Assessing the Need to Educate Prehospital Providers on the Sex Differences in the Clinical Presentation of Acute MI

Keywords

acute MI; sex differences; clinical presentation; prehospital

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Abstract

Medical research has historically underrepresented females. As part of a movement to better represent women in research, U.S. Congress passed the National Institute of Health Revitalization Act of 1993, which mandated the inclusion of women and minority groups in clinical research.1 With the increase in female inclusion, sex differences in the clinical presentations of diseases and responses to medication have emerged. Previous research has found differences in how women and men might present with acute myocardial infarction (MI), with women more often experiencing signs and symptoms that are labeled as 'atypical' or 'nontraditional.'2-8 However, this information has not been robustly incorporated into the prehospital curriculum standards, including education for emergency medical technicians (EMTs) or paramedics.9 This paper investigates whether there is a need for the prehospital curriculum to discuss the lesser-known signs and symptoms of acute MI and the differences in disease presentation between men and women. First, some differences between women's and men's physiology and pathophysiology are explored. Next, the clinical presentation of acute MI is reviewed, including the research supporting the sex differences in clinical presentation. Additionally, the disparities in EMS quality of care will be discussed, as research has shown that women receive lower quality of care in the prehospital setting.10 Social factors that can affect delays to treatment will also be discussed. Since there is substantial evidence that health outcomes of acute MI differ between men and women, EMS education should include and emphasize these topics.

Methodology

This integrative review identified appropriate articles through a search on PubMed with the keywords "acute MI," "sex differences," "gender differences," "sex and gender differences in the clinical presentation," "pathophysiology," "anatomy," "differences in acute MI clinical presentation of transgender individuals," "EMS recognition of acute MI," and "time to treatment and outcome." The PubMed search did not include "chromosomal anomalies," as EMS provider educational standards do not include knowledge of genetic diseases and chromosomal anomalies.9 The search included articles published after 2000. These articles were then assessed and considered relevant if they addressed the following questions:

- Are there sex differences in the clinical presentation of acute MI? Which sexes are discussed in each study?

- Are there anatomical, pathophysiological, or hormonal differences in women and men that affect the development of acute MI? If there are differences, do they affect the signs and symptoms that patients experience?
- Is there an association between time to treatment for acute MI and functional outcomes or mortality? If so, what is the significance in relation to EMS care?
- How accurate is EMS provider recognition of acute MI?
- Is there a difference in the quality of care between EMS providers caring for male and female patients?

Sex and Gender

A person's chromosomal makeup of XX (female) or XY (male) defines one's sex. Other chromosomal anomalies exist, such as XXY (Klinefelter's Syndrome) or X (Turner's Syndrome). Gender is defined as how a person chooses to identify and express themselves. Gender exists as a spectrum and includes categories such as man, woman, transgender man or woman, or nonbinary, as well as others. All the reviewed studies placed patients into binary categories of "male" or "female." None of the reviewed studies included individuals with chromosomal anomalies or those who identify as non-cisgender. Similar to the reviewed studies, this paper will focus on the differences between biological males and females. The conclusion of this paper emphasizes the importance of and the need for acute MI research to encompass a wider spectrum of gender inclusion.

Body

Acute Myocardial Infarction

Most people experiencing an acute MI will present with the well-known signs and symptoms that are taught to healthcare professionals: chest pain, pressure, tightness or discomfort, and diaphoresis. However, numerous studies have found that, compared to men, women more frequently present with additional symptoms that are not as well-taught. Women more commonly present with nausea, vomiting, stomach pain, indigestion, heart palpitations, and dyspnea (2,3). While men more often report pain or discomfort in their left shoulder, women more commonly experience pain or discomfort in their jaw, neck, arms, or between their shoulder blades (2,3). Women are also more likely to have fatigue as their only symptom (3). Although chest pain often accompanies these additional symptoms in both men and women, it may be absent in either sex. However, certain female demographics may disproportionately not experience chest pain at all. Lichtman et al. found that, compared to men, women aged 18 to 55 more often present without chest pain during an ST-elevated acute MI (2). Since EMS providers commonly care for patients experiencing an acute MI, they should be educated about the unfamiliar symptoms that may present with or without chest pain and be informed that women more commonly experience these less frequently emphasized symptoms.

