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Evidence that Gender Effects on Time-to-ECG may be attributable to differences in Atypical Presentations

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Abstract

Electrocardiogram (ECG) completion within 10 minutes for patients with suspected coronary heart disease is a quality marker for acute coronary syndrome (ACS). Controversy exists as to whether differences between genders in the frequency of atypical symptoms cause the observed differences in times to ECG (TECG) acquisition. Our goal was to assess whether delays observed between genders was attributable to differences in atypical symptom rates.

Methods: Retrospective cross-sectional analysis of 8747 patients presenting to a Level 1 trauma hospital with a pre-specified set of "atypical" or "typical" chief complaints for ACS. Three-hundred patients were randomly selected for review. Hypotheses regarding TECG were tested using Kaplan-Meier survival analysis and proportional hazards regression. Chi-square, t-test, and Fisher's exact test were used to compare demographic variables.

Results: The sample consisted of 167 women and 133 men. Atypical complaints, walk-in, lower ESI Triage Criteria, and age <50yrs were each associated with longer TECG. The median TECG was 19 (95%CI 13-94) minutes for males and 83 (95%CI 20- UK) for females. Neither Kaplan Meier Survival analysis nor proportional hazards regression showed a significant difference between the TECG in men versus women or differences in gender within atypical and typical.

Conclusions: There was no statistically significant difference between rates of atypical symptoms between men (43%) and women (57%). Presentation with atypical symptoms affected the likelihood, therefore, speed of TECG. These results suggest that, were there observed differences in atypical symptom rates between genders in other studies; these may have contributed in part or full to any observed differences between genders in TECG.

Keywords: Time to ECG; Door to ECG; Gender; Atypical Presentations; Chest pain; Emergency department

Introduction

The leading cause of death for both men and women in the United States is Coronary Heart Disease (CHD). Interestingly, women experience more complications after Acute Myocardial Infarction (AMI) than men [1]. This seems paradoxical since women, before the age of 50, are generally considered to have better coronary health with a lower short term risk of coronary disease compared with men.

One potential explanation is that women present in a way which may be more difficult to diagnose, leading to improper or delayed care [2]. Studies have shown that a significant number of patients who present with atypical symptoms i.e., without typical angina, receive a delayed diagnosis of AMI and are thus significantly less likely to receive a timely ECG or reperfusion strategies [3]. Insurance coverage appears to also affect treatment in patients with AMI, with insured patients more likely to receive invasive treatments [4]. The effectiveness of thrombolytic therapy and angioplasty are distinctly associated with the time interval between the onset of symptoms and treatment. The shorter the interval, the better the outcome. Despite this knowledge of timely therapy, women continue to have longer times to 911call with increased time from symptom onset to first medical contact [5]. The effects of delays have clearly been documented at a number of treatment points including: arrival at the Emergency Department (ED), initial ECG, decision to administer thrombolytic therapy, and actual infusion of thrombolytic therapy [6]. Recent guidelines recommend that an ECG be obtained within 10 minutes of arrival to the ED in patients in whom ACS is suspected [7]. Insurance coverage has also shown to affect treatment in patients with AMI.

Most patients with Acute Coronary Syndrome (ACS) (53-74%) present with chest pain regardless of gender [8]. However, these estimates still leave a substantial percentage of patients presenting with atypical symptoms. The most frequent atypical symptoms with which patients present are dyspnea, nausea, diaphoresis, syncope, and pain in the arms, epigastrium, neck or jaw. Chest pain itself may present atypically, having been described as not severe or prolonged; a burning, sharp, pleuritic, and positional pain that is reproducible on palpation of the chest wall [9]. Many of these symptoms appear frequently in other diagnosis such as costochondritis, pulmonary embolus and peptic ulcer disease, offering apparently more parsimonious explanations which compete for the treating physician's decision. On balance, patients with ACS presenting with atypical symptoms may falsely be considered low risk for ischemia upon presentation to the ED [10]. Absence of chest discomfort was among the strongest predictor of a missed diagnosis of AMI, lower use of thrombolytic therapy, and ultimately inappropriate discharge from the ED [3]. Studies using data from the National Registry of Myocardial Infarction recently reported that almost one third of the 450,000 patients who had documented AMI did not have chest pain on initial presentation, and that they were at higher risk for less aggressive medical care with poorer outcomes and worsened long term morbidity and mortality [11].

