

## Sex-based Disparities in Myocardial Infarction

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### Introduction

Myocardial infarction, colloquially known as a heart attack, is the leading cause of death in the United States. Annually, around 805,000 Americans experience a heart attack, with about 1 in 6 deaths attributed to coronary heart disease<sup>1</sup>. Characterized by a blockage of coronary blood vessels due to a buildup of cholesterol plaque<sup>2</sup>, myocardial infarction can lead to weakness of cardiac muscles. This makes it more difficult for various parts of the body to receive sufficient amounts of blood, and therefore, oxygen. Myocardial infarction has the potential to increase the long-term risk of fatal cardiovascular issues<sup>3</sup>, including arrhythmia and heart failure. These events can affect individuals of any sex or race, but the risk increases with age. Other key risk factors for heart attacks include family history of heart disease, smoking, high blood pressure, high cholesterol levels, obesity, diabetes, physical inactivity, and poor diet<sup>4</sup>, all of which are highly represented in the US population.

Despite these widespread impacts, there remain major portions of myocardial infarction that are under-researched. Specifically, non-ST elevation myocardial infarction, or nSTEMI, is broadly understudied<sup>5</sup>, leaving medical professionals challenged in effectively recognizing and treating these instances of myocardial infarction, increasing the susceptibility of patients to misdiagnosis. The population demographic that has been affected the most by this disparity in knowledge is women.

Disparities in mortality rates between men and women are substantial, with women having higher mortality rates following a heart attack<sup>6</sup>. This difference is partly attributed to variations in symptoms, as women may experience atypical or less recognizable signs compared to men<sup>7</sup>, leading to delays in diagnosis and treatment. Moreover, there is evidence to suggest that women may receive less treatment for heart attacks compared to men<sup>6</sup>, contributing to poorer outcomes. These disparities underscore the importance of recognizing and addressing sex-specific differences in heart disease presentation, diagnosis, and management to ensure equitable care and to improve outcomes for all individuals.

The purpose and scope of this review paper is to investigate the differences in presentation, diagnosis, and treatment of myocardial infarction between men and women, including varying symptoms, the perceptions of patients and healthcare providers, differences in identification of the issue, and the treatments that each group receives as a result of their diagnosis. Lastly, this paper will also review previous attempts to resolve these disparities and suggest evidence-based solutions to the highlighted issues, including conducting an increased number of research trials that involve women and improving funding for healthcare resources and other types of testing for heart attacks.

### Methodology

Articles submitted to medical research publications and databases such as PubMed, the American Journal of Medicine, and the American Heart Association were reviewed. The searches focused on studies that compared a range of factors of myocardial infarction between men and women, including their symptoms, perception of symptoms, diagnosis, treatment, and long-term cardiovascular health effects. Search terms including “sex disparities in MI”, “men vs women heart attack symptoms”, “men vs women heart attack presentation”, “sex differences in symptom presentation for MI”, “sex differences in heart attack treatment”, and “policies responding to sex disparities in heart attack treatment” were used.

### **Sex-based disparities in MI symptoms**

First, it is important to consider the “classic” symptoms of myocardial infarction at presentation. These include chest pain/tightness, discomfort, fatigue, sudden dizziness, cold sweating, and shortness of breath<sup>8</sup>. Many studies find that, while there are differences in the presentation of atypical symptoms of myocardial infarction, many of the classic symptoms are similar. A study collecting data from 1,941 patients with suspected acute coronary syndrome found that 91.2% of male patients were presented with angina, or chest pain, compared to 92.3% of women<sup>7</sup>. When analyzing specific details, men and women also used similar descriptors for their angina. In the above study, both men and women most often utilized words such as tight, heavy, and stabbing to describe the pain and discomfort. Additionally, men and women generally share other common associated symptoms such as fatigue, shortness of breath, and weakness<sup>9</sup>.

However, women experienced greater rates of atypical symptoms in addition to typical symptoms. According to a 1999 study, women are more likely to experience non-angina symptoms such as mid-back pain (13% of women, 2% of men), nausea and vomiting (30% of women, 16% of men), palpitations (10% of women, 3% of men), and indigestion (22% of women, 12% of men)<sup>10 11</sup>. One study found that approximately 61.9% of women experience >3 associated symptoms, defined as symptoms including epigastric issues, palpitations, and discomfort in other body parts, compared to 54.8% of men<sup>7</sup>. This demonstrates that while men and women share a basic set of classic symptoms, women also have numerous other symptoms that are classified as unconventional.

When considering the factors that lead to differences in presentation of myocardial infarction, a key component is biological. Sex determinants can influence both risk factors and symptoms of men and women relating to cardiovascular disease. A study conducted in Italy found that testosterone in men and 17 $\beta$ -estradiol and progesterone in women affect the mechanisms of the cardiovascular system. As women reach menopause, there is a decline in the levels of these hormones, which can lead to an increased risk of cardiovascular disease. For men, testosterone can have positive effects on the cardiovascular system by maintaining blood vessels and even lowering cholesterol levels<sup>12</sup>. Fluctuation of these hormones as men and women age can influence their respective risks for cardiovascular disease throughout their lives.