The differences between men's and women's vascular physiology and the development of vascular disease may partly account for differences in clinical presentations, though this relationship has yet to be definitively determined. First, women's coronary arteries are narrower than men's, and women have a higher baseline myocardial blood flow (11). Haider et al. suggest that these two factors could contribute to a higher degree of endothelial shear stress, potentially helping to prevent plaque accumulation in women's coronary arteries (11). The pathophysiology of cardiovascular disease has also

been shown to differ between sexes. A study from 2021 found that plaque erosion is responsible for nearly one-third of acute coronary syndrome (ACS) incidents, including unstable angina and acute myocardial infarctions (12). Plaque erosion occurs when the top endothelial layer of a plaque is lifted, and platelets and fibrin deposit there and form a white thrombus (12). Plaque rupture is responsible for the remaining ACS incidents, which can occur when an atherosclerotic plaque partially lifts off the luminal wall of a blood vessel, and fibrin and red blood cells deposit and form a red thrombus at the site of the break (12). Studies have found that plaque rupture is more often experienced by men, and plaque erosion is more commonly experienced by women (11,13). However, one study found that as women's age increased, the prevalence of ACS due to plaque rupture also increased (13). While there is clear evidence that men's and women's vascular physiology and disease development differ, further research is needed to definitively determine whether differing patterns of plaque buildup and thrombosis directly contribute to differences in men's and women's clinical presentation of acute MI.

In addition to vascular pathophysiology, differences in men's and women's hormonal physiology also affect cardiovascular health. Premenopausal women have more circulating estrogen compared to men or postmenopausal women (13). Estrogen has an anti-inflammatory effect on blood vessels and favors low vascular resistance. Studies have shown that premenopausal women have a lower incidence of cardiovascular disease compared to postmenopausal women and men (11,14). Men have more testosterone than women, but research has found conflicting results regarding the overall effect of testosterone on cardiovascular health (15). More research is needed to determine whether there is a direct link between different hormonal profiles and disease presentation. There are studies examining the effects of estrogenic treatments such as oral contraceptive pills and post-menopausal hormone therapy on acute MI risk; however, this information lies outside the scope of EMS education. An in-depth discussion of hormones requires a high-level understanding of endocrinology, which is generally not included in EMS provider education.

Myocardial infarction pathophysiology also differs between women and men. ACS syndromes are classified as Type 1 and Type 2, with ACS Type 1 accounting for roughly 90% of cases and ACS Type 2 accounting for the remaining 10%. ACS Type 1 is defined as an acute atherothrombotic event. A greater proportion of women experience ACS Type 2, which occurs when an infarction is caused by inadequate myocardial oxygenation without injury to the coronary arteries.3 Inadequate oxygenation can occur due to an increase in oxygen demand and/or a decrease in supply. Tachycardia or hypertension can increase myocardial oxygen demand, and hypoxemia, anemia, and hypotension decrease oxygen supply. Often, ACS Type 2 occurs in the presence of more than one of these conditions (16). For instance, ACS Type 2 is associated with operations, sepsis, arrhythmia, and anemia, which all could reasonably lead to an increase in myocardial oxygen demand and/or a decrease in oxygen supply (17). There is limited information discussing sex differences underlying the mechanism of ACS Type 2. Nevertheless, educating prehospital providers about the potential sex differences in heart disease pathophysiology could facilitate their understanding of the differences in men's and women's clinical presentation.

