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Unusual fatigue and failure to utilize EMS are associated with prolonged prehospital delay for suspected acute coronary syndrome

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Abstract

Rapid reperfusion reduces infarct size and mortality for acute coronary syndrome (ACS), but efficacy is time dependent. The aim of this study was to determine if transportation factors and clinical presentation predicted prehospital delay for suspected ACS, stratified by final diagnosis (ACS vs. no ACS). A heterogeneous sample of emergency department (ED) patients with symptoms suggestive of ACS were enrolled at five U.S. sites. Accelerated failure time models were used to specify a direct relationship between delay time and variables to predict prehospital delay by final diagnosis. Enrolled were 609 (62.5%) men and 366 (37.5%) women, predominantly Caucasian (69.1%), with a mean age of 60.32 (± 14.07) years. Median delay time was 6.68 (CI

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Author Contributions:

The concept and design were conceived by HAD, MRD, and AGR. HAD, MRD, and AGR were responsible for the acquisition of the data. MLB and ES were primarily responsible for the analysis of the data. HAD, MRD, EK, AGR, JZH, SM, and SF interpreted the data. HAD drafted of the manuscript. HAD, MRD, AGR, EK, and JZH were responsible for the critical revision of the manuscript for important intellectual content and statistical expertise. All authors edited and approved the final manuscript. HAD received funding for the study.

Conflict of Interest Disclosure

The authors have no conflicts of interest, financial or other, to disclose.

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1.91, 24.94) hours; only 26.2% had a prehospital delay of 2 hours or less. Patients presenting with unusual fatigue (TR=1.71, $p=0.002$; TR=1.54, $p=0.003$, respectively) or self-transporting to the ED experienced significantly longer prehospital delay (TR 1.93, $p<0.001$; TR 1.71, $p<0.001$, respectively). Predictors of shorter delay in patients with ACS were shoulder pain and lightheadedness (TR=0.65, $p=0.013$ and TR=0.67, $p=0.022$, respectively). Predictors of shorter delay for patients ruled out for ACS were chest pain and sweating (TR=0.071, $p=0.025$ and TR=0.073, $p=0.032$, respectively). Patients self-transporting to the ED had prolonged prehospital delays. Encouraging the use of EMS is important for patients with possible ACS symptoms. Calling 911 can be positively framed to at-risk patients and the community as having advanced care come to them since EMS capabilities include 12-lead ECG acquisition and possibly high sensitivity troponin assays.

Keywords

Acute Coronary Syndrome; Prehospital Delay; Emergency Medical Services; Symptoms

Introduction

Acute coronary syndrome (ACS), particularly ST-elevation myocardial infarction (STEMI), is a potentially life-threatening, time-critical emergency. The goal of treatment is reduction of total ischemic time, and studies have documented that rapid reperfusion reduces infarct size and mortality.^{1, 2} Currently, guidelines recommend a door-to-balloon time of <90 minutes for walk-in patients and those transported by emergency medical services (EMS), and <120 minutes for interhospital transfers.³ In the United States, these goals have largely been met or exceeded⁴ following major initiatives such as the American College of Cardiology's D2B Alliance and the American Heart Association's Mission: Lifeline programs.⁵ There has not, however, been a concomitant reduction in overall delay-to-treatment time, suggesting that *prehospital* rather than *in-hospital* delay is now a more relevant contributor to poorer patient outcomes. Accordingly, patient-controlled prehospital delay time is now the most salient and challenging target for reduction.⁶ Multiple individual and transportation factors have been implicated in prehospital delay for potential ACS, in some cases with contradictory findings.

Individual Factors Influencing Prehospital Delay

Demographic factors, including older age, female sex,⁷⁻¹¹ income,¹¹ and Black race¹² or Latino ethnicity have been associated with longer prehospital delay times in some studies. Persons with diabetes, who often present with symptoms other than chest pain, have also been known to have longer prehospital delay times. Health insurance status has been linked to treatment-seeking delay in diverse populations, including those with ACS. ACS patients with no insurance and those with Medicaid have been shown to be more likely than those with private insurance to delay seeking care for symptoms.¹³ Similarly, in several studies, lower household income, low socioeconomic status,¹³ and financial concerns about treatment¹ have been linked to longer prehospital delay times in patients with definite or

probable ACS. Conversely, Nouredine et al. reported that higher income was associated with longer delay times in their study.¹⁴

The presence of underlying comorbid conditions has been linked to a reduction in revascularization procedures,¹⁵ perceived disease severity,¹⁶ and readmission to the ED.¹⁷ There are conflicting findings regarding the relationship between a history of heart disease and prehospital delay. Ironically, some studies show that patients with a history of heart disease actually delay longer, although these findings have not been consistent.^{18, 19} Sullivan et al. found that patients with no history of heart disease delayed longer,²⁰ whereas Sari and colleagues showed that patients with a history of heart disease had shorter delay times.²¹ Also, little is known about the significance or timing of symptom onset upon arrival to the ED. The peak time for the onset of ACS has been reported to be between 6 AM and 12 PM.²²⁻²⁴

Transportation Factors

Despite recommendations to activate EMS for potential ACS symptoms within 5 minutes of symptom onset,²⁵ a substantial number of patients with potential ACS arrive to the ED via personal vehicle or public transportation. In the Rapid Early Action for Coronary Treatment (REACT) trial, EMS use was significantly increased through the use of public health messaging, but prehospital delay (time of symptom onset to ED arrival) did not decrease as patients did not call EMS more quickly.²⁶ Marijon et al. found that calling EMS in response to symptoms was associated with a 32.1% versus 6% ($p < .001$) survival rate compared to those who did not call EMS.

