Does Treatment Change with Gender in Acute Coronary Syndrome?

Ahmad Daraghmeh*, Roshni Shah, George Degheim, Nadir Rehman, Wadie David, Nicholas Tisdale, Shukri David

Abstract
Coronary artery disease (CAD) is the leading cause of death in women, with higher mortality and morbidity compared to men. We sought to evaluate whether an inequality in the primary medical treatment of acute myocardial infarction (AMI) exists in a sample population in a tertiary care hospital setting. There were no statistically significant differences in use of beta receptor blockers, aspirin, cholesterol lowering agent or clopidogrel in both genders. However, women were slightly more likely to receive angiotensin converting enzyme inhibitor. There is an extensive literature suggesting gender bias in the management of patients with AMI, with women being treated less intensively than men. Our research highlights the fact that there were no statistically significant differences in the AMI medical management. Clinical management of men and women with AMI is similar and should follow the standard of care recommended by the related guidelines.

Keywords — coronary artery disease, gender, treatment difference

Cite this article as: Daraghmeh A, Shah R, Degheim G, et al. Does Treatment Change with Gender in Acute Coronary Syndrome? JCvD 2014. In press

I. INTRODUCTION
Coronary artery disease (CAD) is the leading cause of death in women. It has higher mortality and morbidity compared to men, because of higher prevalence of comorbidities, baseline CAD risk factors and older age at the time of presentation (1-12). The incidence of acute myocardial infarction (AMI) in women, although lower than men, increases dramatically after the menopause (13).

The Global Burden of Disease study classified ischemic heart disease as the leading cause of global mortality. In 2010, the leading risk factors for global disease burden were arterial hypertension and tobacco smoking. The reason for the enormous burden of hypertension has been reported in numerous studies, showing that hypertensive disease is strongly associated with overall cardiovascular risk (25).

In one cohort study, women were found to be less likely to undergo diagnostic catheterization when present with AMI, less likely to receive thrombolytic therapy within 60 minutes and aspirin within 24 hours after arrival at the hospital and were less likely to be discharged on aspirin or beta-blockers when compared to men (17). These gender differences did not translate into differences in hospital outcome, but may highlight differences in quality of care and alarm the care providers for importance of performance improvement (16, 18). Other studies demonstrated that there are currently no gender biases in key cardiac interventions after AMI and that lower procedure rates for females were completely explained by their older age profile (22).

The evidence behind gender-based discrimination of care for patients with AMI is mixed and the results are very conflicting. We conducted this study to evaluate the inequality “if any” in the primary medical treatment of AMI that includes ST-elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI) between men and women in a tertiary hospital setting.

II. METHODS
Objective
We sought to determine whether women with acute myocardial infarction in the Southfield Providence Hospital and Medical Centers (PHMC) System receive the same medical therapeutic interventions as their male counterparts.

Study design
This is a observational, single center, retrospective study based on an electronic medical system review.

Null hypothesis
Women don’t get equal medical therapeutic intervention for AMI compared to men.

Subjects
Our study population included all adult patients > 18 years old admitted or discharged with the diagnosis of AMI at PHMC in Michigan between 2008 and 2012. The diagnosis of AMI was based on at least one cardiac enzyme assay result (Troponin I)
above twice the limit of normal, or AMI code as the principal diagnosis in the hospital patient administration system. Seven hundreds twenty one patients (485 men and 236 women) fulfilled the criteria, demographic and clinical data including CAD risk factors, left ventricular ejection fraction, use of the standard of care medications after AMI diagnosis and length of stay were gathered by reviewing the preeminent cardiovascular data repository (NCDR®). The (NCDR®) was developed in 1997 by the American College of Cardiology (ACC) for collecting and implementing clinical data in order to improve cardiovascular care (table 1). PHMC is a tertiary medical center is an active participant in the NCDR® registry data collection.

Statistical analysis

Patient characteristics and in-hospital medical treatments for men and women were compared using either the Mann-Whitney non-parametric test (for non-normal) or students’ T-test (for normal) continuous variables.

Categorical variables were compared utilizing the maximum likelihood Chi-square test. Significance was established at the 5% level. Statistical software for the analysis was statsoft STATISTICA ‘99 Edition.

III. RESULTS

Patients’ characteristics

AMI was confirmed in 236 women (32.7%) and 485 men (67.3%). Patient characteristics are shown in table (1). Men were younger than women (P= 0.00002), and significantly had a shorter hospitalization course and length of stay (P= 0.0009).

Women were more likely to have a history of hypertension, and diabetes, but less likely to have a history of smoking or high cholesterol compared to men. Figure (2) demonstrates the left ventricular ejection fraction distribution among the study sample population. Combined age and sex distribution for the study sample distribution is shown in figure (3).