The patient's self-reported history can significantly impact the prehospital provider's understanding of the patient's condition. Interestingly, Lichtman et al. found that women were more likely to perceive their symptoms as anxiety or stress, whereas men were more likely to perceive the symptoms as muscle pain (2). Therefore, a woman with chest pain and lesser-

known acute MI symptoms may tell the prehospital provider that her symptoms are anxiety-related. If the EMS believes the patient is experiencing acute anxiety and does not evaluate for an acute MI, several unfortunate scenarios could result in worse outcomes for the patient. Theoretically, EMS may fail to perform an EKG, assign the patient as low priority, which places the patient at risk of seriously deteriorating as they wait for an emergency department (ED) assessment. Or worse, EMS may recommend that the patient try to remain calm at home and call 911 again if they still have symptoms later. In either case, the patient would experience a delay in treatment and potentially worse outcomes. Another factor that may contribute to more women misperceiving their symptoms is that, compared to men, more women had visited their primary doctor for symptoms related to an acute MI before being hospitalized (2). During these visits, women were more often told that their symptoms were not heart-related and instead were likely gastrointestinal or stress-related (2). If a patient explains to EMS that their doctor said their symptoms are gastrointestinal or stress-related, the prehospital provider may believe the patient and may not perform investigative interventions. Prehospital providers should be made aware of how patients may perceive their symptoms. This knowledge may enable EMS providers to overcome bias brought on by the patient's symptoms and history.

Conscious or unconscious gender biases can affect a prehospital provider's clinical decisions. Previous studies have found discrepancies in the performance of EMS interventions between male and female patients. For instance, a national study by Lewis et al. found that compared to men younger than 65 years old, women under 65 were significantly less likely to receive aspirin or nitroglycerin for chest pain (18). This study did not control for reasons not to administer these medications, such as patient administration before EMS arrival or an allergy (18). However, another possible reason not to administer medication for chest pain is a low suspicion of a cardiac event, which may be due to unconscious provider bias or inadequate training. Another observed discrepancy between women and men is that, for patients with chest pain, women under 65 were less likely to be transported using lights and sirens compared to men of similar age (18). Occasionally, a patient will request not to be transported with lights and sirens, but otherwise, lights and sirens are used to transport high-priority patients. These discrepancies in treatment and transport methods likely involve gender bias or disbelief of symptoms. Bringing awareness to discrepancies surrounding prehospital interventions may affect EMS providers' patient care decisions, which ideally should be equally performed for women and men.

Failure to investigate the patient's signs and symptoms could also lead to a delay in treatment. When paramedics suspect a cardiac emergency, they should perform an electrocardiogram (EKG). EKGs can show ST-elevated myocardial infarctions (STEMIs) or non-ST-elevated myocardial infarctions (NSTEMIs). The EKG reading can help paramedics assign a patient's priority level, which EMS uses in their report while en route to their destination hospital. EMS providers assign patients experiencing a life-threatening medical emergency with a high priority. Once an EMS provider calls the destination hospital and gives a verbal report, the ED will prepare a room and the appropriate resources for high-priority patients before they arrive at the ED. Assigning a patient with a high priority likely decreases their time to imaging and/or treatment compared to patients assigned with lower priority. One concern that may arise is that basic life support crews (BLS), who are unable to conduct EKGs, may unnecessarily make an acute MI notification to the destination hospital based purely on signs and symptoms. The hospital may use

unnecessary resources, and the patient may undergo avoidable stress from the experience. While it is best to send an advanced life support (ALS) crew to someone experiencing an acute MI, BLS crews may be sent if all other ALS crews in the area are busy. Nevertheless, both BLS and ALS providers should be aware of unfamiliar signs and symptoms of life-threatening disease states so that they may perform appropriate investigative interventions and decrease the possibility of delaying hospital evaluation.

During an acute MI, time to treatment can impact a patient's outcome. Lichtman et al. found that women aged 18-65 had a longer time from symptom onset to hospital presentation (2). Deluca et al. found that each 30-minute delay from the onset of acute MI symptoms to a primary angioplasty was associated with both an increased relative risk of mortality in one year and an increased risk of having a pre-discharge ejection fraction of less than 30%.19 A normal ejection fraction is 52% to 72% for men and 54% to 74% for women (20). Per the American College of Cardiology, an ejection fraction below 30% is considered severely dysfunctional (20). A low ejection fraction indicates that the left ventricle is unable to pump blood to the rest of the body effectively, which can lead to further heart complications. Though EMS does not spend hours with a patient, they can potentially shorten the time to treatment if they recommend that the patient go to the hospital. Obtaining an EKG may especially benefit patients experiencing an MI who present with unfamiliar signs and symptoms and attribute their symptoms to other causes.

