# Women Who Experience Myocardial Infarction at a Young Age Have Worse Outcomes Compared With Men: Results From the YOUNG MI Registry

# Women Who Experience Myocardial Infarction at a Young Age Have Worse Outcomes Compared with Men: Results from the YOUNG MI registry

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## ABSTRACT

**Background**: Prior studies have highlighted known sex differences among patients experiencing a myocardial infarction (MI), but there is a scarcity of data regarding young patients presenting with a first MI, particularly regarding long-term outcomes. Our aim was to investigate differences in risk factors, clinical presentation, management, and all-cause mortality among men and women who experience their first MI at a young age.

**Methods**: We retrospectively included all consecutive patients with age ≤ 50 years, presenting to two large medical centers with a Type 1 MI from 2000 through 2016. The presence and type of MI was adjudicated based on the Third Universal Definition on MI. Vital status was identified by the Social Security Administration's Death Masterfile. Cause of death was adjudicated using electronic health records and death certificates.

**Results**: 2097 individuals had an MI (mean age 44±5.1 years, 73% white, 53% STEMI) with median follow-up of 11.2 years (interquartile range: 7.3-14.2). Women presented with greater risk factor burden and had a longer median length of stay (4.0 vs. 3.0 days, p=0.012). Women were less likely than men to undergo invasive coronary angiography (93.5% vs. 96.7%, p=0.003) and coronary revascularization procedures (82.1% vs. 92.6%, p<0.001), and were less likely to be discharged with appropriate post-MI medications. While there was no significant difference in hospital mortality between men and women, among those who survived to hospital discharge, women had a higher long-term mortality (adjusted HR=1.51, p=0.009).

**Conclusions**: Women who experienced their first MI under the age of 50 had a higher burden of traditional risk factors compared to men, and were less likely to be undergo coronary revascularization and treated with guideline-directed post MI medical therapies. Furthermore, women who survived hospitalization experienced significantly higher all-cause mortality than

men. A better understanding of the mechanisms underlying these disparities may lead to improved care for young women with cardiovascular disease.

## INTRODUCTION

Even in the contemporary era, sex differences in presentation, treatment and outcomes of myocardial infarction (MI) have been well-demonstrated in the cardiovascular literature. Studies have shown that women present with MI at a later age, with greater risk factor burdens, and with worse outcomes(1-9). Women are also less likely than men to receive standard-of-care therapies, including invasive coronary angiography and reperfusion, and to be prescribed necessary cardiovascular medications at discharge (10,11). However, most studies on sex differences have primarily focused on older populations. There is a scarcity of data regarding MI in young people. Such data is especially important because patients younger than 55 years of age presently account for 23% of all patients with acute coronary syndrome in the United States(12). Furthermore, while the rates of MI have been declining overall in the United States, rates of MI in young people have not seen similar decreases(13).

While most reports suggest that young women who experience an MI have significantly worse long-term mortality compared with men (14-19), other studies find no such significant differences after adjustment for age, comorbidities and treatment (20-23). These contradictions emphasize the need to better understand sex differences in outcomes among young individuals following acute MI. Our aims were to investigate differences in risk factors, clinical presentation, , hospital management, and long-term mortality among men and women who experience their first MI at a young age.

## METHODS

### Study Population

The design of the YOUNG-MI registry has been previously described (24). In brief, this is a retrospective cohort study from Brigham and Women's Hospital and Massachusetts General Hospital that included patients who experienced a first MI at or before 50 years of age. All records were adjudicated by a team of study physicians, as previously described (24), using the Third Universal definition of MI (25). For the present analysis, only patients with Type 1 MI were included. Individuals with known coronary artery disease (CAD), defined as prior MI or revascularization, were excluded.

### Risk Factors

Presence of cardiovascular risk factors was ascertained by a review of electronic medical records during or before the index admission. Hypertension was defined as a systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or diagnosis/treatment of hypertension. Diabetes was defined as fasting plasma glucose >126 mg/dl or hemoglobin A1c ≥6.5% or diagnosis/treatment for diabetes. Diabetic complications ascertained included nephropathy, neuropathy, and retinopathy. Dyslipidemia was defined as diagnosis or treatment of dyslipidemia prior to MI. Obesity was defined as a body mass index ≥ 30 $kg/m^2$ or a diagnosis of obesity. Peripheral artery disease was defined as prior peripheral arterial revascularization or a diagnosis of peripheral artery disease or limb claudication.

Family history of premature CAD was defined as stroke, MI, or CABG occurring before age 55 years for male family members and before age 65 years for female family members, in

first-degree relatives. Depression was defined by a prior diagnosis/treatment of depression. Rheumatologic conditions consisted of a documented history of either systemic lupus erythematosus or rheumatoid arthritis. Smoking status was defined as current (tobacco products used within the last month), former, or never. Illicit substance use was defined as history of using marijuana or cocaine, , as documented by admission notes or detected on toxicology.

**Hospital Presentation**

Time-to-hospital-presentation was defined as time from most recent episode of angina or anginal equivalent to time of presentation. Stuttering chest pain was defined as chest pain that occurred intermittently in the day(s) leading up to presentation (26); intervals were defined as: none, <1 day, 1-3 days, 4-7 days, or >7 days, unknown. Other symptoms such as shortness of breath, radiation to arm/jaw/neck, palpitations, heartburn, nausea, and fatigue were identified through review of admission notes.