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It has previously been demonstrated that women are more likely than men to have atypical ACS symptoms, although the magnitude of this difference and the significance of the difference on outcome is controversial [12]. Despite the limited evidence, it is important to consider the potential to place women at increased risk or a falsely low ACS rating. Triage decisions are dependent on the knowledge and experiences of emergency nurses and front line Emergency Medicine health care providers. Emergency Medicine Services personnel, ED nurses or providers who fail to associate middle-aged women's atypical CHD presenting symptoms with ACS unwittingly create delays in ECG acquisition and the initiation of timely and appropriate treatment thus further contributing to the increased morbidity and mortality in these patients if they are having an AMI [13]. That is, the observed differences between genders may be attributable to greater rates of atypical symptoms in women. By logical extension, raising awareness and training regarding atypical symptomology would indirectly correct the gender discrepancy in ACS outcomes.

Controversy exists as to whether differences between genders in the frequency of atypical symptoms cause the observed differences in times to ECG acquisition. Prior studies that have shown gender differences in Time to ECG (TECG) and rates of atypical symptoms have been conducted retrospectively on patients with diagnoses of ACS. Our goal was to assess whether the delays observed between genders was attributable to differences in atypical symptom rates by testing whether the effects of gender were present or of different magnitude, depending on whether patients presented with typical or atypical symptoms.

Methods

Study Design and Setting

We conducted a retrospective study of a random sample of patients who had presented to a large urban Level I trauma center. It is the main teaching hospital for a medical school and serves a large heterogeneous population including a substantial inner city dwelling, minority, and lower SEP patients. The ED is a regional cardiac referral center with 24 hour access to cardiac catheterization laboratory located in the ED. The ED uses an electronic medical record to document nursing care, order entry, patient flow, and discharge and a templated written chart for physicians. The hospital's institutional review board approved the study.

Inclusion and Exclusion Criteria

Investigators identified a set of typical and atypical symptoms associated with ACS and AMI after reviewing studies of presenting symptoms suggestive of CHD (Figure 1) [14]. Typical symptoms included chest pain, left arm pain and dyspnea. Atypical symptoms were defined as palpitations, jaw pain, back pain, epigastric pain, nausea, vomiting, indigestion, weakness, fatigue, syncope or dizziness. The electronic medical record and patient tracking system allowed investigators to identify patients who had been treated in the ED having presented with these symptoms. Trained Research Assistants (RAs) reviewed the charts of adult patients (age ≥ 18 years) who presented to the ED from January 2009 to June 2009 with at least one of the following chief complaints as recorded in the triage electronic nursing notes: a) Typical Chief Complaints - Chest pain, Left Arm Pain, Dyspnea or b) Atypical Chief Complaints - limited to Palpitations, Jaw Pain, Back Pain, Epigastric Pain, Nausea or Vomiting, Weakness, Fatigue, Dizziness and Syncope.

Because atypical CHD symptoms can be ambiguous and can be associated with a number of other non-cardiac pathologies, investigators examined the recorded chief complaint in the triage nursing notes for descriptors of definitive alternative non-cardiac pathology. A pre-defined list was created which served as exclusion criteria: gastrointestinal bleeding (vomiting blood, vomiting coffee grounds, bloody stool, black or tarry stools); two or more neurologic complaints (weakness or numbness) or one neurologic complaint involving a lower extremity (dysarthria + left arm weakness or weakness + lower extremity complaint); trauma; back pain with lower extremity, genital, or urinary complaints (back pain + radiates to leg); current alcohol intoxication (intoxicated + nausea); insect or animal bite; rash; fever; seizure; pregnancy; Sickle Cell Crisis; intracranial hemorrhage.