The objective of this study was to identify predictors of prehospital delay, defined here as time of symptom onset to arrival in the ED, for suspected ACS by final diagnosis (ACS vs. no ACS), including patient, timing of symptom onset, and transportation factors (EMS vs. self-transport). We hypothesized that there are individual and external factors that contribute to prehospital delay in patients with suspected ACS presentations.

Methods

Design, Sample, and Setting

This was a secondary analysis of data from the *Think Symptoms* study.²⁷ We used the methodological structure for secondary analyses of existing data proposed by Doolan & Froelicher²⁸ to guide the design of the study. The *Think Symptoms* study was a prospective study that enrolled patients presenting to the ED with symptoms suggestive of ACS. Patients were enrolled in the study from January, 2011 to December, 2014. Aims were to evaluate for sex differences in the occurrence, severity, and distress of ACS symptoms and establish the sensitivity, specificity, and predictive value of each symptom as an indicator of ACS for women and men. Data were collected directly from patients in the ED and abstracted from their medical record. Symptoms were measured with the 13-item ACS Symptoms Checklist.²⁹ Symptoms are recorded as present or absent. Time and place of symptom onset, clinical characteristics, diagnostic testing, and functional status were also measured. Prehospital delay time was calculated by subtracting the time of symptom onset from the time of

registration in the ED. While time from symptom onset to first medical contact (within the control of the patient) is now the accepted definition of prehospital delay, we did not have data on first medical contact for patients who called EMS. Therefore, we used time of registration in the ED in calculating prehospital delay. Time was rounded to the nearest quarter hour. For example, if the patient was registered in the ED at 11:07 AM and stated that their symptoms began at 8:15 AM, total delay time was recorded as 2 hours and 45 minutes. If the patient was registered at 11:08 AM, total delay time was recorded as 3 hours.

The original dataset included 1064 patients, 400 women and 664 men, from four academic and one nonacademic medical center in four distinct regions of the United States. Characteristics of the original cohort included 474 patients ruled-in for ACS and 590 patients ruled-out for ACS with an age range from 21-98. The participants were 69% Caucasian and 31% minority group members.

Data Quality

Rigorous quality control and transparency measures were addressed through design, peer-review processes, and comparison of our findings to the literature. During the design phase of the study, we used the *Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines*³⁰ as a blueprint for helping to ensure the rigor and transparency of our dataset. This included a strong scientific rationale, clear objectives, detailed methods, identification of data sources, assessment of bias, sample size, heterogeneous sample, statistical methods, descriptive data, outcomes data, and the funding source.³¹ The original study was approved by the institutional review boards (IRBs) of the sponsoring institutions and all clinical sites. This study received IRB exemptions from the sponsoring institutions. Finally, to ensure transparency, we have made our data available to other investigators³² and will continue to do so in the future.

Statistical Analyses

Data files were carefully built using the SPSS (Chicago, IL) statistical package. The data were systematically examined for out-of-range values, missing data, and data inconsistencies and double entered into SPSS for accuracy. Significance was set at $p < 0.05$ for all statistical tests. Analyses included descriptive statistics on delay time and possible predictors for the sample as a whole and separately for patients ruled in and those ruled out for ACS. Chi-square tests, Wilcoxon rank sum tests, or t tests, as appropriate to distributional characteristics, were used to describe simple differences between ACS and non-ACS groups for each possible predictor.

To evaluate predictors of delay time, we used an accelerated failure time (AFT) model, a parametric model for survival analysis, which specifies a direct relationship between delay time and the possible predictors. The log-normal error distribution was selected based on likelihood ratio tests. For ACS patients, the log likelihood (LL) for the lognormal model was -1605.5 (vs. -1992.0 to -1617.9 for other distributions). For patients without ACS, the LL for the lognormal model was -2037.8 (vs. -2508.6 to -2049.3 for other distributions). The results of the AFT provide time ratios (TR), computed as exponential (β coefficients), allowing ready interpretation of results. A TR of more than 1 for a predictor indicates that

the characteristic is associated with a longer delay time; a TR of less than 1 indicates a shorter delay time.

For parsimony, a two-stage estimation procedure was used. As a preliminary step, unconditional relationships were estimated for each of the 19 possible predictors considered for this analysis. Those with $p < 0.25$ for either the ACS or non-ACS subgroup in unconditional relationships were included in a multivariable model. In order to explore predictors for patients ruled in and those ruled out for ACS, models were estimated separately for the two groups. A sensitivity analysis was completed by applying linear regression on the log transformed delay time; results were equivalent to those of the AFT model. However, coefficients (relating to predicting the log of delay time) were not as easily interpretable in the linear regression model and appear in Supplemental Table 1.

Results

Sample Description

The sample was 62.5% male, 69.1% Caucasian and had a mean age of 60 years; 66.4% had income levels of \$50,000 or less, and most had some health coverage (including 32% with private insurance through an employer, 34% with Medicare, and 22% with other insurance, primarily Medicaid). The most prevalent symptoms at presentation to the ED were chest discomfort (70%), chest pain (69%), chest pressure (65%), and shortness of breath (56%). The least prevalent symptoms were indigestion (24%), palpitations (26%), and upper back pain (27%). Detailed characteristics of the study cohort are described in Table 1.

