Sex-Based Differences in Diagnosis of Acute Coronary Syndrome

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Introduction

Acute coronary syndrome (ACS) is a term used to define a variety of conditions in which the muscle of the heart suffers from ischemia due to a sudden decrease in blood flow (Oosterhout et al. 2020a). It is the worlds leading cause of death, with over 9 million deaths in 2015 (Roth et al. 2017). ACS includes unstable angina (chest pain due to ischemia), non-ST-segment-elevation myocardial infarction (NSTEMI), or ST-segment-elevation myocardial infarction (STEMI). Despite being the leading cause of death for women as well as men, ACS in women is often overlooked due to "atypical" symptoms and the false perception that women are at lower risk (Oosterhout et al. 2020b). Prior meta-analyses have found that women with ACS experience a delay in time to treatment, are less likely to be treated invasively (such as with cardiac catheterization or surgery), and have worse short- and long-term all-cause mortality compared to males (Lunova, Komorovsky, and Klishch 2023).

The objective of this study was to compare men and women presenting to the emergency room with a chief complaint of "chest pain" to determine the percentage of women vs men diagnosed with acute coronary syndrome. A subanalysis to determine overall emergency department cost between the two genders was also performed. We hypothesize that due to the atypical nature of symptoms for women with ACS compared to men, that less women presenting with chest pain would receive a diagnosis of ACS. Additionally, we predicted that costs for women would be lower either due to less medical work-up for ACS or less aggressive treatment.

Methods

Study Design and Participants

This study was a retrospective review of patients treated at a single urban academic institution from January 1, 2015 to December 31, 2025. The research was approved by the Institutional Review Board. A query was run through the institution's electronic medical record of all

patients seen in the Emergency Department during this time period. When patients present to the Emergency Department, they provide a "chief complaint" to the triage registered nurse, which is documented in the electronic medical record. All patients who reported "chest pain" as their chief complaint were identified and included in this study. Adults age 18 and older were included and there was no upper age restriction. Patients who presented to the Emergency Department unable to voice a chief complaint (ex. if actively being resuscitated, non-verbal, intubated, etc.) were excluded. Patients who eloped without being seen by an emergency department provider were excluded.

Data Collection

After patients were identified through the electronic medical record as meeting inclusion criteria, a chart review was performed by a trained research team member. Variables collected included sex, age, history of smoking, final diagnosis, and cost of emergency department visit. These variables were documented and verified by a second research team member.

Definitions

In this case, sex was defined as biological sex at birth and treated as a categorical variable. History of smoking was self-reported by the patient and was defined as at least 20 pack-years (the equivalent to smoking an average of one pack (20 cigarettes) per day for 20 years), and who currently smoke or quit within the last 15 years. Age was documented at time of encounter. Emergency department cost was available within the electronic medical record and includes costs of laboratory and radiology tests, medications, provider services, hospital services, and any procedure costs.

Statistical Analysis

The primary outcome was diagnosis of acute coronary syndrome. We performed a Pearson's Chi-squared test for categorical variables and Wilcoxon rank sum test to compare the frequency of diagnosis of ACS between men vs women as well as median age, history of smoking, and cost of Emergency Department visit. Statistical significance was set at $p<0.05$ and analysis was performed using R Statistical Software (v4.4.1; R Core Team 2021).

A multivariate logistic regression comparing the incidence of ACS by sex, age, and history of smoking was performed. The equation is shown below. Y=Diagnosis of ACS, A is age as a continuous variable, B1 is the slope by sex (1=female, 0=male), and B3 is the slope by History of Smoking (0= No history of smoking, 1= history of smoking).

$$Y = \alpha + \beta_1(\text{sex}) + \beta_2(\text{age}) + \beta_3(\text{smoke}) + \varepsilon$$

Results

Cohort Overview

Of 120,000 patients who presented to the Emergency Department during the study time frame, 5,000 were identified as adult patients reporting chest pain as their chief complaint and were included in analysis. In regards to the overall cohort, 2,774 (55%) were female and 2,226 (45%) were male. The average age was 44 years, with an age range of 18 to 70 years. In the overall cohort, there were 250 diagnoses of ACS (5%), 789 (16%) patients had a history of smoking, and median cost was $9,143 (Interquartile range 8,874, 9,427). The minimum cost was $7,878 and the maximum cost was $10,790.