In addition to provider recognition of a patient's disease severity, social factors can also influence a patient's time to treatment. Patient characteristics associated with prehospital delay include non-white race, low socioeconomic status, diabetes, and hypertension (21). A non-white race or low SES may be associated with a prehospital delay due to a lack of medical knowledge and mistrust in the healthcare system. Additionally, women are more likely to have a longer delay in seeking care (21). The reasons for the prolonged time to seek medical attention also tend to differ between women and men. Men who reported a mismatch between their expected and actual symptoms of an acute MI, had a low education level, did not call 911 or did not ride in an ambulance tended to have a prolonged time to seek treatment21. Meanwhile, women with a longer delay were older, single, alone during symptom onset, or did not want to trouble anyone (21). Interestingly, men with a history of an acute MI had a shorter delay in seeking treatment, while women with this history had a longer delay in seeking treatment (21). Though prehospital providers cannot impact these social factors, they potentially expedite getting the patient to definitive imaging and care. Suppose prehospital providers are aware of less common acute MI presentations. In that case, they may be able to advocate for a patient with a less common presentation and eliminate delays in the ED.

Conclusion

Since women are more likely to present with lesser-known signs and symptoms of acute MI and are less likely to receive the highest quality of care, there is a need to implement the above findings in prehospital education. This may be through classroom curriculum for future EMS providers and continuing education classes for current providers. EMS providers who understand that acute MI can present with lesser-known signs/symptoms may be more likely to obtain a detailed history and perform interventions, which subsequently may paint a clearer picture for emergency department providers.

The goal of educating the prehospital provider about sex differences in acute MI is to increase

awareness of how life-threatening conditions can manifest beyond the well-known textbook definitions and encourage providers to deliver higher-quality patient care. The curriculum should discuss trends in men's and women's clinical presentations and emphasize how women more often experience unfamiliar symptoms. To supplement this information, discussing underlying differences in male and female physiology could provide greater context for different trends in presentation. The physiology discussion should be tailored to either a more basic level for EMTs or a more detailed level for paramedics. The curriculum should also emphasize the current discrepancies in performing interventions and providing high-quality care between patient sexes. Due to these current discrepancies, the course should review EMS protocols for suspected acute MI. Additionally, the curriculum should reframe the language used to describe lesser-known signs and symptoms. Labeling the symptoms more commonly experienced by women as 'atypical' or 'non-traditional' diminishes their clinical importance. Emerging literature and curriculum should consider placing these signs and symptoms into a category that frames them as likely and valid disease indicators, such as 'additional signs and symptoms.'

In addition to cisgender women and men, future research is needed to assess whether acute MI presents differently in non-cisgender individuals. About 1.6% of the U.S. population identifies as transgender or nonbinary, with a greater proportion under 30 years old (22). Transgender people may undergo hormone treatment or gender reconstruction surgery, and these procedures may affect the risk of developing acute MI. For instance, one study found that transgender men undergoing gender-affirming hormone therapy had an increased risk of MI compared to cisgender women and men (23). Transgender women undergoing gender-affirming hormone therapy may have an increased risk of an MI (23). Due to these increased risks, it may be helpful to compare the acute MI presentation of transgender populations to cisgender women and men. Another challenge that future research may face is collecting patient information. Transgender and non-binary patients do not always disclose their true gender identity to providers. For instance, the U.S. Transgender Survey reports that almost one-third of transgender people did not inform their healthcare providers that they were transgender (24). There are many reasons that people may not wish to disclose their gender, including prior discrimination, fear of mistreatment, and avoiding invasive questions (24). The transgender and non-binary individuals have especially experienced negative interactions with healthcare providers. The responsibility to make a patient feel comfortable falls on the medical provider, and, therefore, providers should have adequate training on how to care for transgender and nonbinary populations. The medical community must continue to acknowledge its biases and adjust providers' approach to patient care so that patients of all genders may one day receive similar quality of care.

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