Differences in Prehospital Delay and Transportation Factors by Diagnosis

The median delay time was 6.68 hours for the sample as a whole; 26.2% had a delay time of 2 hours or less. Arrival times at the ED were predominantly during the daytime. Thirty-eight percent of patients presented between 6 AM and 12 PM and 37.4% arrived between 12 PM and 6 PM. Mode of arrival was more often by self-transport (53.6%). Only 44.4% of patients arrived by EMS and 2% were interhospital transfers. While patients with and without ACS did not differ significantly in delay time or mode of arrival to the ED, they did differ in the time of arrival, with a greater percentage of patients with ACS arriving in the evening and nighttime hours (6 PM-6 AM) compared to patients ruled out for ACS (31.7% vs. 18.0%). Further, when time of arrival to the ED was divided into 6-hour increments, patients arriving between the hours of 12 AM and 5:59 AM with or without ACS had shorter delays time compared to all other times (Supplemental Tables 4 and 5). Patients ruled out for ACS, transported by EMS, had a median delay time that was shorter than those who self-transported or were transferred from another facility (Supplemental Table 6). We then examined diagnosis and EMS use between those presenting to the ED during the day versus night. Those arriving between 6pm and 6am were more likely to have arrived by EMS compared to those arriving between 6am and 6pm (56% vs 42%; $\chi^2=13.59$, $p<.001$). This pattern was true for those ruled in and ruled out for ACS. Fifty-seven percent of ACS patients arriving at night came via EMS compared to 43% during the day. Fifty-four percent of patients ruled out for ACS arrived via EMS at night vs. 41% during the day. The two groups also differed significantly on several clinical characteristics, including age (ACS

older than non-ACS group), sex (more males in ACS group), and income (ACS had higher income than non-ACS group), and on symptoms, including chest pain and arm pain (reported more often with ACS than non-ACS group), and lightheadedness, shortness of breath, unusual fatigue, and palpitations (reported less often by ACS than non-ACS group).

Predictors of Delay Time

In the multivariable model, significant predictors included selected symptoms and mode of arrival. For ACS patients, those with shoulder pain or lightheadedness had approximately 30% shorter prehospital delay times compared to those not reporting these symptoms (TR=0.65, $p=0.013$ and TR=0.67, $p=0.022$, respectively; Table 2). ACS patients presenting with unusual fatigue experienced significantly longer delay than those without this symptom (TR=1.71, $p=0.002$). Importantly, ACS patients arriving by EMS had delay times approximately 50% shorter than those arriving by self-transport (TR=0.52, $p<0.001$), and those transferring from another facility also had significantly shorter delay times than those arriving by self-transport (TR=0.34, $p=0.018$).

For patients ruled out for ACS, those with chest pain or sweating had nearly a 25% shorter delay time compared to those without these symptoms (TR=0.71, $p=0.025$ and TR=0.73, $p=0.032$, respectively; Table 3). Patients without ACS complaining of unusual fatigue or indigestion had longer delay times (TR=1.54, $p=0.003$ and TR=1.37, $p=0.045$, respectively). Patients ruled out for ACS who arrived by EMS also had shorter delay times (TR=0.58, $p<0.001$) compared to those self-transporting. Likelihood ratio tests indicated that models for both groups were significantly better than an intercept-only model. However, McFadden's R^2 indicated that the models were relatively low in predictive capability (0.017 and 0.014 for ACS and non-ACS groups, respectively) indicating that there were likely other factors contributing to prehospital delay that were not measured in the study.

Exploratory Analysis

A minority of patients (26.2%) had a delay time of 2 hours or less; therefore, we performed an exploratory analysis and stratified participants into two groups, those who arrived to the ED more than 2 hours after symptom onset and those who arrived in 2 hours or less, to further explore differences in delay times (Supplemental Table 2). There were far more similarities in demographic characteristics and symptoms between groups. Patients were more likely to experience delays lasting more than 2 hours if they reported unusual fatigue or self-transported to the hospital. A history of diabetes was also associated with a delay > 2 hours; however, this difference did not meet statistical significance ($p=0.051$). When we conducted further regression modeling by diagnosis, we found that patients ruled in for ACS delayed longer if they reported lightheadedness and self-transported to the hospital (Supplemental Table 2). Lastly, those ruled out for ACS delayed longer if they experienced unusual fatigue and self-transported to the hospital (Supplemental Table 3).

Discussion

The aims of this study were to identify predictors of prehospital delay for suspected ACS, stratified by final diagnosis (ACS vs. no ACS), by examining patient, timing of event, and

transportation factors. We hypothesized that there are individual and external factors that contribute to prehospital delay in suspected ACS that vary by diagnosis. Key findings included that patients delay too long in presenting to the ED and that patients with ACS had significantly shorter delay when experiencing shoulder pain or lightheadedness and significantly longer delay if experiencing unusual fatigue. No symptoms were defined for the patients, patients simply responded yes or no to whether they experienced each of the 13 symptom. However, when developing the 13-item ACS Symptoms Checklist, we purposefully used the term “unusual” fatigue to denote serious and debilitating fatigue. McSweeney and colleagues noted in their study of prodromal myocardial infarction symptoms that women described fatigue as “so severe that they could not make a bed without resting.”³³ This is the concept of fatigue that we tried to capture. Patients ruled out for ACS had a significantly shorter delay if they reported chest pain or sweating and a significantly longer delay if they reported indigestion. Importantly, patients ruled in and ruled out for ACS had a significantly shorter prehospital delay if they were transported via EMS.

