

## Gender-Based Delays in Acute Coronary Syndrome and Their Impact on Outcomes

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### ABSTRACT

Cardiovascular disease (CVD) remains the leading cause of death in the United States, with gender disparities in presentation and outcomes increasingly recognized. Women with acute coronary syndrome (ACS) often experience atypical symptoms and are subject to care-seeking delays, potentially contributing to poorer prognoses. This literature review aimed to evaluate the extent of treatment delay in female patients with ACS and to assess its relationship with clinical outcomes. Using a structured search of the PubMed database, 14 articles published in the past decade were initially identified, with 11 meeting inclusion criteria following relevance screening. Among the selected studies, five reported statistically significant delays in treatment for women compared to men, with women more likely to present later after symptom onset and experience additional in-hospital delays. These delays were associated with increased short-term mortality, with one study reporting a twofold increase in 30-day mortality among women. Conversely, five studies did not find statistically significant differences, though several showed trends toward longer delays in women. Variability in findings may be attributed to small sample sizes or improved public awareness of sex-specific ACS symptoms in recent years. Several studies identified atypical symptom perception, lack of symptom recognition, and social factors as key contributors to delayed care-seeking behavior among women. Interviews with female patients revealed that many did not perceive their symptoms as consistent with myocardial infarction, leading to delayed presentation. These findings highlight the continued presence of gender-based disparities in ACS treatment and outcomes. Efforts to educate both patients and healthcare providers about atypical symptomatology in women, as well as system-level interventions to reduce delays, may improve timely care and reduce mortality. Further research is needed to better understand modifiable barriers to prompt treatment in women and to design targeted strategies that address these gaps.

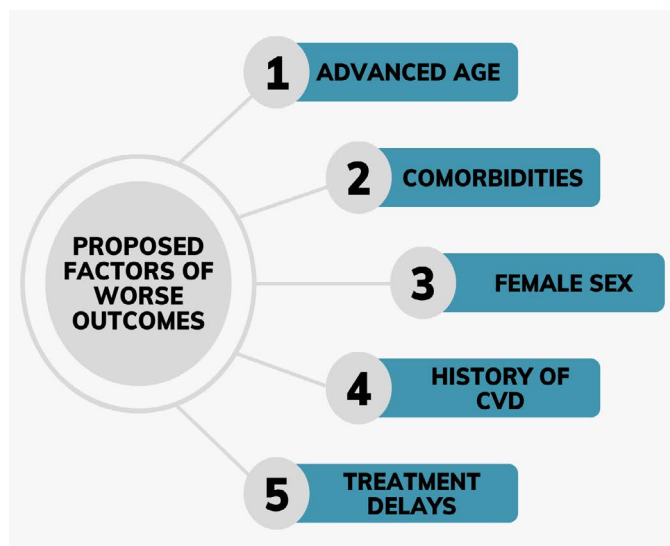
**Keywords:** women health, acute coronary syndrome, myocardial infarction, treatment delay

### 1. Background

Cardiovascular disease (CVD) is the leading cause of death in the United States, but the importance of gender differences in the prevalence and burden of various CVD has only been acknowledged since the mid-eighties.<sup>8</sup> Beyond the basic

description and quantification of these gender differences, some researchers have attempted to identify bias and develop hypotheses related specifically to gender-specific CVD treatment and outcomes. One of the physicians at the forefront of this research was Dr. Bernadette Healy, who in 1991 was the first to present on Yentl Syndrome, which suggested gender bias in coronary

heart disease.<sup>9</sup> For over three decades the debate has continued regarding which gender has a poorer prognosis following myocardial infarction, and if women do have worse outcomes, why? In 2016, the American Heart Association released their first scientific statement regarding acute myocardial infarction in women, specifically sex-specific differences in presentation, pathophysiology, and outcomes.<sup>13</sup> Proposed reasons for women having poorer prognoses have included age at time of symptom presentation, higher number of comorbidities, underlying gender differences in pathophysiology, and delays seeking care, and these factors are outlined in **Figure 1**. Most of these aspects, like age or pathophysiology, are not directly modifiable. Reducing delays in seeking care, a behavioral change, is a potentially modifiable variable, making it very important to study due to the direct impact on decreasing female patients' CVD morbidity and mortality. However, determining the factors contributing to the delay in care-seeking behavior is the first step before attempting to influence women's choices in receiving timely CVD treatment. This literature review specifically addressed female patients with acute coronary syndrome and sought to identify any relationships between delayed care-seeking behavior and disease prognosis.