The multivariate model demonstrated that women had an associated decrease in the likelihood of a diagnosis of ACS of 0.088 units ($p<0.001$), whereas having a history of smoking was associated with a 0.141 unit increase in the likelihood of a diagnosis of ACS ($p<0.001$). Age was not significantly associated ($p=0.101$) (Table 1).

Analysis by Sex

When the cohort was compared by sex, the median age was similar; for women median age was 43 years and for men was 45 years ($p=0.064$) (Table 2). The rates for history of smoking were the same, at 16% in both cohorts ($p=0.9$). However, there was a significant difference in the rates of diagnosis of ACS between men and women; 9.9% (n=221) of men presenting with chest pain were diagnosed with ACS compared to 1.0% (n=29) of women (p=<0.001) (Table 2, Figure 1). Similarly, the cost of an Emergency Department visit was significantly higher for men ($9,300) compared to women ($9,013), p=<0.001 (Table 2, Figure 2).

Table 1: Table 1: Multivariate Model Results

	(1)
(Intercept)	0.063
	(0.010)
female	-0.088
	(0.006)
age	0.000
	(0.000)
smoke	0.141
	(0.008)
Num.Obs.	5000
R2	0.097
AIC	-1544.7
BIC	-1512.1
Log.Lik.	777.365
RMSE	0.21

Characteristic	**Female** N = 2,774[1]	**Male** N = 2,226[1]	**p-value**[2]
History of Smoking	436 (16%)	353 (16%)	0.9
Age	43 (30, 57)	45 (31, 57)	0.064
ACS	29 (1.0%)	221 (9.9%)	<0.001
Cost	9,013 (8,756, 9,281)	9,300 (9,045, 9,586)	<0.001

[1]n (%); Median (Q1, Q3)

[2]Pearson's Chi-squared test; Wilcoxon rank sum test

Figure 1: Number of Patients Diagnosed with ACS by Sex

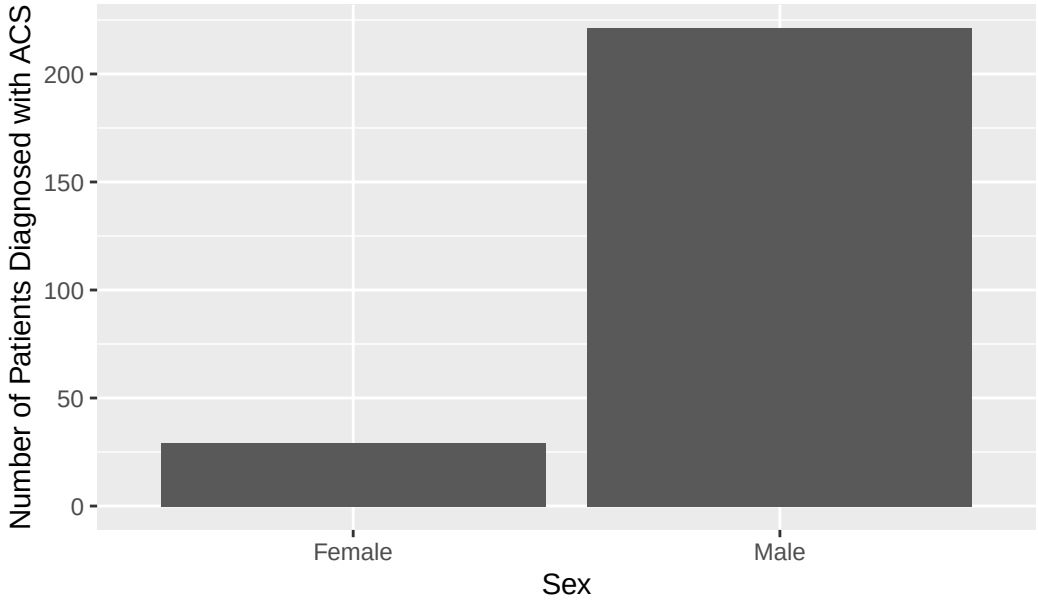
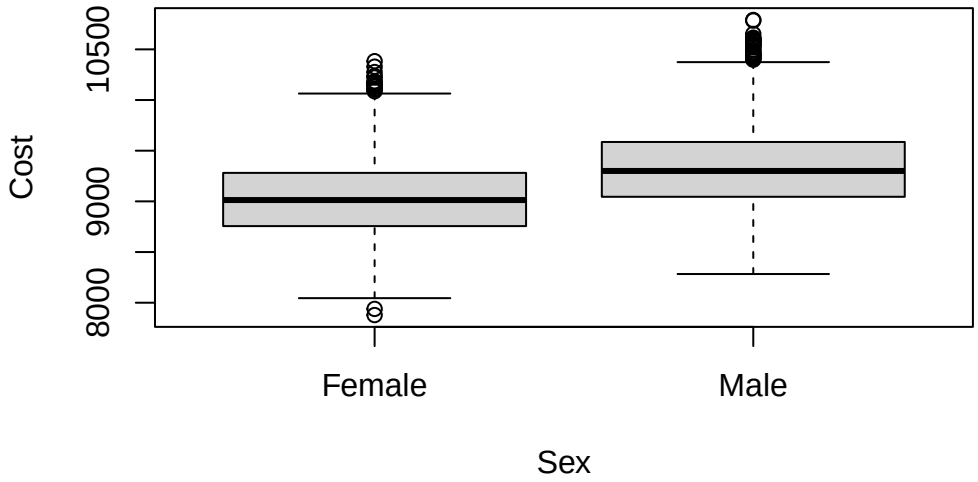