Data Abstraction

The investigators used well established and published data sources (LifeLinks and MedHost). Studies based on these sources have been published in the past [15,16]. ECG's are date and time stamped in Life Links and can be extracted directly along with ECG readings and patient-linked reports, laboratory results, transcribed copies of dictated notes and discharge summaries, scanned ED physician encounter notes, transcriptions of stress test interpretations, and radiologic materials including reports and electronic images. Further MedHost is used for ED nurse charting the entire course of each patient's visit including disposition, chief complaints, orders, medication(s) administered, labs,

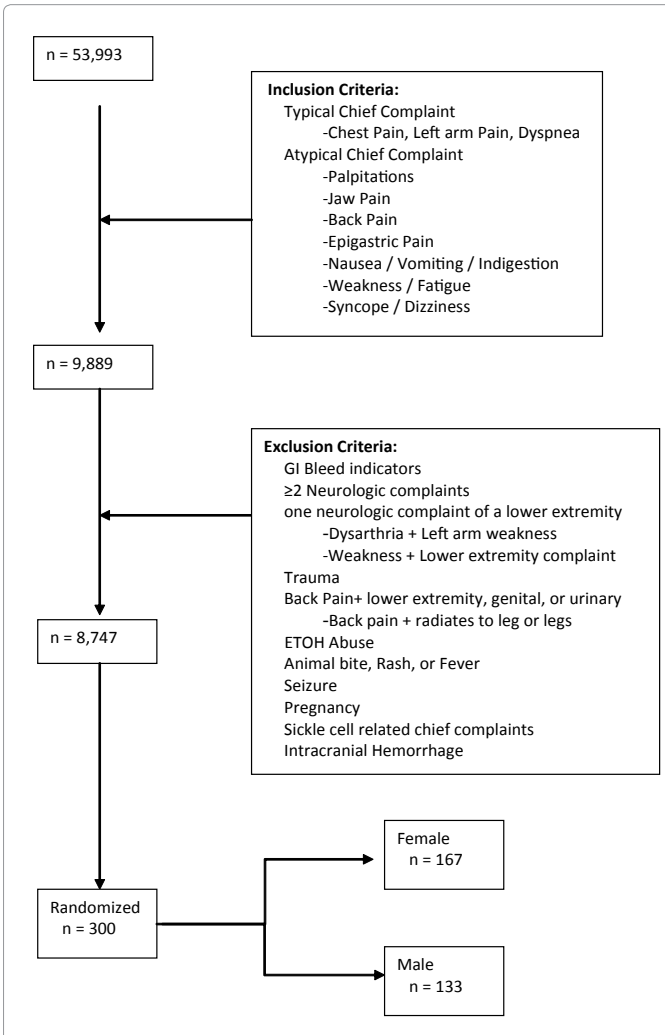

Figure 1: Patient Flow.

x-ray reports, and disposition. The investigators queried the MedHost record to discover the chief complaints in the triage system for each patient visit during the study period.

Trained RAs recorded data in a standardized data extraction form. RAs were blinded to the hypothesis of the study. They recorded patient demographic information (Age, Race, Gender, Age, Insurance status) and ED visit information (Date, Time of day, Emergency Severity Index (ESI) Triage Designation, Arrival Method). They also entered the patient's time of ED registration and chief complaint at the time of ED registration. Time of 1st ECG was obtained from the scanned ECG in LifeLinks. If a scanned ECG was not electronically available in LifeLinks, the RAs searched MedHost Nursing Notes in the patient's electronic chart for time of 1st ECG. RAs clearly indicated if no ECG was scanned or documented for a particular patient. RAs recorded patient disposition, noting whether the patient was Discharged or Admitted to the Chest Pain (Observation) Unit, Medical Floor, or Cardiac Care Unit. They also recorded additional outcome measures including: Diagnosis, Cardiac enzymes (CPK and Troponin), the occurrence or non-occurrence of cardiac stress testing during the patient's admission. For the purposes of this study, only Stress Testing done during the course of the patient's admission was noted.