Prehospital Delay Time

The length of time a patient takes to seek care for symptoms suggestive of ACS is critical to eligibility for reperfusion,³⁴ reperfusion success,³⁵ recovery,³⁶ and long-term outcomes.^{37, 38} Median delay time of 6.68 hours is excessively long and exceeds guidelines from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology.^{39, 40} In addition, only 26.2% of patients had a delay time of 2 hours or less. Frisch et al. found that 54% of patients, with and without ACS, sought treatment within the 2-hour window of symptom onset; however, their study focused solely on high-risk chest pain patients transported by EMS.⁴¹ These results confirm the need to shift our focus on prehospital delay now that in-hospital delay factors have been largely addressed.⁴ Other factors relevant to reducing prehospital delay include irreversible myocardial tissue necrosis during this critical period⁴², a fragmented healthcare system, and high hospital costs and insurance premiums.⁴³ For example, EMS transport charges between \$600 and \$2500 dollars, the average ED work-up for chest pain runs in the range of \$2000 if the patient is ruled out for ACS and is much higher for those individuals that rule in for ACS.⁴⁴

Patient Characteristics by Diagnosis

Patients Ruled In for ACS.—Patients with ACS complaining of unusual fatigue had longer delay times (TR=1.71, p=0.002). Other studies have found that patients with symptoms of ischemic heart disease, such as weakness or fatigue, as opposed to chest pain, have longer prehospital delay.⁴¹ In addition, pain that the patient labeled as “epigastric” was most commonly attributed to noncardiac causes among those with ACS.⁴⁵ It may be that the patient’s interpretation of symptoms as being not serious and/or the attribution of their symptoms to a noncardiac cause result in prolonged prehospital delay. Albarquoni et al. found that patients with fatigue and indigestion were less likely to recognize and interpret their symptoms correctly as a heart attack.⁴⁶ Finnegan et al. found that patients and bystanders expected a myocardial infarction to present as sharp, crushing chest pain referred to as a “Hollywood heart attack.”⁴⁷ Prehospital delay has been linked to non-classic ACS symptoms; therefore, associated symptoms, such as unusual fatigue, may confuse

individuals and lead to delayed treatment seeking.⁴⁸ Symptoms that have been associated with reduced prehospital delay include chest pain^{9, 10} and left arm pain.⁹ In a cross-sectional study of 486 patients with myocardial infarction (MI), Albarqouni et al. found that a large majority of patients correctly recognized chest pain (94.8%) and shoulder pain (83.2%) as classic symptoms of MI. The authors also observed that knowledge of MI symptoms had a significant impact on prehospital delay time, with more knowledgeable patients having a 50% higher chance of arriving to the ED in less than 2 hours compared to patients with inadequate knowledge of symptoms.⁴⁶ Our findings suggest that, in most cases, symptoms are unlikely to help the patient make a decision to seek care quickly given that chest pain and dyspnea, symptoms commonly focused on by EMS and ED personnel, did not significantly predict delay for the most vulnerable patients, those with ACS. As the population ages and providers see fewer classic presentations (ie chest pain, shortness of breath, or sweating), we need to rethink the symptoms-based strategy of risk stratification.

Patients Ruled out for ACS.—For patients ruled out for ACS, those with chest pain or sweating had nearly a 25% shorter delay time. These results suggest that prior public health messaging campaigns and patient education have been successful in alerting individuals to the most commonly experienced symptoms of MI. Allana et al. found that patients with ACS believe that sweating is a symptom that requires urgent cardiac treatment. Also, more women than men considered chest pain and sweating as symptoms requiring urgent treatment.⁴⁵ Chest pain and sweating are well-known symptoms of ACS for the lay public and likely spur people to rapid action. Why this only occurred in patients ruled out for ACS in our study is puzzling. It is possible that those with prior disease took a wait-and-see approach. Sweating is an objective sign associated with STEMI. It is possible that the sample size of STEMI patients was too small to detect differences in symptoms by sub-diagnosis.

Time of Presentation to the Emergency Department and Use of EMS

Patients arriving to the ED at night (6 PM–6 AM) were more likely to have ACS (31.7% vs. 18.0%), compared to those ruled out. Wouters et al. conducted a cross-sectional study of 1655 patients who called the out-of-hours primary care services for chest discomfort. The authors found that patients with chest discomfort who called the out-of-hours primary care services between 12 AM and 9 AM had nearly double the likelihood for a diagnosis of ACS, compared to patients calling at other hours and after adjustment for sex and age.⁴⁹ The higher incidence of ACS between 6 PM and 6 AM in our study could partly be explained by the fact that most primary care offices are closed during these hours. Only 44.4% of patients in our study arrived by EMS, which is below the national average.⁵⁰ The proportion of patients with MI arriving via EMS nationally has ranged from 49.8%–60%.^{50–52} In the REACT trial, it was reported that 50% or more of individuals with ACS did not use EMS.²⁶ The fact that more patients, both ruled in and ruled out for ACS arrived via EMS between 6pm and 6am portends well for time to treatment and could result in improved outcomes.

The benefits of EMS use are well known, including 24-hour, 365-days-a-year availability; 12 lead ECG is now standard of care; many departments can transmit data and activate the cardiac catheterization laboratory for STEMI or STEMI equivalents; aspirin therapy can be

given; advanced cardiac life support can be provided; and EMS provides more direct entry into the ED. Under use of EMS, which are staffed with highly skilled paramedics and medications, is a call to action, if we are to reduce prehospital delay and improve patient outcomes. Future studies should examine barriers to EMS use such as cost, concerns about privacy, individual beliefs that EMS may be delayed and self-transport is faster, and the lack of understanding of the advanced capabilities of EMS personnel.