Physical examination findings were identified from review of admission documentation, and included: jugular venous distension (JVD), crackles/pulmonary edema, pedal edema, no congestive heart failure (CHF) symptoms, and unknown, if insufficient information regarding physical examination was provided.

**Outcomes**

Our primary outcome was all-cause death. Vital status of the study patients at follow-up was assessed using the Social Security Administration's Death Master File, the Massachusetts Department of Vital Statistics, as well as a longitudinal follow-up within our electronic health

records system. Non-deceased patients were censored on the date of querying the Death Master File.

Death was recorded as occurring in-hospital or post-discharge. Secondary outcomes included cardiovascular mortality, and in-hospital mortality. The cause of death was categorized into cardiovascular death, non-cardiovascular death, or undetermined cause of death. If cause of death was unable to be determined, patients were conservatively analyzed as non-cardiovascular death. The definition of cardiovascular death was adapted from the 2014 ACC/AHA definitions for cardiovascular endpoint events (27) and was previously detailed in the study design publication (24) . Cardiovascular deaths included death from a cardiovascular cause within 30 days of acute MI, heart failure, sudden cardiac death, ischemic stroke, non-traumatic hemorrhagic stroke, immediate complications of a cardiovascular procedure, cardiovascular hemorrhage, and other cardiovascular causes such as pulmonary embolism or peripheral arterial disease.

**Data management**

Study related data for all patients who met inclusion criteria were stored on our customized secure electronic adjudication system and REDCap, an electronic data capture platform. The YOUNG-MI registry has been approved by the Institutional Review Board at Partners HealthCare.

**Statistical analysis**

Categorical variables are reported as frequencies or proportions and compared with the chi-square test or Fisher's exact test, as appropriate. Continuous variables were reported as mean with standard deviation or median with interquartile range and compared with a t-test or non-parametric Mann-Whitney U test, as appropriate. Cox proportional hazards modeling was

performed for all cause death and cardiovascular death. Patients were censored on the date of querying the Social Security Administration Death Master File or Massachusetts State Department of Vital Statistics.

We constructed Kaplan-Meier failure curves for all patients as well as those who survived hospitalization to illustrate time-to-death. Multivariable models were constructed to assess whether sex is an independent predictor of treatment with invasive coronary angiography, all-cause mortality and cardiovascular mortality. Variables for each model were selected based on examining the univariate association of each variable with the outcome of interest, as well as selecting clinically relevant variables that have a known association with the outcome of interest. The socioeconomic status was estimated based on median incomes for the patient's designated zip code (US Census). In order to adjust for comorbidities, we also calculated the Charlson Comorbidity Index (CCI) for each patient, which is a method of predicting the risk of mortality based on co-morbidities of patients, as determined by ICD diagnosis codes. The CCI was computed by applying the Charlson command within STATA to the set of International Classification of Diseases (ICD), ninth revision, billing codes associated with the index hospitalization(28). For patients within the sample who were not coded for MI, we added an additional ICD code of "410" – the ICD-9 code corresponding to acute myocardial infarction – prior to calculating the CCI. The variables in the score include age, diabetes mellitus, liver disease, solid tumor, AIDS, presence of moderate to severe chronic kidney disease, congestive heart failure, myocardial infarction, chronic obstructive pulmonary disease, peripheral vascular disease, cerebrovascular event or transient ischemic attack, dementia, hemiplegia, connective tissue disease, leukemia, malignant lymphoma, and peptic ulcer disease.

## RESULTS

### Study Population

Our study population consisted of 2097 patients with a first-MI, of whom 404 (19%) were women and 1693 (81%) were men. The median age was 45 (interquartile range 41-48), 1531 (73%) were White, and 1121 (53%) had STEMI.

### Risk Factors

Baseline characteristics stratified by sex are provided in **Table 1**. Women had a significantly higher proportion of diabetes (21.4% vs 14.6%, $p < 0.001$), obesity (40.3% vs 31.9%, $p = 0.03$), rheumatologic conditions (6.7% vs 1.3%, $p < 0.001$), and depression (24.0% vs 10.3% $p < 0.001$) compared to men. In addition, women had a significantly higher mean CCI (1.8 vs 1.5, $p < 0.001$). Men were significantly more likely to have hyperlipidemia (62.6% vs 44.8%, $p < 0.001$).

Of those with diabetes, women were significantly more likely to be on insulin therapy (57.9% vs. 37.5%, $p < 0.001$), to have had the diagnosis for 10 years or longer (61.3% vs. 29.1%, $p < 0.001$), and to have experienced diabetic complications. Substance abuse was less prevalent in women, (11.4% vs. 7.7%, $p < 0.001$). Notably, family history of premature CAD was common, and was present in 28.6% (n=116) of women and 27.5% (n=465) of men (p=0.63). **Figure 1** illustrates prevalence of risk factors stratified by sex.

### Sex Differences in Hospital Presentation

Most women (68.1%) and men (68.0%) presented to the hospital within 6 hours of their last onset of symptoms. Chest pain was the most common presenting symptom in both men

(90%) and women (88%), p = 0.25. However, women were significantly more likely to present with atypical symptoms, including shortness of breath (36.5% vs 31.0%, p = 0.03), palpitations (7.2% vs 2.8%, p < 0.001) and fatigue (5.4% vs 2.7%, p = 0.007). See **Figure 2**. More than half of men (54.5%) and women (51.4%) experienced stuttering chest pain prior to presentation (p=0.26). Notably, up to 16.5% (n=66) of women and 15.8% (n=262) of men had greater than 7 days of stuttering pain (p=0.76) prior to their presentation.