Figure 2: Average ED Visit Cost by Sex



Discussion

In this single institution cohort of patients presenting to the Emergency Department with Chest pain, female patients were less likely to be diagnosed with acute coronary syndrome compared to males, even though age and history of smoking were similar between groups. The overall cost of the Emergency Department visit was less for women compared to men, though from this data we are unable to determine why this may be the case.

These findings support prior work in the literature that demonstrate that women are less likely to be treated for acute coronary syndrome despite the fact that ischemic heart disease is the number one cause of mortality for women(Lunova, Komorovsky, and Klishch 2023). This has previously been attributed to differences in presenting symptoms; however, this study was unique in that all patients included presented with the same "classic" symptom of chest pain(DeVon, Mirzaei, and Zègre-Hemsey 2020). Therefore, further work is needed to determine what factors may play a role in this underdiagnosis of ACS in women. Prior studies have suggested there is inherent bias regarding women presenting with chest pain, and that they are more likely than men to be diagnosed with anxiety or other mental health disorders(Carmin et al. 2008).

This work is limited by the small number of variables collected; additional confounders such as family or personal history of heart disease, body mass index, or diabetes mellitus, were not included. Additionally, we do not have details of what tests were ordered to arrive at the final diagnosis. For example, we are unable to determine if women are not being diagnosed with ACS because they did not meet laboratory or electrocardiogram requirements for the diagnosis or if the appropriate tests were never ordered. Additionally, we do not have follow-up data to determine mortality or morbidity after initial Emergency Department visit. Finally, we do not have detailed cost-break down of the Emergency Department visit; it would be valuable to understand the amount of money being spent on laboratory or radiology tests vs treatment.

While these results are from a single institution they may be generalized to other urban high-volume academic institutions in the United States. Further work is needed to better understand the cause of these findings.

Conclusion

This large retrospective cohort study of 5,000 patients presenting to an urban academic Emergency Department with chief complaint of chest pain demonstrated that men had a much higher percentage of diagnosis of Acute Coronary Syndrome (9.9% vs 1.0%, $p<0.001$) and higher Emergency Department Visit costs despite similar risk factors of age and smoking history. This work raises questions regarding the rate at which women with a classic presenting symptom for ACS are accurately being diagnosed.

I did not use generative AI technology to complete any portion of this work.

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