have been linked to increased readmission rates in ACS patients: female sex, increased age, lower income, cigarette smoking, history of diabetes, history of hypertension, history of pulmonary disease, history of anemia, and history of renal disease (Rashidi et al., 2021). Nurses may use these clinical factors to identify high-risk individuals, counsel them on modifiable risk factors, and perform individualized discharge planning (Rashidi et al., 2021).

The results of our study may have significant implications in clinical practice. Patient outcomes may be improved by identifying clinical variables present at initial ED assessment that may affect a patient's eligibility for reperfusion and risk for negative clinical outcomes based on their treatment-seeking delay time.

7.0 Conclusion

It is crucial for patients with suspected ACS to present rapidly to the ED for prompt assessment and time-sensitive reperfusion therapy, if indicated. Reducing treatment-seeking delay is critical in reducing total ischemic time to limit final infarct size and preserving myocardial function. In our study cohort, over half (55%, n = 655), of our patients presented greater than 12 hours after symptom onset, which is longer than the cutoff for initiating reperfusion therapy for those with confirmed ACS (O'Gara et al., 2013).

ED nurses should be familiar with the presentation and characteristics of patients with suspected ACS who are at increased risk of adverse clinical outcomes, like MACE and hospital utilization, in order to appropriately risk stratify these patients and ensure appropriate resources are being focused on these individuals. ED nurses should also be aware that early presenters with symptoms suspicious of ACS may have a greater likelihood of hospital utilization.

Future research may focus on analyzing the patients with extreme outliers of treatment-seeking delay times and ways to change behavior for a potentially life-threatening condition with effective but time-dependent therapies.

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