**Acute MI Care**

When examining in-hospital length of stay, women had longer lengths-of-hospital-stay compared to men (4 days vs. 3 days, p=0.012).

Women were less likely than men to undergo invasive coronary angiography (93.5% vs. 96.7%, p=0.003) (**Table 3**). The difference persisted in both women with STEMI (96.8% vs. 98.2%, p=0.227) as well as those presenting with NSTEMI (90.4% vs. 95.0%, p=0.020), however these differences did not persist in a multivariable model (**Supplemental Table 1**).

Similarly, women were also less likely to undergo coronary revascularization than men (82.1% vs. 92.6%, p<0.001). This difference persisted for both women presenting with STEMI (87.7% vs. 96.2%, p<0.001) and those presenting with NSTEMI (77.0% vs. 87.9%, p<0.001).

**Medications at Discharge**

Women were significantly less likely to be discharged on guideline-directed medical therapy, including beta-blockers (86.7% vs. 90.3%, p = 0.03), ACE inhibitors/ARBs (52.8% vs. 62.4%, p < 0.001), and statins (82.4% vs. 88.4%, p = 0.002), as shown in Table 3. There were

no significant differences in prescriptions for aspirin and P2Y12 inhibitors at discharge, or referrals to cardiac rehabilitation.

**All-cause death and cardiovascular death**

Over a median follow-up time of 11.2 years (interquartile range: 7.3-14.2), there were 254 (12%) deaths in our cohort, representing 14% of women and 11% of men (p=0.087). When examining all patients in our cohort, including those who died in the hospital, there was a strong trend for women to have higher all-cause death compared with men was (HR=1.338, p=0.053). After adjustment for baseline covariates, the hazard ratio increased to 1.432, p=0.032. **See Table 4, Figure 3**. When analyzing sex based difference in cardiovascular death among all patients (including those who died in the hospital), there was no significant differences by sex, 5.9% vs. 5.2%, p=0.64.

While 38 (2.2%) men and 5 (1.2%) women died while in-hospital, these differences were not statistically significant (p=0.24). When examining only patients who survived their initial hospitalization, women had higher all-cause mortality (the unadjusted hazard ratio =1.511, p=0.009. After adjustment for baseline covariates, the hazard ratio attenuated to 1.477, but remained significant (p=0.025). **See Table 5, Figure 4**. Analysis for cardiovascular death did not show any significant differences between men and women, 4.3% vs. 4.5%, p=0.862.

## DISCUSSION

Our study is one of the largest to examine differences in long term outcomes between young men and women presenting with a first MI. Over a median follow-up of 11.2 years, young women who survived their initial hospitalization had significantly worse all-cause mortality when compared with young men. This finding remained significant even after adjustment for

important differences in baseline characteristics, laboratory values, and treatment. Our study found that women were less likely to undergo invasive coronary angiography, less likely to be treated with coronary revascularization, less likely to be prescribed statins and beta blockers upon discharge.

While many studies found that young women have significantly worse long-term mortality compared with men (14-19), other studies found no such significant differences after adjustment for age, comorbidities and treatment (20-23). Our study – one of the largest to examine sex differences in long-term mortality following a first MI at a young age – shows that even after adjustment for differences in risk factors and treatment, women have a higher long term all-cause mortality. While these differences may be due to underlying baseline differences in risk factors, and treatment that we are unable to account for, our results suggest that there may be inherent excess risk in young women.

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Prior studies have shown that women who experience an MI – irrespective of age -- are more likely to present with greater risk factor burden, are more likely to present with atypical symptoms, and are less likely to receive invasive therapies when compared with men (29-31). Our study extends these prior results by showing that these differences in presentation and treatment are also found in young women, when compared to young men.

*Potential Mechanism for increased risk*

There are several possible mechanisms to explain these differences. A plausible explanation is that estrogen has cardioprotective effects in premenstrual young women (32). Therefore, in order for women to have an MI, this protective effect may have to be overridden by a higher burden of risk factors, which may include both measured and unmeasured factors.

*Potential Mechanism for differences in invasive coronary angiography and coronary revascularization*

Young women are also known to have a higher incidence of non-obstructive coronary atherosclerosis, smaller coronary vessels, and microvascular dysfunction compared with men. These findings likely reflect different patterns of atherosclerosis between men and women, which have been documented in prior studies (33-35). Some of these patterns of disease may be associated with increased risk and thus could account for some of the excess risk observed in our study.

Since our study did not evaluate data from cardiac angiography, we cannot ascertain if women received lower rates of revascularization due to appropriate or inappropriate clinical decision-making. For instance, in addition to having more non-obstructive CAD, women are also more likely to have MI related to spontaneous coronary artery dissections, a condition which generally is not treated with revascularization. Nevertheless, women were also less likely to undergo invasive coronary angiography, and these differences persisted even after accounting for possible confounders. A potential explanation for these differences in treatment is that there is physician bias related to the evaluation and treatment of women,(40), which leads to women receiving fewer therapies than their male counterparts.

Women had less coronary revascularization, in part because they had less invasive coronary angiography. Additionally, studies have shown that women are less likely to undergo coronary revascularization when compared with men. In part this may be due referral bias, as well as technical reasons. For example, women have smaller coronary vessels which may make it more technically challenging to perform percutaneous or surgical coronary revascularization (4,36-39)

*Comparison with the VIRGO study*

The Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients Study (VIRGO study) (32) is the largest prospective observational study of young patients (⩽55 years) hospitalized for MI ($n$ = 3501). The study demonstrated that young women presenting with MI had higher risk factor burdens, more delays in presentation, were less likely to undergo revascularization procedures, and were less likely to receive timely primary reperfusion therapies (31,32,41). However, VIRGO only examined patients for 1-year post-MI, and did not report any data on differences in mortality between men and women due to a low event rate.