Data Analysis

RAs entered all the data that they collected into an Excel spreadsheet. The data was then imported into Statistical Analysis System (SAS) version 9.2 (The SAS institute, Cary, NC) for analysis. The probability of obtaining an ECG was modeled as a function of the time from ED registration to ECG. Covariates were analyzed using the Kaplan-Meier (K-M) survival method and the primary hypothesis was analyzed using a proportional hazards regression with effects for age, gender, atypical symptomology, and the interaction between atypical symptoms and gender. The log-rank Chi-square statistic was used for testing the difference between K-M survival curves that had been generated as a function of gender, atypical versus typical presentation, insurance versus none, race, mode of arrival, ESI, and age (both continuous and dichotomized at 50 years of age). The interaction between gender and presentation with atypical versus typical symptoms was tested in a proportional hazards regression. Alpha was set to 0.05 for all analyses and, where necessary, follow-up comparisons were adjusted using the Tukey-Kramer method to maintain this alpha.

Based on t-test, a sample of 272 (136 males and 136 females) was necessary to maintain a power of greater than or equal 80% to detect a statistically significant difference at a 2-tailed alpha of 0.05 at the time of analysis, given an effect size of Cohen's d=0.343. We chose to inflate this sample size to 300 in anticipation of unanticipated data quality issues during the medical record chart review process that might lead to missing one or more of the variables necessary for analysis.

Results

The MedHost search identified 53,993 patients during the specified six month period. By applying the inclusion criteria, 9889 patients with the previously specified CHD related chief complaints were chosen. After applying the exclusion criteria, investigators removed 1142 of these. The sample size determination was based on an estimated effect size of d=0.27. Given this effect size, and the likely ratio of females to males near 50%, we estimated a total sample size of 300 patients. Of the remaining 8747 charts, investigators generated a randomly assigned value to each record using electronic software Stata (StataCorp). The records were then sorted in the dataset by the random number. The first 300 records were segregated to produce the final study list.

Primary Hypotheses: Age, Gender, Symptomology, and Time to ECG

The final sample consisted of 167 women and 133 men (300 total). Approximately equal percentages of patients presented with typical and atypical symptoms (55%, 166/300), but contrary to our expectations, there was no statistically significant difference in the percent of men (43%, 71/133) and women (57%, 95/167) who presented with atypical symptoms (p=0.5444).

As differences in presentation was our primary theory as to how gender differences might emerge in times to ECG, it was not surprising that there was no statistically significant difference between genders with regards to times to ECG (Figure 2, Log-Rank p=0.1358). Consistent with our expectation, there was a profound difference between patients with atypical presentations and those with typical presentations (Figure 3, Log-Rank p<.0001). More specifically, 50% of patients presenting with typical symptoms received an ECG within 9 minutes (95%CI 8-10 minutes), and 75% received an ECG within 14 minutes (95%CI 12-17 minutes). In contrast, fewer than 25% of patients presenting with atypical symptoms ever received an ECG within 2 hours. Also consistent with the atypical versus typical symptom distinction, older patients tended to have shorter times to ECG both model as a continuous covariate (Log-Rank p=0.0001), and comparing patients who were younger than 50 years to those who were 50 or older (Log-Rank p<.0001). A subsequent multiple proportional hazards regression including age as a covariate found no statistically significant difference in the degree to which atypical presentation increased the times to ECG in men and women relative

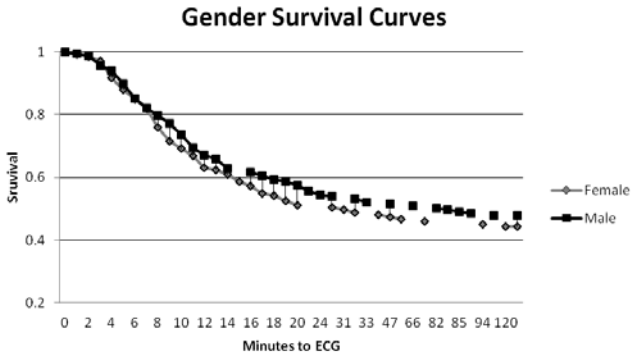

Figure 2: Time to ECG Gender Survival Curves.