Limitations

There are some limitations to this study. Although we performed meticulous statistical analysis, there is a possibility that some associations may have occurred by chance. Wide confidence intervals for some tests suggest that sample sizes for some subgroups may be a limitation. Our study did not evaluate the patient's state of mind in relation to delay in seeking medical care. Future studies could benefit from evaluating why the patient did or did not call EMS upon symptom onset.⁵³ Lastly, the predictive capability of our multivariable model was lower than expected. Additional prehospital factors should be considered in future work.

Conclusion

Prehospital delay for symptoms suggestive of ACS remains excessive. A relatively small number of symptoms and self-transport to the ED predicted prehospital delay for patients with and without a final diagnosis of ACS in our study. Encouraging the use of EMS is an important and modifiable factor that may result in expedited diagnosis and treatment for patients with suspected ACS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Stone GW, Selker HP, Thiele H, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. *J Am Coll Cardiol*. 2016;67(14):1674–1683. [PubMed: 27056772]
2. Cullen L, Greenslade JH, Menzies L, et al. Time to presentation and 12-month health outcomes in patients presenting to the emergency department with symptoms of possible acute coronary syndrome. *Emerg Med J*. 6 2016;33(6):390–395. [PubMed: 26781459]
3. O'Gara PT, Kushner FG, Ascheim DD, et al. 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. *J Am Coll Cardiol*. 2013;61(4):e78–e140. [PubMed: 23256914]
4. Menees DS, Peterson ED, Wang Y, et al. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med*. 9 5 2013;369(10):901–909. [PubMed: 24004117]

5. Granger CB, Bates ER, Jollis JG, et al. Improving care of STEMI in the United States 2008 to 2012: a report from the American Heart Association Mission: Lifeline program. *Journal of the American Heart Association*. 2019;8(1):e008096. [PubMed: 30596310]
6. Isaksson RM, Holmgren L, Lundblad D, Brulin C, Eliasson M. Time trends in symptoms and prehospital delay time in women vs. men with myocardial infarction over a 15-year period. The Northern Sweden MONICA Study. *Eur J Cardiovasc Nurs*. 6 2008;7(2):152–158. [PubMed: 17980668]
7. DeVon HA, Hogan N, Ochs AL, Shapiro M. Time to treatment for acute coronary syndromes: the cost of indecision. *J Cardiovasc Nurs*. Mar-Apr 2010;25(2):106–114. [PubMed: 20142752]
8. Higginson R. Women's help-seeking behaviour at the onset of myocardial infarction. *Br J Nurs*. 1 10–23 2008;17(1):10–14. [PubMed: 18399391]
9. Kirchberger I, Heier M, Wende R, von Scheidt W, Meisinger C. The patient's interpretation of myocardial infarction symptoms and its role in the decision process to seek treatment: the MONICA/KORA Myocardial Infarction Registry. *Clin Res Cardiol*. 2012;101(11):909–916. [PubMed: 22618810]
10. Isaksson R-M, Brulin C, Eliasson M, Näslund U, Zingmark K. Older women's prehospital experiences of their first myocardial infarction. *J Cardiovasc Nurs*. 2013;28(4):360–369. [PubMed: 22495804]
11. Moser DK, Kimble LP, Alberts MJ, et al. Reducing delay in seeking treatment by patients with acute coronary syndrome and stroke: a scientific statement from the American Heart Association Council on cardiovascular nursing and stroke council. [Reprint in *J Cardiovasc Nurs*. 2007 Jul-Aug;22(4):326–43; PMID: 17589286]. *Circulation*. 2006;114(2):168-182. [PubMed: 17589286]
12. DeVon HA, Burke LA, Nelson H, Zerwic JJ, Riley B. Disparities in patients presenting to the emergency department with potential acute coronary syndrome: It matters if you are Black or White. *Heart Lung*. Jul-Aug 2014;43(4):270–277. [PubMed: 24992880]
13. Foraker RE, Rose KM, McGinn AP, et al. Neighborhood income, health insurance, and prehospital delay for myocardial infarction: the atherosclerosis risk in communities study. *Arch Intern Med*. 2008;168(17):1874–1879. [PubMed: 18809814]
14. Noureddine S, Adra M, Arevian M, et al. Delay in seeking health care for acute coronary syndromes in a Lebanese sample. *J Transcult Nurs*. 10 2006;17(4):341–348. [PubMed: 16946116]
15. Passamonti E, Pirelli S. The impact of comorbidity in the management of octogenarians with non-ST-elevation acute coronary syndrome. *Ital Heart J Suppl*. 11 2004;5(11):855–860. [PubMed: 15633429]
16. Nau DP, Ellis JJ, Kline-Rogers EM, Mallya U, Eagle KA, Erickson SR. Gender and perceived severity of cardiac disease: evidence that women are “tougher”. *Am J Med*. 11 2005;118(11):1256–1261. [PubMed: 16271910]
17. Wang HY, Chew G, Kung CT, Chung KJ, Lee WH. The use of Charlson comorbidity index for patients revisiting the emergency department within 72 hours. *Chang Gung Med J*. Sep-Oct 2007;30(5):437–444. [PubMed: 18062175]
18. Kluz K, Parenica J, Kubkova L, et al. Unstable angina pectoris prior to ST elevation myocardial infarction in patients treated with primary percutaneous coronary intervention has no influence on prognosis. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 6 2015;159(2):251–258. [PubMed: 24457834]
19. Ribeiro S, Gaspar A, Rocha S, et al. Predictors of pre-hospital delay in patients with ST-segment elevation myocardial infarction. *Rev Port Cardiol*. 10 2010;29(10):1521–1532. [PubMed: 21265494]
20. Sullivan AL, Beshansky JR, Ruthazer R, Murman DH, Mader TJ, Selker HP. Factors associated with longer time to treatment for patients with suspected acute coronary syndromes: a cohort study. *Circ Cardiovasc Qual Outcomes*. 1 2014;7(1):86–94. [PubMed: 24425697]
21. Sari I, Acar Z, Ozer O, et al. Factors associated with prolonged prehospital delay in patients with acute myocardial infarction. *Turk Kardiyol Dern Ars*. 4 2008;36(3):156–162. [PubMed: 18626207]