In many respects, our study complements VIRGO's important contributions by providing long term data. In addition, our study design allowed to us to include all patients presenting to our healthcare with MI, while the VIRGO study only include patients who were able to provide informed consent. Consequently, we included sicker patients who are often the ones who are unable to provide informed consent(32).

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*Limitations*

There are several limitations to our study which deserve mentioning. While our study utilized careful chart reviews to identify all known risk factors, laboratory values, and therapies provided, we were unable to account for some of the potential variables that may be associated with outcome or patient management. For instance, we did not have data on invasive angiography findings, patient preferences (42), or psychosocial factors (43)-- all important variables that have an important impact on patient outcomes.

However, our retrospective design, did allow us to include a large number of young patients experiencing their first MI, and enrolling a similar number of patients using a

prospective design would take over 15 years to conduct.

Our cohort included a smaller proportion of women with MI than men, as would be expected for a younger population of patients with MI. Thus, our power to assess for differences in cardiovascular mortality was limited. Furthermore, our ability to access for sex differences in in-hospital mortality was likely impeded by too few deaths. We also did not account for pre-hospital deaths, further limiting our ability to study early mortality in young patients with MI.

The association between patient sex and cardiovascular outcomes may be driven by confounders including lifestyle and behavioral factors. While we adjusted for an extensive array of baseline co-variates including demographics, comorbidities, laboratory values, revascularization procedures, and medications, we realize that other unmeasured confounders may remain.

*Conclusion*

In summary, women who experienced their first MI under the age of 50 had a higher burden of traditional risk factors compared to men, and were less likely to be treated with coronary revascularization and guideline-directed post MI medical therapies. Furthermore, women who survived hospitalization experienced significantly higher all-cause mortality than men. Future studies should seek to understand the mechanisms underlying these disparities, leading to improved care for young women with cardiovascular disease.

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**Table 1: Baseline Risk Characteristics by Sex**

| Baseline Risk Characteristics by Sex | | | |
|---|---|---|---|
| **Name** | **Men (n=1693) 81%** | **Women (n=404) 19%** | **p-value** |
| **Demographics** | | | |
| Age at Event, Median IQR | 45.0 (41.0,48.0) | 45.0 (42.0,48.0) | 0.99 |
| White | 1241 (73.3%) | 290 (71.6%) | 0.49 |
| STEMI | 934 (55.2%) | 187 (46.2%) | **0.001** |
| Length of stay, median (IQR) | 3.0 (2.0, 5.0) | 4.0 (2.0, 6.0) | **0.015** |
| Charlson Index, mean (SD) | 1.5 (0.9) | 1.8 (1.3) | **<0.001** |
| **Income** | | | |
| Median (IQR), in dollars | 72568 (54883, 87412) | 65334 (50865, 83438) | **<0.001** |
| Lower Tertile | 76 (4.5%) | 22 (5.4%) | **0.006** |
| Middle Tertile | 1048 (61.9%) | 279 (69.1%) | **0.006** |
| High Tertile | 569 (33.6%) | 103 (25.5%) | **0.006** |
| **Past Medical History** | | | |
| Hypertension | 775 (46.3%) | 195 (48.5%) | 0.42 |
| Dyslipidemia | 1049 (62.6%) | 180 (44.8%) | **<0.001** |
| Diabetes | 244 (14.6%) | 86 (21.4%) | **<0.001** |
| Former Smokers | 237 (14.2%) | 40 (9.9%) | **0.025** |
| Current Smokers | 843 (50.4%) | 223 (55.3%) | 0.073 |
| Substance Abuse | 342 (20.2%) | 54 (13.4%) | **<0.001** |
| Obesity | 454 (31.9%) | 150 (40.3%) | **0.003** |
| Peripheral Vascular Disease | 34 (2.0%) | 7 (1.7%) | 0.71 |
| Sleep Apnea | 93 (5.6%) | 15 (3.7%) | 0.14 |
| Depression | 167 (10.3%) | 93 (24.0%) | **<0.001** |
| Rheumatologic Diseases | 21 (1.3%) | 27 (6.7%) | **<0.001** |
| Family History of Premature CVD | 465 (27.5%) | 116 (28.6%) | 0.63 |
| **Laboratories (in mg/dL)** | | | |
| Normalized troponin, median (IQR) | 43.7 (11.6, 150.7) | 30 (7.0, 148.5) | **0.015** |
| Creatinine, mean (SD) | 1.1 (0.4) | 0.9(0.4) | **<0.001** |
| Total Cholesterol, mean (SD) | 193.6 (56.8) | 186.8 (55.2) | **0.042** |

| | | | |
|---|---|---|---|
| LDL cholesterol, mean (SD) | 120.4 (46.7) | 114.0 (47.0) | **0.021** |
| HDL Cholesterol, mean (SD) | 36.2 (9.3) | 39.9 (13.1) | **<0.001** |
| Triglycerides, median (IQR) | 155.0 (105.0, 228.0) | 130.0 (89.0, 187.0) | **<0.001** |