**Figure 1:** Proposed Factors Contributing to Worse Outcomes Among CVD Patients.

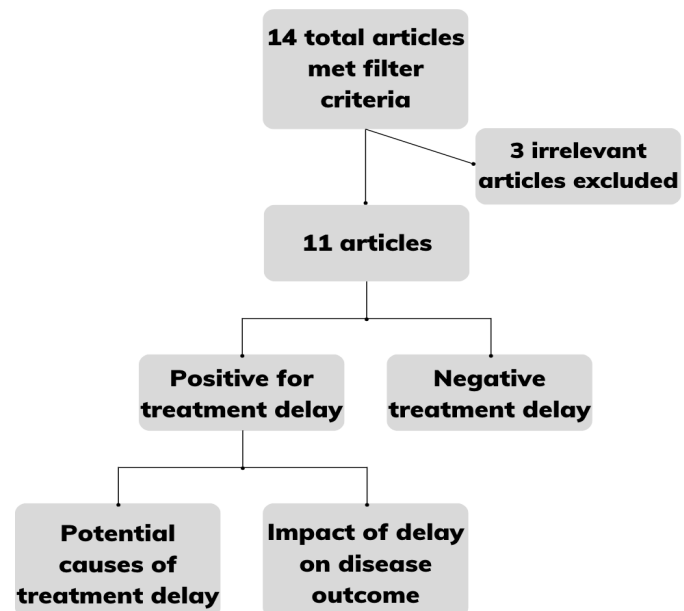
### 3. Objective

To complete a literature review to identify factors contributing to delayed care-seeking behavior in female patients with acute coronary syndrome (ACS) and assess how these factors impact disease prognosis.

### 4. Methods

The sources for this review were selected using a methodological filter search on the PubMed database. The key terms used in the search were “women,” “treatment delay,” and “acute myocardial infarction”. Additional inclusion criteria included publication within the past ten years and the article being written in English. Additional filters were applied to specify the publications be classical articles and include datasets, multicenter and observational studies, and randomized controlled trials, resulting in a set of fourteen articles. Of the fourteen articles meeting the search criteria, three were excluded due to irrelevance to this review's objective and research question, leaving eleven articles for final inclusion. The eleven

sources were then methodically analyzed. Key information extracted from each study included the type, purpose, location, study population, independent and dependent variables, and key outcomes pertinent to the research question. The articles were then separated into those with supporting evidence for women with ACS having increased treatment delay compared to men and those that concluded the opposite. Lastly the sources finding women having increased treatment delay were further analyzed to identify potential causes for the delay and, if included, the resultant impact on disease prognosis. This process is depicted in **Figure 2**.



**Figure 2:** Article Sorting Method.

### 5. Results

Following the filter search identifying published studies in the past decade with data regarding treatment delay in women with ACS, eleven sources were generated. All sources from this search were methodically analyzed and relevant data extracted. Among the analyzed sources, five presented data supporting significant treatment delays in female patients. An observational study published in 2017 in the Journal of the American Heart Association analyzed a dataset of 6,022 patients and found the median time from symptom onset to diagnosis of myocardial infarction was 270 minutes for women compared to 240 minutes for men.<sup>5</sup> Similar findings were found in multiple other sources, with men receiving care for acute cardiac events significantly faster than women.<sup>6,11,12</sup> Women were also found to be more likely to present to the emergency department more than twelve hours after symptom onset compared to men.<sup>5</sup> A separate study related to hospital admission times had comparable results, with the analysis of 2,596 patients with acute coronary syndrome indicating men were significantly more likely to have a less than 120 minute delay from symptom onset to hospital admission.<sup>6</sup> Another analysis of treatment delays found women had a delay between symptom onset and their presentation to the hospital. There were also delays from the time the women presented to the hospital and when they received medical intervention. However, the delay between symptom onset and presentation was found to be four times longer than the delay experienced when they received medical intervention compared to males with the same clinical presentation.<sup>11</sup>