22. Cohen MC, Rohtla KM, Lavery CE, Muller JE, Mittleman MA. Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death. *Am J Cardiol.* 6 01 1997;79(11):1512–1516. [PubMed: 9185643]
23. Mahmoud KD, Lennon RJ, Ting HH, Rihal CS, Holmes DR. Circadian variation in coronary stent thrombosis. *JACC Cardiovasc Interv.* 2011;4(2):183–190. [PubMed: 21349457]
24. Edahiro R, Sakata Y, Nakatani D, et al. Association of lifestyle-related factors with circadian onset patterns of acute myocardial infarction: a prospective observational study in Japan. *BMJ open.* 2014;4(6):e005067.
25. Antman EM. Time is muscle: translation into practice. *J Am Coll Cardiol.* 2008;52(15):1216–1221. [PubMed: 18926324]
26. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA.* 2000;284(1):60–67. [PubMed: 10872014]
27. DeVon HA, Burke LA, Vuckovic KM, et al. Symptoms Suggestive of Acute Coronary Syndrome: When Is Sex Important? *J Cardiovasc Nurs.* 6 08 2016.
28. Doolan DM, Froelicher ES. Using an existing data set to answer new research questions: a methodological review. *Res Theory Nurs Pract.* 2009;23(3):203–215. [PubMed: 19769213]
29. Devon HA, Rosenfeld A, Steffen AD, Daya M. Sensitivity, specificity, and sex differences in symptoms reported on the 13-item Acute Coronary Syndrome Checklist. *J Am Heart Assoc.* 2014;3(2):e000586. [PubMed: 24695650]
30. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology [STROBE] statement: guidelines for reporting observational studies. *Gac Sanit.* 2008;22(2):144–150. [PubMed: 18420014]
31. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *International Journal of Surgery.* 2014;12(12):1495–1499. [PubMed: 25046131]
32. Knight EP, Shea K, Rosenfeld AG, Schmiede S, Hsu C-H, DeVon HA. Symptom Trajectories After an Emergency Department Visit for Potential Acute Coronary Syndrome. *Nurs Res.* 2016;65(4):268–278. [PubMed: 27362513]
33. McSweeney JC, Cody M, O’Sullivan P, Elberson K, Moser DK, Garvin BJ. Women’s early warning symptoms of acute myocardial infarction. *Circulation.* 11 25 2003;108(21):2619–2623. [PubMed: 14597589]
34. American College of Emergency P, Society for Cardiovascular A, Interventions, et al. 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. *J Am Coll Cardiol.* 1 29 2013;61(4):e78–140. [PubMed: 23256914]
35. Kristensen SD, Laut KG, Fajadet J, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries. *Eur Heart J.* 8 1 2014;35(29):1957–1970. [PubMed: 24419804]
36. Christiansen EC, Wickstrom KK, Henry TD, et al. Comparison of functional recovery following percutaneous coronary intervention for ST elevation myocardial infarction in three age groups (<70, 70 to 79, and >=80 years). *Am J Cardiol.* 8 1 2013;112(3):330–335. [PubMed: 23642505]
37. Collins SD. Acute myocardial infarction in women: is there a sex disparity between door-to-balloon time and clinical outcomes? *Cardiovasc Revasc Med.* 2012;13(2):125–127. [PubMed: 22154718]
38. Giustino G, Baber U, Stefanini GG, et al. Impact of Clinical Presentation (Stable Angina Pectoris vs Unstable Angina Pectoris or Non-ST-Elevation Myocardial Infarction vs ST-Elevation Myocardial Infarction) on Long-Term Outcomes in Women Undergoing Percutaneous Coronary Intervention With Drug-Eluting Stents. *Am J Cardiol.* 9 15 2015;116(6):845–852. [PubMed: 26174605]
39. American College of Emergency P, Society for Cardiovascular A, Interventions, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart

- Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 1 29 2013;61(4):485–510. [PubMed: 23256913]
40. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 1 7 2018;39(2):119–177. [PubMed: 28886621]
 41. Frisch SO, Faramand Z, Li H, et al. Prevalence and Predictors of Delay in Seeking Emergency Care in Patients Who Call 9–1-1 for Chest Pain. *J Emerg Med.* 11 2019;57(5):603–610. [PubMed: 31615705]
 42. Benjamin EJ, Muntner P, Bittencourt MS. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation.* 2019;139(10):e56–e528. [PubMed: 30700139]
 43. Smolderen KG, Spertus JA, Nallamothu BK, et al. Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *JAMA.* 4 14 2010;303(14):1392–1400. [PubMed: 20388895]
 44. Yau AA, Nguyendo LT, Lockett LL, Michaud E. The HEART Pathway and hospital cost savings. *Crit Pathw Cardiol.* 2017;16(4):126. [PubMed: 29135619]
 45. Allana S, Moser DDK, Ali DTS, Khan DAH. Sex differences in symptoms experienced, knowledge about symptoms, symptom attribution, and perceived urgency for treatment seeking among acute coronary syndrome patients in Karachi Pakistan. *Heart Lung.* 11 2018;47(6):584–590. [PubMed: 30107891]
 46. Albarqouni L, Smenes K, Meinertz T, et al. Patients' knowledge about symptoms and adequate behaviour during acute myocardial infarction and its impact on delay time: Findings from the multicentre MEDEA Study. *Patient Educ Couns.* 11 2016;99(11):1845–1851. [PubMed: 27387122]
 47. Finnegan JR Jr, Meischke H, Zapka JG, et al. Patient delay in seeking care for heart attack symptoms: findings from focus groups conducted in five US regions. *Prev Med.* 2000;31(3):205–213. [PubMed: 10964634]
 48. DeVon HA, Ryan CJ, Ochs AL, Shapiro M. Symptoms across the continuum of acute coronary syndromes: Differences between women and men. *Am J Crit Care.* 1 2008;17(1):14–24; quiz 25. [PubMed: 18158385]
 49. Wouters LT, Zwart DL, Erkelens DC, et al. Chest discomfort at night and risk of acute coronary syndrome: cross-sectional study of telephone conversations. *Fam Pract.* 1 30 2020.
 50. Tataris K, Kivlehan S, Govindarajan P. National trends in the utilization of emergency medical services for acute myocardial infarction and stroke. *West J Emerg Med.* 2014;15(7):744. [PubMed: 25493113]
 51. Mathews R, Peterson ED, Li S, et al. Use of Emergency Medical Service Transport Among Patients With ST-Segment–Elevation Myocardial Infarction. Findings From the National Cardiovascular Data Registry Acute Coronary Treatment Intervention Outcomes Network Registry–Get With the Guidelines. 2011;124(2):154–163.
 52. Mirzaei S, Steffen A, Vuckovic K, et al. The association between symptom onset characteristics and prehospital delay in women and men with acute coronary syndrome. *Eur J Cardiovasc Nurs.* 2019;1474515119871734.
 53. Rosenfeld AG, Lindauer A, Darney BG. Understanding treatment-seeking delay in women with acute myocardial infarction: descriptions of decision-making patterns. *Am J Crit Care.* 2005;14(4):285–293. [PubMed: 15980419]

Table 1

Sample Characteristics by Diagnosis

Variable	Total Cohort (n=975)	ACS (n=439)	No ACS (n=536)	p value
Delay Time in hours, mean (SD)	20.24 (27.72)	19.01 (26.04)	21.24 (29.00)	0.212
Delay Time in hours, median [IQR]	6.68 [1.91, 24.94]	6.47 [1.67, 24.46]	6.73 [2.15, 25.27]	0.195
Age in years, mean (SD)	60.32 (14.07)	61.77 (12.12)	59.13 (15.40)	0.004
Age in years, median [IQR]	60.0 [51.0, 70.0]	61.0 [53.0, 70.0]	59.0 [49.0, 70.0]	0.011
Age				<0.001
<40	62 (6.4)	11 (2.5)	51 (9.5)	
40 to <60	407 (41.7)	189 (43.1)	218 (40.7)	
60 to <80	414 (42.5)	201 (45.8)	213 (39.7)	
80+	92 (9.4)	38 (8.7)	54 (10.1)	
Sex				<0.001
Male	609 (62.5)	316 (72.0)	293 (54.7)	
Female	366 (37.5)	123 (28.0)	243 (45.3)	
Race/ethnicity				0.318
White or Caucasian	672 (69.1)	296 (67.6)	376 (70.3)	
Black or African American	127 (13.1)	56 (12.8)	71 (13.3)	
Hispanic	76 (7.8)	42 (9.6)	34 (6.4)	
Other	98 (10.1)	44 (10.0)	54 (10.1)	
Health Insurance				0.537
Private from employer	303 (31.6)	139 (32.5)	164 (30.9)	
Private paid by patient	94 (9.8)	40 (9.3)	54 (10.2)	
Medicare	326 (34.0)	136 (31.8)	190 (35.8)	
Govt Insurance or other	115 (12.0)	52 (12.1)	63 (11.9)	
Not Insured	121 (12.6)	61 (14.3)	60 (11.3)	
Income				0.001
<\$20,000	291 (33.1)	107 (27.5)	184 (37.5)	
\$20,000 - \$50,000	293 (33.3)	133 (34.2)	160 (32.6)	
\$50,000 - \$100,000	174 (19.8)	97 (24.9)	77 (15.7)	
\$100,000+	122 (13.9)	52 (13.4)	70 (14.3)	
Diabetes	279 (28.7)	129 (29.5)	150 (28.0)	0.627
Symptoms on Presentation to ED				
Chest Pressure	630 (64.7)	290 (66.2)	340 (63.4)	0.367
Chest Discomfort	682 (70.0)	306 (69.9)	376 (70.1)	0.923
Chest Pain	672 (69.0)	317 (72.4)	355 (66.2)	0.039
Shoulder Pain	341 (35.0)	158 (36.1)	183 (34.1)	0.530
Arm Pain	351 (36.0)	176 (40.2)	175 (32.6)	0.015
Upper Back Pain	261 (26.8)	104 (23.7)	157 (29.3)	0.052
Lightheadedness	433 (44.5)	164 (37.5)	269 (50.2)	<0.001