**Table 2: Presentation Characteristics by Sex**

| Presentation Characteristics by Sex | | | |
|---|---|---|---|
| **Name** | **Men** | **Women** | **p-value** |
| **Symptoms** | | | |
| Chest Pain | 1485 (89.9%) | 352 (88.0%) | 0.25 |
| Shortness of Breath | 524 (31.0%) | 148 (36.5%) | **0.030** |
| Radiation to arm/jaw/neck | 710 (41.9%) | 204 (50.4%) | **0.002** |
| Palpitations | 47 (2.8%) | 29 (7.2%) | **<0.001** |
| Heartburn | 146 (8.6%) | 37 (9.1%) | 0.77 |
| Nausea | 689 (40.7%) | 185 (45.7%) | 0.068 |
| Fatigue | 45 (2.7%) | 22 (5.4%) | **0.007** |
| Pain at Rest | 383 (22.6%) | 92 (22.7%) | 0.97 |
| **Time to Hospital Presentation** | | | |
| < 6 hours | 1124 (68.0%) | 273 (68.1%) | 0.96 |
| 6-24 hours | 236 (14.3%) | 55 (13.7%) | 0.78 |
| 1-3 days | 56 (3.4%) | 16 (4.0%) | 0.55 |
| > 3 days | 36 (2.2%) | 7 (1.7%) | 0.59 |
| Unknown | 202 (12.2%) | 50 (12.5%) | 0.89 |
| **Stuttering of Chest Pain** | | | |
| None | 753 (45.5%) | 195 (48.6%) | 0.26 |
| < 1 day | 188 (11.4%) | 47 (11.7%) | 0.84 |
| 1-3 days | 167 (10.1%) | 34 (8.5%) | 0.33 |
| 4-7 days | 142 (8.6%) | 24 (6.0%) | 0.086 |
| > 7 days | 262 (15.8%) | 66 (16.5%) | 0.76 |
| Unknown | 202 (12.2%) | 50 (12.5%) | 0.89 |
| **Physical Exam** | | | |
| Elevated JVD | 47 (2.8%) | 14 (3.5%) | 0.46 |
| Crackles/Pulmonary Edema | 113 (6.7%) | 39 (9.6%) | **0.039** |
| Pedal Edema | 49 (2.9%) | 24 (5.9%) | **0.003** |
| No CHF Findings | 1268 (74.9%) | 295 (72.8%) | 0.39 |
| Unknown | 205 (12.1%) | 43 (10.6%) | 0.40 |

**Table 3: In-Hospital and Discharge Care**

| In-Hospital and Discharge Care | | | |
|---|---|---|---|
| **In-Hospital Cardiac Procedures** | | | |
| | **Men** | **Women** | **p-value** |
| Catheterization Performed | 1597 (96.7%) | 375 (93.5%) | **0.003** |
| Revascularization Performed | 1479 (87.4%) | 307 (76%) | **<0.001** |
| PCI | 1308 (77.3%) | 266 (65.8%) | **<0.001** |
| CABG | 145 (8.6%) | 32 (7.9%) | 0.77 |
| POBA | 26 (1.5%) | 9 (2.2%) | 0.38 |
| **In-Hospital Events** | | | |
| In-Hospital Mortality | 38 (2.2%) | 5 (1.2%) | 0.244 |
| **Medications at Discharge** | | | |
| Aspirin | 1576 (93.1%) | 369 (91.1%) | 0.17 |
| P2Y12 Inhibitors | 1270 (75.0%) | 293 (72.3%) | 0.27 |
| Beta-Blocker | 1528 (90.3%) | 351 (86.7%) | **0.034** |
| Spironolactone | 45 (2.7%) | 12 (3.0%) | 0.73 |
| ACE Inhibitor | 1056 (62.4%) | 214 (52.8%) | **<0.001** |
| Statin | 1497 (88.4%) | 334 (82.5%) | **0.002** |
| Rehab after First MI | 188 (11.1%) | 36 (8.9%) | 0.19 |

**Table 4: All-Cause Mortality for All Patients (Including Patients with In-Hospital Death)**

| ALL-CAUSE MORTALITY | | | | |
|---|---|---|---|---|
| | UNIVARIATE | | MULTIVARIATE | |
| **Factor** | **Hazard Ratio** | **p-value** | **Hazard Ratio** | **p-value** |
| Female Sex | 1.338 | 0.053 | 1.437 | 0.031 |
| Age at Event | 1.034 | 0.018 | 1.032 | 0.055 |
| Hypertension | 1.586 | <0.001 | 1.352 | 0.047 |
| Diabetes | 2.268 | <0.001 | 1.856 | <0.001 |
| Obesity | 1.082 | 0.593 | -- | -- |
| Peripheral Vascular Disease | 5.464 | <0.001 | 1.991 | 0.023 |
| Sleep Apnea | 1.130 | 0.668 | -- | -- |
| Depression | 1.266 | 0.205 | -- | -- |
| Rheumatologic Diseases | 1.758 | 0.097 | -- | -- |
| Family History of CVD | 0.698 | 0.036 | -- | -- |
| Current Smoking | 1.129 | 0.351 | -- | -- |
| Substance Abuse | 1.508 | 0.006 | 2.054 | <0.001 |
| Statin at Discharge | 0.285 | <0.001 | 0.519 | 0.001 |
| P2Y12 Inhibitors at Discharge | 0.422 | <0.001 | 0.667 | 0.030 |
| Beta-Blockers at Discharge | 0.364 | <0.001 | -- | -- |
| ACE Inhibitors/ARBs | 1.530 | 0.127 | -- | -- |
| Invasive Coronary Angiography Performed | 0.386 | <0.001 | 0.877 | 0.694 |
| Revascularization Performed | 0.544 | <0.001 | 0.844 | 0.497 |
| Length-of-Stay (days) | 1.044 | <0.001 | 1.026 | 0.003 |
| LDL Cholesterol (mg/dL) | 0.997 | 0.103 | -- | -- |
| HDL Cholesterol (mg/dL) | 0.969 | <0.001 | 0.977 | 0.004 |
| Triglycerides (mg/dL) | 1.000 | 0.002 | -- | -- |
| Creatinine (mg/dL) | 2.383 | <0.001 | 1.482 | <0.001 |