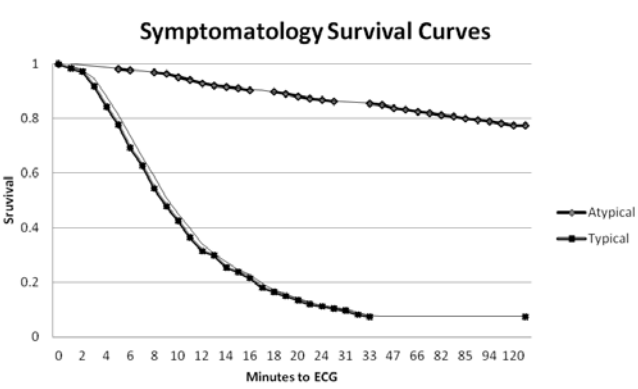

Figure 3: Time to ECG Symptomatology Survival Curves.

to typical presentation (gender x presentation p=0.4417) while atypical presentation (regardless of gender) remained statistically significant (p<.0001) with neither gender (p=0.4783) nor age (p=0.4319) being statistically significant. Once the interaction was removed from the model, the symptomology hazard ratio suggested the probability of patients presenting with atypical symptoms receiving an ECG at any given moment after arrival was only 8.5% that of those presenting with typical symptoms.

Of the typical chief complaints, chest pain was the most common descriptive symptom (96% Table 1). Of the atypical presentations, back pain (39%) and gastrointestinal upset (36%) were the most common with weakness/fatigue (19%) and epigastric pain (12%) also frequent.

Secondary Hypotheses: Mode of Arrival, ESI, Race, and Insurance

Patients arriving by ambulance (46%) had significantly shorter times to ECG than those arriving as walk-ins (50%) (adj. p=0.0031), with those arriving by ambulance having median times to ECG of 17 (95%CI 14-32) minutes and only 45% of walk-ins ever receiving recorded ECGs (Table 2). Time to ECG increased significantly (ADJ. p<.05) with each increase in ESI Triage Category, with ESI category 2 having a median time to ECG of 2 (95%CI 10-14), 3 having a median time to ECG of 76 (95%CI 17-Undeterminable), and none of the ESI 4 receiving a recorded ECG. There were no statistically significant differences in times to ECG between races (p=0.9671) or by insurance status (p=0.7360).

Discussion

Based on previous literature, the investigators anticipated that women would be more likely to have a significant delay in TECG, because of the greater probability that the women would present with atypical symptoms of possible acute coronary syndrome than the men [6,12]. Our results showed no statistically significant difference between men and women in the probability of an atypical presentation of possible acute coronary syndrome. Not surprisingly, then, we found no statistically significant difference in TECG between the men and the women in our study; however, there was a strikingly significant TECG difference between patients presenting with typical versus atypical symptoms of possible ACS. Both men and women presenting with atypical symptoms of possible ACS had delays in TECG and there was no difference based on the sex of the patient with atypical symptoms.

Many studies now suggest that patients with atypical symptoms of possible ACS represent a large segment of the MI population and, that these patients are more likely to delay seeking medical attention, receive less aggressive medical treatment, and have higher in-hospital mortality [3]. Our study provides evidence that these differences in treatment and outcome begin in the ED with a delay in TECG acquisition. Our study also demonstrates that female gender is not an independent factor in delays in TECG; we demonstrated no difference in TECG with respect to gender. Improved education of triage nursing about atypical presentations of possible ACS may lead to more effective identification of these patients regardless of patient gender. Decreasing TECG in these patients presenting atypically may hasten appropriate diagnosis and treatment thus improving these patient's outcomes and decreasing the morbidity and mortality associated with a delayed, incorrect, or missed diagnosis [11,17].