Variable	Total Cohort (n=975)	ACS (n=439)	No ACS (n=536)	p value
Short of Breath	544 (55.9)	214 (48.9)	330 (61.6)	<0.001
Sweating	343 (35.2)	164 (37.4)	179 (33.4)	0.188
Unusual Fatigue	458 (47.0)	173 (39.5)	285 (53.2)	<0.001
Nausea	367 (37.7)	161 (36.8)	206 (38.4)	0.592
Palpitations	254 (26.1)	91 (20.8)	163 (30.4)	0.001
Indigestion	236 (24.2)	105 (24.0)	131 (24.4)	0.865
ACS Diagnosis				<0.001
No ACS	536 (55.0)	0 (0.0)	536 (100.0)	
UA & NSTEMI	327 (33.5)	327 (74.5)	0 (0.0)	
STEMI	112 (11.5)	112 (25.5)	0 (0.0)	
Charlson Comorbidity Index, mean (SD)	1.83 (1.87)	1.96 (1.73)	1.73 (1.98)	0.061
Charlson Comorbidity Index				0.095
0 to 1	520 (54.3)	223 (51.6)	297 (56.5)	
>1 to 4	351 (36.6)	174 (40.3)	177 (33.7)	
>4	87 (9.1)	35 (8.1)	52 (9.9)	
Mode of Arrival				0.170
Self-Transport	520 (53.6)	222 (50.9)	298 (55.7)	
EMS	431 (44.4)	202 (46.3)	229 (42.8)	
Transfer from another facility	20 (2.0)	12 (2.8)	8 (1.5)	
Time of Arrival				<0.001
6 am – 11:59 am	374 (38.4)	157 (35.8)	217 (40.6)	
12 pm – 5:59 pm	364 (37.4)	143 (32.6)	221 (41.4)	
6 pm – 11:59 pm	136 (14.0)	78 (17.8)	58 (10.9)	
12 am – 5:59 am	99 (10.2)	61 (13.9)	38 (7.1)	

Note. Bolding indicates significance at <.05. ACS is acute coronary syndrome; SD is standard deviation; IQR is interquartile range; Govt is government; ED is emergency department; UA is unstable angina; NSTEMI is non-ST elevation myocardial infarction; STEMI is ST elevation myocardial infarction; EMS is emergency medical services. Bolded numbers indicate statistical significance.

Table 2

Multivariable Accelerated Failure Time Model (Log Normal) Predicting Delay Time for Patients Ruled In for ACS (n=432 in model)

Variables	Time Ratio (TR)	95% CI	p-value
Race			0.654
White or Caucasian (Reference)			
Black or African American	1.11	(0.71, 1.73)	0.661
Hispanic	0.87	(0.52, 1.45)	0.585
Other	1.50	(0.92, 2.46)	0.106
Diabetes	1.32	(0.95, 1.84)	0.100
Shoulder Pain	0.65	(0.46, 0.91)	0.013
Lightheaded	0.67	(0.48, 0.94)	0.022
Short of Breath	1.19	(0.87, 1.63)	0.283
Unusual Fatigue	1.71	(1.23, 2.40)	0.002
Chest Pressure	0.87	(0.62, 1.21)	0.408
Chest Pain	1.09	(0.77, 1.54)	0.625
Upper Back Pain	1.40	(0.96, 2.03)	0.077
Sweating	0.90	(0.65, 1.25)	0.538
Indigestion	1.07	(0.75, 1.53)	0.706
Mode of Arrival			0.005
Emergency Medical Services (Reference)			
Self-Transport	1.93	(1.43, 2.60)	<0.001
Transfer from Another Facility	0.65	(0.26, 1.61)	0.349
Time of Arrival			0.244
6 am - 11:59 am (Reference)			
12 pm - 5:59 pm	1.19	(0.75, 1.90)	0.457
6 pm - 11:59 pm	1.79	(1.12, 2.88)	0.015
12 am - 5:59 am	1.56	(0.93, 2.64)	0.094

Note. ACS is acute coronary syndrome

Table 3

Multivariable Accelerated Failure Time Models (log normal) Predicting Delay Time for Patients Ruled Out for ACS (n=531 in model)

Variables	Time Ratio (TR)	95% CI	p-value
Race/ethnicity			0.694
White or Caucasian (Reference)			
Black or African American	0.88	(0.59, 1.29)	0.508
Hispanic	1.09	(0.63, 1.88)	0.759
Other	1.38	(0.89, 2.13)	0.148
Diabetes	1.05	(0.78, 1.41)	0.754
Shoulder Pain	0.89	(0.66, 1.20)	0.439
Lightheadedness	0.94	(0.70, 1.26)	0.690
Short of Breath	1.11	(0.83, 1.48)	0.499
Unusual Fatigue	1.54	(1.16, 2.05)	0.003
Chest Pressure	0.91	(0.68, 1.22)	0.528
Chest Pain	0.71	(0.53, 0.96)	0.025
Upper Back Pain	1.29	(0.95, 1.74)	0.105
Sweating	0.73	(0.55, 0.97)	0.032
Indigestion	1.37	(1.01, 1.86)	0.045
Mode of Arrival			0.015
Self-Transport (Reference)			
Emergency Medical Services	0.58	(0.45, 0.76)	<0.001
Transfer from Another Facility	1.46	(0.50, 4.25)	0.487
Time of Arrival			0.895
6 am – 11:59 am (Reference)			
12 pm – 5:59 pm	1.23	(0.73, 2.10)	0.437
6 pm – 11:59 pm	1.32	(0.78, 2.23)	0.302
12 am – 5:59 am	1.34	(0.72, 2.50)	0.354
Note. ACS is acute coronary syndrome; CI is confidence interval.			
Log Likelihood Multivariable Model	-2037.8		
Log Likelihood Model with Intercept Only	-2065.9		
McFadden's R2	0.014		