**Table 5: All-Cause Mortality for All Patients (Excluding Patients with In-Hospital Death)**

| ALL-CAUSE MORTALITY POST-DISCHARGE | | | | |
|---|---|---|---|---|
| | UNIVARIATE | | MULTIVARIATE | |
| **Factor** | **Hazard Ratio** | **p-value** | **Hazard Ratio** | **p-value** |
| Female Sex | 1.511 | 0.009 | 1.481 | 0.024 |
| Age at Event | 1.039 | 0.015 | 1.025 | 0.149 |
| Hypertension | 1.825 | <0.001 | 1.478 | 0.015 |
| Diabetes | 2.309 | <0.001 | 1.767 | 0.001 |
| Obesity | 1.111 | 0.502 | -- | -- |
| Peripheral Vascular Disease | 5.99 | <0.001 | 2.778 | 0.001 |
| Sleep Apnea | 1.139 | 0.675 | -- | -- |
| Depression | 1.379 | 0.100 | -- | -- |
| Rheumatologic Diseases | 1.383 | 0.434 | -- | -- |
| Family History of CVD | 0.777 | 0.160 | -- | -- |
| Current Smoking | 1.190 | 0.218 | 1.281 | 0.120 |
| Substance Abuse | 1.781 | 0.006 | 1.965 | 0.002 |
| Statin at Discharge | 0.526 | <0.001 | 0.857 | 0.521 |
| P2Y12 Inhibitors at Discharge | 0.647 | 0.005 | 0.912 | 0.654 |
| Beta-Blockers at Discharge | 1.067 | 0.805 | -- | -- |
| ACE Inhibitors/ARBs | 1.193 | 0.229 | -- | -- |
| Invasive Coronary Angiography Performed | 0.491 | 0.002 | 0.858 | 0.673 |
| Revascularization Performed | 0.599 | 0.003 | 0.688 | 0.151 |
| Length-of-Stay (days) | 1.045 | <0.001 | 1.038 | <0.001 |
| LDL Cholesterol (mg/dL) | 1.000 | 0.799 | -- | -- |
| HDL Cholesterol (mg/dL) | 0.982 | 0.03 | 0.989 | 0.201 |
| Triglycerides (mg/dL) | 1.002 | 0.187 | -- | -- |
| Creatinine (mg/dL) | 2.114 | <0.001 | 1.479 | 0.001 |