While biological factors can influence the symptoms of patients with myocardial infarction, patient perception of symptoms also plays a significant role. Several studies have found that women are likely to delay seeking medical attention despite the onset of myocardial infarction

symptoms. One study attributes this to symptom uncertainty due to atypical symptoms, inadequate patient-physician interaction, competing social demands, and structural barriers to healthcare<sup>13</sup>. Another study from 2013 illustrated that even when women were aware that their symptoms were heart-related, they delayed their decision to acquire care<sup>14</sup>. On average, women delay a median of 5.4 hours before they seek medical attention<sup>15</sup>.

Another crucial factor to note is that women are much more likely to perceive their symptoms as being related to stress and anxiety compared to men<sup>7</sup>. One 2018 study found that around 20.9% of women with angina and other symptoms associated with MI perceived their symptoms to be related to stress and/or anxiety. 11.8% of men felt the same way<sup>16</sup>. This indicates that societal and psychological influences also play a role in the identification and perception of symptoms of myocardial infarction.

### **Sex-based disparities in MI diagnosis**

There are several diagnostic tests that are typically used to identify myocardial infarction in patients. Blood tests are used in the diagnosis of myocardial infarction, measuring the concentration of troponin in the bloodstream. Troponin is a protein in cardiac muscle cells, and when these cells necrose due to inadequate oxygenation and perfusion, troponin is released into the bloodstream, providing a readout for myocardial infarction. Blood samples are effective at identifying myocardial infarctions that may occur without ST-segment elevation, or nSTEMI<sup>17</sup>.

Generally, an electrocardiogram, or ECG, is another initial test that is conducted. An ECG is capable of identifying myocardial infarction through ST-segment elevation, or STEMI<sup>18</sup>, as well as other changes.

Coronary angiography is another method used to identify blockages in the coronary arteries. This procedure involves percutaneously directing a catheter through the patient's vasculature, typically by way of the radial artery. The doctor then injects contrast dye into the patient's coronary vessels and examines how the contrast flows through the vessels. Identifying blockages can assist physicians in diagnosing myocardial infarction<sup>19</sup>.

Studies have shown that myocardial infarction is under-recognized and misdiagnosed more in women compared to men. Acute coronary syndrome (ACS) is nearly twice as likely to be misdiagnosed in women—one study encompassing 12 years found that 5% of ACS was misdiagnosed in women compared to 3% in men<sup>20</sup>. In the study, ACS was identified as a possible issue in 39% of women and 44.5% of men, showing that the risk of myocardial infarction was incorrectly estimated in women. The impact of these errors can be fatal; in over 50% of acute myocardial infarctions that result in death, patients are discharged and die outside of the hospital without receiving treatment<sup>21</sup>.

There are several challenges that can potentially lead to late diagnosis and misdiagnosis. First, as discussed earlier, atypical cardiovascular symptoms may contribute to both patients and their providers incorrectly assessing the cause and severity of symptoms. When looking at how providers often analyze and respond to symptoms, it has been identified that providers are more

likely to determine that men's symptoms are heart-related compared to women. The 2018 study noted above about patient and provider perception found that approximately 36.7% of providers for men believed that their symptoms were not heart-related. This is a substantial difference from 53.4% of providers for women<sup>17</sup>. Despite patients presenting with similar symptoms, the sex of the patients was shown to affect how healthcare providers assess the symptoms.

Additionally, similar to patients, providers were also more likely to believe that stress and/or anxiety was the cause of women's myocardial infarction symptoms. The same 2018 study found that the perceived cause of symptoms was stress or anxiety in 25% of female patients, compared to 15.2% in male patients<sup>17</sup>.

The misunderstanding of symptoms in women eventually culminates in differences in diagnostic testing. One 2001 study found that in general, women were "undertreated" in the early progression of acute myocardial infarction. They were found to be half as likely as men to undergo acute catheterization, angioplasty, or coronary bypass surgery<sup>22</sup> (odds ratio 0.5). A study in 2022 demonstrated these statistics with a large sample size of 141,459 patients. The study found that, of the patients evaluated for myocardial infarction through coronary angiography (CAG), 31.4% were women<sup>23</sup>. A similar study found that, especially in nSTEMI cases, women in all age groups were significantly less likely to receive coronary angiography as a diagnostic test<sup>6</sup>.

### **Sex-based disparities in MI treatment and outcome**

There are various treatment options that healthcare providers use after an MI diagnosis. Percutaneous coronary intervention is a treatment procedure for myocardial infarction that involves ballooning and/or inserting a stent into narrowed arteries to improve blood flow to the heart<sup>24</sup>. Other treatment options can be long-term medications to prevent future coronary blockages, including platelet inhibitors, which reduce the ability of platelets to adhere and aggregate<sup>25</sup>, and statins, which reduce the cholesterol produced in the liver and also reduce inflammation in artery walls<sup>26</sup>.