Medical therapy before discharge

Treatment received in hospital is shown in table 2. There were no statistically significant differences in use of intravenous or oral beta receptor blockers (BB), aspirin (ASA), cholesterol lowering agent or Clopidogrel (Plavix) in both genders. However, women were slightly more likely to receive angiotensin converting enzyme inhibitor (ACEI). Women and men were both equal in the prevalence of AMI complicated by left ventricular dysfunction with an average left ventricular ejection fraction (47.9% in female group v 47.7% in male group with p=0.7875).

| General characteristics | Female (n.236) | Male (n.485) | P - value |
|--------------------------|---------------|--------------|-----------|
| Age (years) (Mean)       | 64.9          | 60.4         | 0.00002*  |
|                         | 63            | 60           | 0.00007*  |
| Length of stay (Mean)    | 3.8           | 2.8          | 0.0009*   |
|                         | 2             | 2            | 0.014*    |
| Ejection fraction % (Mean)| 47.9%          | 47.7%        | 0.7875    |
|                         | 50            | 50           | 0.58      |
| Hypertension (n, %)      | 200 (84.7%)   | 342 (70.5%)  | 0.00002*  |
| Diabetes Mellitus (n, %) | 94 (40%)      | 137 (28.24%) | 0.0019*   |
| Smoking (n, %)           | 84 (35.6%)    | 226 (46.6%)  | 0.0049*   |
| High cholesterol (n, %)  | 137 (58.05%)  | 290 (59.8%)  | 0.6552    |

* < 0.05 statistically significant
Figure (2): Ejection fraction distribution among the study sample population for the patients admitted with AMI

![Ejection fraction distribution](image)

Figure (3): Age and sex distribution among the study sample population admitted with AMI

![Age and sex distribution](image)

Table (2): Sex differences in treatment of AMI

| Medication used in the hospital for managing AMI | Female (n. 236) | Male (n. 485) | P-value |
|------------------------------------------------|----------------|---------------|---------|
| ASA                                            | 229 (97%)      | 474 (97.7%)   | 0.46    |
| PLAVIX                                         | 221 (93.6%)    | 454 (93.6%)   | 0.97    |
| BB                                             | 222 (94%)      | 458 (94.4%)   | 0.84    |
| ACEI                                           | 190 (80.5%)    | 360 (74.2%)   | 0.05    |
| STATIN                                         | 221 (93.6%)    | 456 (94%)     | 0.75    |

IV. DISCUSSION

There is an extensive literature suggesting gender bias in the management of patients with coronary artery disease, with women being treated less intensively than men \(^{(24)}\). Some studies showed that the clinical management of men and women after AMI was very similar \(^{(22)}\), but other studies have shown prominent differences \(^{(16)}\).

In setting of hospitalization for CAD, women were found to have a higher incidence of CAD risk factors like diabetes and systemic hypertension, were less likely to be smokers \(^{(14)}\) but they presented more frequently with heart failure due to diastolic dysfunction which may explain their higher unadjusted in-hospital mortality rates in AMI \(^{(15, 16 & 17)}\). Clinical management of men and women with AMI is similar and should follow the standard of care recommended by the related guidelines, though there are still small but significant differences in some areas.

Over the last decade, in-hospital AMI mortality rates declined for every age and sex group except males less than 55 years \(^{(19)}\). Higher risk of in-hospital mortality in younger women compared to younger men is more evident in patients presenting as STEMI \(^{(20)}\). There is an interaction between age and sex and it manifests as larger sex difference in younger than older patients. A large cohort study, showed that women with AMI arrived later at the emergency department, were less likely to be given aspirin therapy acutely, and had longer door-to-needle times \(^{(21)}\). Also on the day of discharge from the hospital, they were less likely to be prescribed beta-blockers. The above evidence showed some signals that indicate the in-equalities in management of women compared to men.

Accumulating literature evidence showed that women receive less medical and invasive treatments after AMI compared with men \(^{(15, 17, 21)}\). On the other hand, other investigators showed that in a sample of population included patients admitted with AMI for the first time without significant stenosis based on diagnostic heart catheterization, women were found to share the same prospects as men regarding long-term prognosis and the extent of secondary preventive medical treatment \(^{(23)}\).

Many investigators have reported higher rates of coronary interventions for males when compared to females after AMI that may indicate more aggressive management for males \(^{(14)}\). However, others have reported no significant gender differences, whether the MI alert was initiated in the ED or in the prehospital field, after controlling for age, resulting in uncertainty about the existence of a true gender bias in cardiac care \(^{(22)}\).

Our research highlighted the fact that there were no statistically significant differences in the AMI medical management including the use of aspirin, beta-blockers, Plavix or statin between both genders and that the average length of stay for women with AMI in the hospital was higher than male. Women in our study were slightly more likely to receive ACE inhibitors despite the fact that both genders are equal in the prevalence of AMI complicated by left ventricular dysfunction with an average left ventricular ejection fraction (47.9% in female group v 47.7% in male group with p=0.7875).
Our findings of the initial clinical profile between both genders were congruent with findings from large national and global studies. A study using data from the Global Registry for Acute Coronary Events (GRACE) that examined 43,393 patients (14,180 women and 29,213 men) with acute coronary syndromes from 14 countries observed similar patterns. In the GRACE study, women with ACS were more likely to be older, have higher rates of hypertension, diabetes, whereas men were more likely to smoke (16).

Limitations of our study were: a) retrospective b) nonrandomized c) conducted in a single center. However, the results can be generalized to other hospitals in the same region. Patients were unselected and are from an area of mixed ethnic origin and social status. The physicians treating those patients were not aware that we would be examining treatment differences by sex.

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