**Figure 1: Risk Factors by Sex**

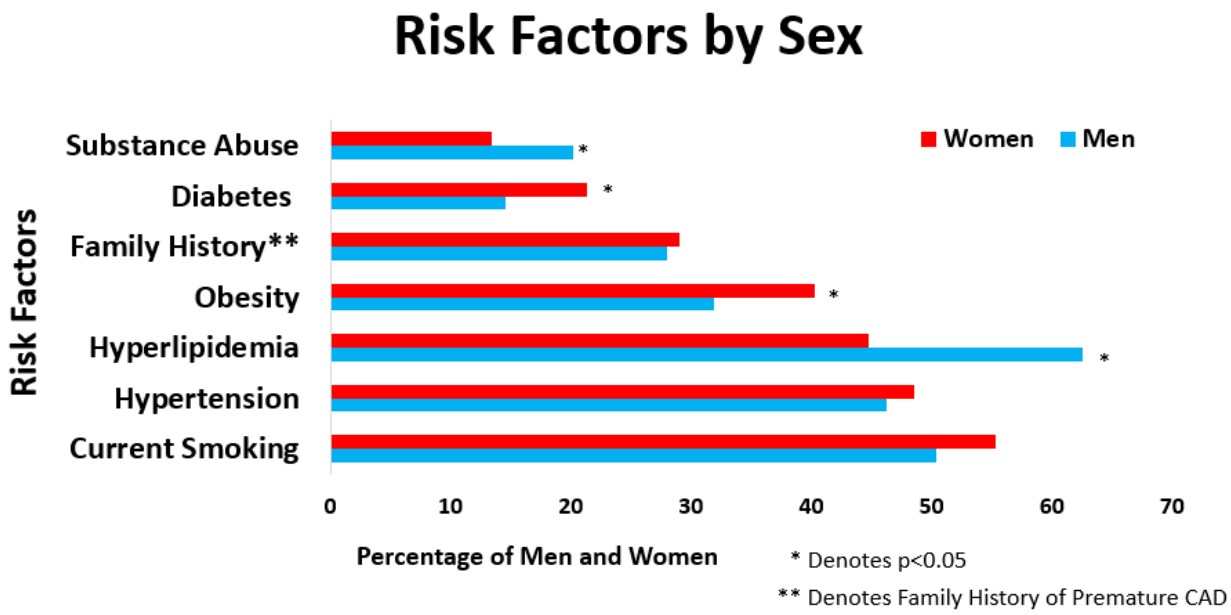


**Figure 2: Presentation Symptoms by Sex**

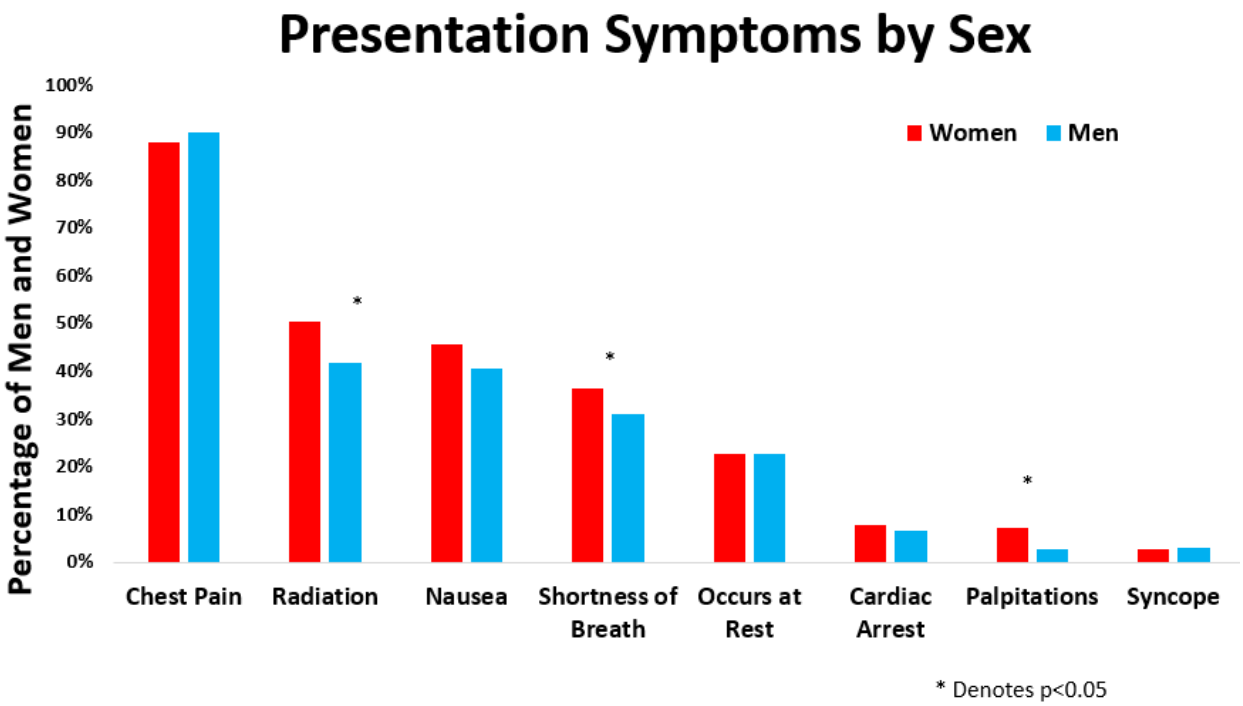



**Figure 3: Kaplan-Meier Failure Estimates for All-Cause Death (Including Patients with In-Hospital Death)**

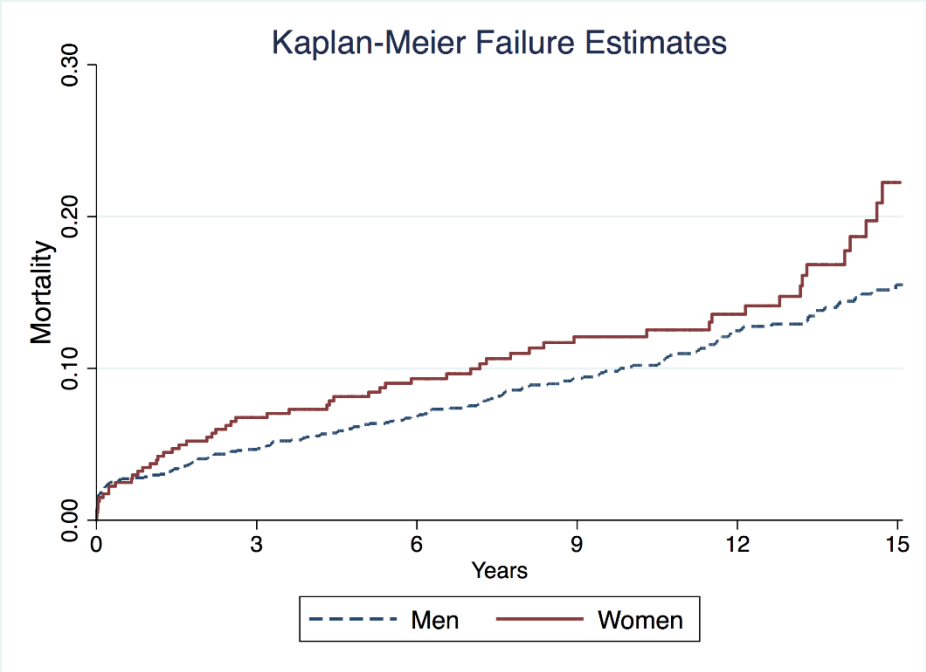
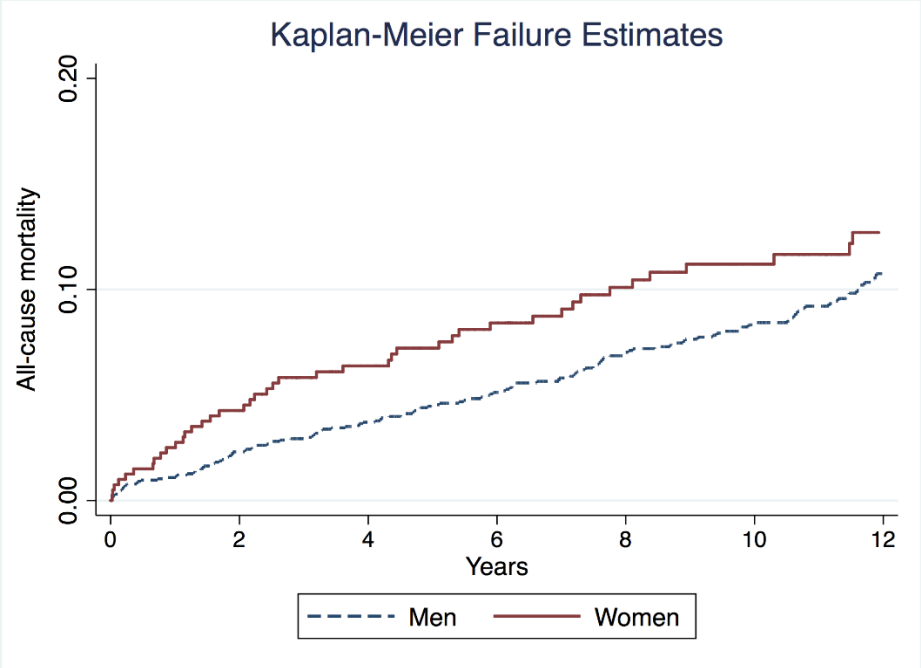