The disparities continue in the treatment of women with myocardial infarction. Approximately 22.2% of the women identified with coronary blockages undergo percutaneous coronary interventions (PCI) to clear those blockages. This small percentage suggests that despite diagnosis of myocardial infarction, women may be still less likely to receive treatment as opposed to men<sup>24</sup>.

Women are also less likely to receive long-term treatment options, such as blood thinners. A few notable differences in medication disparities for patients diagnosed with MI include >1 platelet inhibitor (83.9% of women, 90.8 of men) and statins (82.9% of women, 92.1% of men)<sup>6</sup>.

Predictably, the discrepancy in medical intervention, in part, results in elevated mortality rates for women with myocardial infarction. In the United States, myocardial infarction is the leading cause of mortality among women. Specifically, one study tested the differences in mortality rate

between men and women after 28 days following their first acute myocardial infarction. Mortality was later retested after 6 months. It was found that the 28-day mortality rate was significantly higher for women (18.5% of women, 8.3% of men). Similarly, women had higher 6-month mortality rates (23.3% of women, 12.2% of men)<sup>27</sup>.

## Treatments and solutions

While sex disparities continue to exist within cardiovascular health, substantial progress has been made. The medical industry has increased research into sex-specific risk factors for myocardial infarction, improved recognition of atypical symptoms, and expanded the understanding of treatment risks and options for women post-diagnosis of MI<sup>28</sup>. One article found that since 1997, awareness of cardiovascular disease and MI has doubled, and the death rate resulting from CVD has decreased by nearly half. There has also been research conducted regarding prevention of myocardial infarction, including the impacts of various medications on MI risk in women<sup>29</sup>.

However, noting the current impacts of myocardial infarction, it is crucial to continue to work towards solutions to improve health outcomes for women with MI. There is still much unknown regarding specific cardiovascular conditions that are associated with myocardial infarction, such as spontaneous coronary artery dissection, or SCAD, which one study states occurs almost solely in women<sup>30</sup>. Additionally, early diagnosis is one of the most important factors in the current disparity in health outcomes and continues to be unresolved.

One intervention that may reduce delays in diagnosis is improved patient education and awareness. A 2019 study found that while many American adults recognize chest pain as a symptom of myocardial infarction, atypical symptoms are less recognized (47% of adults surveyed were unable to identify each symptom presented as a potential sign of MI). The rate was higher among women and also of population demographics at lower income levels, likely due to limited access to higher education<sup>31</sup>. Strategies to improve awareness include collaboration with local health providers to offer educational materials to families, as well as emphasize the need of regular testing and health screenings. Additionally, cooperating with community-based organizations that have established a network with local populations can be an additional method of outreach to spread information regarding symptoms of MI and what actions to take in the event of experiencing such symptoms.

As identified above, delays in diagnosis are not solely attributable to patients with MI. Since providers are significantly more likely to conclude that a woman's MI symptoms are not heart-related, it is essential to integrate knowledge about atypical MI symptoms into medical education. Combining newer research with the current content of the exams and continued medical education program which allow providers to maintain their certificate of practice can ensure that providers are up to date with findings regarding sex-specific protocol for diagnosing MI.

Finally, but perhaps most importantly, continued research is essential to enhance our current understanding of myocardial infarction in women. A key obstacle to advanced research in this

area is a lack of funding—one study established a link between inadequate funding and quality medical studies over the past several decades. It argued that improved funding mechanisms can facilitate more effective study designs and techniques, amplify collaboration between institutions, and supplement existing resources<sup>32</sup>. Addressing the funding shortfall requires not only efforts from local organizations and governments, but from regional and national establishments. While efforts to enhance awareness on an individual level are necessary, it is imperative for policymakers to acknowledge the impact of myocardial infarction on individuals and their families to catalyze enduring and impactful policy reforms.

## Conclusion

Sex-based disparities within myocardial infarction extend across various aspects including symptoms, diagnosis, and treatment. Women are more likely to have non-angina symptoms compared to men, which can be caused by biological factors. Additionally, women generally assess their symptoms to be not heart-related, leading to delays in seeking treatment. When it comes to diagnosis, women are less likely to receive certain diagnostic tests including coronary angiography, especially in nSTEMI cases, resulting in women having a higher rate of misdiagnosis of MI compared to men. This is attributable to provider perception of patients' symptoms—providers were 9.8% more likely to believe that the symptoms of women were caused by stress and/or anxiety. These differences eventually contribute to distinctions in treatment options, both short-term (such as percutaneous coronary intervention) and long-term (such as statins and platelet inhibitors). Overall, women have a significantly higher mortality rate from myocardial infarction.

Actions have been taken to reduce disparities, including research and increased awareness among women, but continued efforts are necessary to reduce persisting impacts of sex disparities in cardiovascular health. These efforts could include community outreach to expand awareness, requiring that providers remain up to date with novel medical knowledge, and increasing funding for research initiatives that are focused on women.

Ultimately, addressing disparities in myocardial infarction requires action from all stakeholders, including healthcare providers, researchers, policymakers, and individual patients. By improving collaboration and working towards evidence-based strategies, it may be possible to attain a future where all individuals receive equitable care and have the best outcomes following myocardial infarction, regardless of sex.

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