Conversely, five of the eleven selected sources did not find a difference in pre-treatment delays between men and women with acute coronary syndrome. One study analyzed both pre-hospital presentation delay and in-hospital treatment delay. While an increased numerical value for women regarding both types of delays were found (227 vs. 209 min and 35 vs. 30 min, respectively), these values were analyzed and not found to be statistically significant.<sup>3</sup> Two other studies had similar findings with raw data indicating a trend towards longer time between symptom onset and presentation to the hospital among female patients, but the differences were statistically insignificant after adjusting for baseline variables.<sup>4, 8</sup> Another source analyzed time from symptom onset to first electrocardiogram among 3,658 patients with acute myocardial infarction from the Acute Coronary Syndrome Israeli Survey. The survey results showed less than half of all patients received a timely electrocardiogram, but there was not a significant difference between men and women in pre-treatment delay. However, when analyzing time to invasive treatment, female sex was found to be an independent factor of delayed treatment times.<sup>2</sup> Finally, an assessment of the Multicenter Munich Examination of Delay in Patients Experiencing Acute Myocardial Infarction analyzed the impact of Generalized Anxiety Disorder (GAD) on delay treatment times. In the context of GAD, the study found men to experience longer treatment delays than women.<sup>7</sup> of the sources that found an increase in delayed treatment times for women, several discussed potential reasons for these delays and the associated outcomes. To determine causes of delayed treatment seeking behavior, one report conducted interviews with women with acute myocardial infarction regarding their individual rationale for when they sought care.<sup>10</sup> This report found that 70% of women delayed seeking medical care because “their symptoms were not severe and therefore did not meet their expectations for an AMI.”<sup>10</sup> Another study found among patients who experienced fear of death as a symptom of acute myocardial infarction, men were more likely to report symptoms as meeting their expectation for myocardial infarction than women.<sup>1</sup> Beyond quantifying the time from symptom onset to medical intervention, many sources analyzed the impact of treatment delay on disease outcome. One source found among patients with myocardial infarction, 30-day mortality was two times higher in women than men.<sup>5</sup> Additionally, when the data was broken into subgroups based on treatment delay times, a strong relationship between 30-day mortality and treatment delay was found, “with the risk decreasing at every time decrement of the delay.”<sup>25</sup> Another source also found female sex among those with myocardial infarction to be an independent contributing factor to the outcome of mortality. Congruous findings to other research were reported, such as the result of death being two times higher in women than men, and every minute in delay contributing to the risk of mortality.<sup>6,7</sup>

## 6. Discussion

This article synthesizes findings from studies done in the last decade regarding delayed care seeking behavior among women with acute coronary syndromes, reasons for treatment delay, and the impact of delay on disease prognosis. Articles were found using a methodological search with filters from the PubMed database. Analysis of the eleven sources found meeting the specific search criteria showed conflicting evidence for differences in treatment delays between men and women. Some sources reported significant differences while others reported

numerical increases measured in time for women when compared to men, but the differences were insignificant following statistical analysis.<sup>3,4,8</sup> One reason for the lack of significant findings could be the studies’ small patient populations. These analyses could be replicated with a much larger *n*, which could result in a statistically significant difference being found. Additionally, in the past ten years much work has been done to promote awareness and educate patients about gender specific presentations of acute coronary syndromes. These efforts to reach the public may have increased awareness about how women might present with acute coronary syndromes, which could have resulted in improved self-identification of symptoms and reduced delays in seeking medical treatment. Conversely, many sources reviewed did find longer times in treatment delay among women that were statistically significant. These results suggest disparities in time from symptom onset to treatment may still exist between men and women with acute coronary syndromes.<sup>5,6,11,12</sup> Another proposed explanation regarding the delay in care for women relates to the documented atypical physical symptom presentation of ACS in female patients. Women supported this hypothesis in interviews and reported atypical symptoms as a reason for their delayed treatment seeking behavior. Women were more likely to report their physical symptoms as not meeting their expectation for acute coronary syndrome and perceived their symptoms as less severe. Inaccurate expectations and perception of symptoms may directly contribute to a longer delay in seeking medical attention, and ultimately treatment.<sup>10</sup> Educating both the public and healthcare providers about atypical presentation of acute coronary syndromes in women may result in decreased treatment delays and reduced morbidity and mortality. Of the sources finding a significant treatment delay, many also analyzed the impact the delay had on disease prognosis. A delay in treatment for acute coronary syndromes was found to increase mortality among women. Sources also found a direct relationship to the length of the delay and the severity of the outcome, with the longer the delay, the more mortality increased.<sup>5-7</sup> This correlation between delay and mortality was also found to be stronger in women than men. These findings indicate delays in care have detrimental effects on disease prognosis. Also, any amount of delay could negatively impact disease prognosis. These findings suggest interventions to decrease treatment delay times could positively impact disease outcome.

## 7. Conclusion

This literature review underscores the persistent issue of gender-based disparities in the treatment of acute coronary syndrome (ACS), highlighting significant delays experienced by female patients compared to their male counterparts. Such delays are notably associated with atypical symptom presentation and misperceptions regarding symptom severity, leading women to delay seeking timely medical attention. The clinical consequences of these delays are substantial, with evidence clearly linking increased treatment delays to poorer outcomes, including elevated short-term mortality rates among women. Despite conflicting findings in some studies, the preponderance of data supports targeted interventions aimed at both public education and healthcare provider awareness to recognize and promptly address ACS in women. Future research should focus on identifying modifiable barriers more precisely and developing tailored strategies to reduce these delays, thereby improving clinical outcomes and narrowing the gender disparity in cardiovascular care.

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## 9. Conflicts of interest

None, consent for publication was obtained from all authors.

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