**Figure 4: Kaplan-Meier Failure Estimates for All-Cause Death (Excluding Patients with In-Hospital Death)**



# SUPPLEMENTAL MATERIAL

## Table of contents:

1. Association of Sex with Treatment with Invasive Coronary Angiography (Online Tables 1)
2. Cardiovascular Death (Online Tables 2)
3. Kaplan-Meier Failure Estimates for Cardiovascular Death (Excluding Patients with In-Hospital Death) (Online Figures 1)

**Table S1: Association of Sex with Treatment with Invasive Coronary Angiography**

| Logistical Regression for Catheterization | | | | |
|---|---|---|---|---|
| | UNIVARIATE | | MULITVARIABLE | |
| **Factor** | **Odds Ratio** | **p-value** | **Odds Ratio** | **p-value** |
| Female Sex | 0.486 | 0.003 | 0.610 | 0.123 |
| Charlson Comorbidity Index | 0.625 | <0.001 | 0.651 | <0.001 |
| STEMI | 0.333 | <0.001 | 0.411 | 0.004 |
| Length-of-Stay | 0.981 | 0.117 | 0.990 | 0.547 |
| Creatinine | 0.427 | <0.001 | 0.445 | <0.001 |
| Age at Event | 0.990 | 0.673 | 0.991 | 0.742 |
| Normalized Troponin | 1.00 | 0.230 | 1.000 | 0.373 |
| Income | 1.000 | 0.001 | 1.000 | 0.007 |
| Substance Abuse | 0.462 | 0.008 | 0.376 | 0.008 |
| Diabetes | 0.588 | 0.037 | 2.048 | 0.058 |
| Cardiogenic Shock | 0.907 | 0.822 | 1.191 | 0.751 |
| Current Smoking | 1.239 | 0.348 | 1.284 | 0.400 |
| **Time to Hospital Presentation** | | | | |
| 6-24 Hours | 3.287 | 0.023 | 13.111 | 0.013 |
| 1-3 Days | 0.779 | 0.638 | 3.323 | 0.272 |
| >3 Days | 0.940 | 0.932 | 2.335 | 0.419 |
| Unknown | 1.237 | 0.558 | 1.629 | 0.281 |

**Table S2: Cardiovascular Death**

| Cardiovascular Death | | | | |
|---|---|---|---|---|
| | UNIVARIATE | | MULITVARIATE | |
| Factor | Hazard Ratio | p-value | Hazard Ratio | p-value |
| Female Sex | 0.959 | 0.862 | 0.956 | 0.870 |
| Age at Event | 1.035 | 0.018 | 1.019 | 0.418 |
| Hypertension | 1.586 | <0.001 | 1.410 | 0.134 |
| Diabetes | 2.268 | <0.001 | 2.071 | 0.005 |
| Creatinine | 2.383 | <0.001 | 1.390 | 0.013 |
| HDL Cholesterol (md/dL) | 0.970 | <0.001 | 0.975 | 0.037 |
| Substance Abuse | 1.510 | 0.006 | 1.534 | 0.087 |
| Statin at Discharge | 0.285 | <0.001 | 0.437 | 0.003 |
| P2Y12 Inhibitors at Discharge | 0.422 | <0.001 | 0.463 | 0.002 |
| Cardiovascular Shock | 3.172 | <0.001 | 4.348 | <0.001 |
| Cardiac Rehabilitation | 0.311 | 0.001 | 0.335 | 0.066 |
| Cancer | 4.153 | <0.001 | 1.294 | 0.562 |
| Charlson Index | 1.527 | <0.001 | 1.085 | 0.890 |

**Figure S1: Kaplan-Meier Failure Estimates for Cardiovascular Death (Excluding Patients with In-Hospital Death)**