Parameter	n (%)
Typical Chief Complaint	
Chest Pain	129 (96.3)
Left arm Pain	1(0.7)
Dyspnea	15(11.2)
Atypical Chief Complaint	
Palpitations	8(4.8)
Jaw Pain	6(3.6)
Back Pain	64(38.6)
Epigastric Pain	20(12.1)
Nausea / Vomiting / Indigestion	60(36.1)
Weakness / Fatigue	32(19.3)
Syncope / Dizziness	11(6.6)

Table 1: Patient Chief Complaint Characteristics.

Parameter, n (%)	Atypical Chief Complaint	Typical Chief Complaint
Female	71 (23.7)	62 (20.7)
Patient Age		
18-49	104 (34.7)	67 (22.3)
50-64	32 (10.7)	32(10.7)
≥65	30 (10.0)	35 (11.7)
ED Presentation		
Time of the day		
Midnight to 7:59am	28 (9.3)	31 (10.3)
8:00am to 3:59pm	94 (31.3)	50 (16.7)
4:00pm to 11:59pm	44 (14.7)	53 (17.7)
Race		
White	111 (37.0)	89 (29.7)
African American	36 (12.0)	32 (10.7)
Other	19 (6.3)	13 (4.3)
ESI Triage Designation		
ESI 1-2	36 (12.0)	61 (20.3)
ESI 3-5	130 (43.3)	73 (24.3)
Arrival Type		
Walk-in	96 (32.0)	54 (18.0)
EMS	63 (21.0)	75 (25.0)
Not recorded	7 (2.3)	5 (1.7)
Insurance		
Private	43 (14.3)	28 (9.3)
Public	83 (27.7)	71 (23.7)
Private + Public	17 (5.7)	13 (4.3)
Self Pay	23 (7.7)	22 (7.3)

Table 2: Patient Demographics and Visit Information Related to Chief Complaint.

Currently the published literature lacks evidence based standardization of atypical presentations and the relationship of a range of those symptoms to the likelihood of ACS [13]. Our study begins to elucidate concerning delays in TECG for patients presenting with atypical symptoms of possible ACS regardless of gender. We have demonstrated an important link between delays in TECG and the typicality or atypicality of presenting symptoms of possible ACS, while calling into question the notion that patient gender is a primary factor in atypical presentation of possible ACS with an associated delay in TECG. A critical step in diagnosing and treating the undifferentiated population of both men and women with typical and atypical symptoms of ACS in the ED is obtaining a timely electrocardiogram. We plan to broaden the protocol driven Triage symptom criteria for timely ECG acquisition in our ED regardless of patient gender. Further investigating TECG and patient outcomes in this new larger pool of patients will evaluate effectiveness of casting a wider net.

Limitations

This study has several limitations. Firstly, the retrospective chart based approach to patient selection and data acquisition precluded our ability to understand the reasoning of triage nurses and clinicians who ordered the ECGs and made it impossible to consider dynamic changes in patient symptoms after initial evaluation but before ECG acquisition. Secondly, there were a surprising number of patients chosen for review

in our study who did not receive an ECG during their ED visit. We had not considered this possibility when we performed our power analysis when we were planning the study. Thus we may not have evaluated enough patients to show difference in TECG based on gender and atypical presentation. Fourthly, it is possible that our exclusion criteria may have led to our excluding patients from review who had a true ACS event. Fifthly, when the ECG was missing from the patient's chart, the time to ECG was taken from the recorded documentation in the nurses charting notes. This recorded time may have been inaccurate although it is unclear in which direction the error may have been introduced. Finally, our results are from a single, urban academic center with high patient volume. Our results may not be valid for other practice settings with different triage protocols for obtaining an ECG.

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