

# Myocardial Infarction in Young Women

## An Unrecognized and Unexplained Epidemic

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There has been considerable progress in the prevention and treatment of coronary heart disease in the United States and other Western nations over the past 40 years, with substantial declines in heart disease mortality. However, concern has been raised that young adults, and young women in particular, may have benefited less from these favorable trends in recent years. Heart disease mortality rates have declined less in this group than in other segments of the population since 1990,<sup>1</sup> and studies both in the United States and in other developed nations have reported rising hospitalization rates for myocardial infarction (MI) in younger women.<sup>2–4</sup> The prehospital case fatality of MI has similarly declined less in young women than in men.<sup>5</sup> These recent statistics have raised alarm and require possible explanations.<sup>6</sup> However, much of the available data regarding time trends in coronary heart disease come from mortality statistics and administrative databases, which can be incomplete and inaccurate.

In this issue of *Circulation*, Arora et al,<sup>7</sup> using data from the ARIC (Atherosclerosis Risk in Communities) surveillance study, examined trends in the incidence and management of MI for the period between 1995 and 2014, with a focus on young adults. The authors analyzed surveillance data in the 4 US ARIC communities, which allowed the examination of incident MI based on adjudicated events rather than a reliance on hospital billing codes. To collect these data, the ARIC surveillance study abstracted and reviewed more than 15 000 medical records. The authors report a staggering increase in the annual incidence of hospitalized MI among young women (35–54 years old), whereas the incidence decreased among men in the same age bracket. During the study period, the percentage of women and men who were 35 to 54 years old declined relative to the total population. Despite the increased proportion of older patients in the surveilled population, the proportion of MI admissions for young women (35–54 years old) increased, from 21% in 1995 to 1999 to 31% in 2010 to 2014, while it remained relatively stable among young men (from 30% to 33%). When examined by race, the proportion of MI admissions occurring in the young population increased by 41% in white women and by 19% in black women, whereas it did not significantly change among men of either race. Although this study did not provide data on people who were older than 54 years, the increasing proportion of incident MI in young adults implies a parallel declining incidence in older groups, which is consistent with reports from other developed countries.<sup>2,4,8</sup>

What explains these worrisome trends for women? Young women with MI were more likely than their male counterparts to have comorbidities, including hypertension, diabetes mellitus, chronic kidney disease, and prior stroke, but they were less likely to smoke and more likely to have medical insurance. They also more often

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experienced heart failure and pulmonary edema during the hospitalization than similarly aged men. These data are in agreement with other studies of young MI patients regarding the higher burden of comorbidities in women.<sup>9,10</sup> However, it is unlikely that an increase in risk factors and comorbidities during the study period explains the rise in MI incidence in women, because both young men and young women with MI showed similar changes in risk factors in the study time frame, with parallel increases in diabetes mellitus and hypertension and declining smoking. However, data on time trends in risk factors were not available in the entire ARIC surveillance communities, but only in the subset who were hospitalized with MI. The latter may not necessarily mirror the underlying population, in which risk factors may have followed different trajectories in women and men. Other studies have suggested that young people and women have experienced the largest increase in diabetes mellitus since the 1980s,<sup>11</sup> and young women have also exhibited the largest increase in the prevalence of obesity.<sup>12</sup> Given that data on risk factors were not available for the entire surveilled population, no inference can be made on whether a disproportionate worsening of cardiovascular risk profile among women had an impact on their rising MI incidence.

In the study by Arora et al,<sup>7</sup> young women had a lower probability of receiving guideline-based MI therapies and interventions than young men, including lipid-lowering medications, nonaspirin antiplatelet agents, coronary angiography, and revascularization. These differences were substantial (in most cases >10%) and persisted when analyzed in subgroups of MI type (non-ST-segment elevation MI or ST-segment elevation MI) and race, when limiting the analysis to patients with first-time MI, and when adjusting for hospital clinical complications and comorbidities. Notably, there was no indication that the sex-related treatment gap improved between 1995 and 2014; if anything, there was a tendency for the disparities to worsen over time, especially for lipid-lowering agents and coronary revascularization. Despite these treatment differences and the higher prevalence of comorbidities and risk factors in young women with MI than in their male counterparts, their case fatality rate was similar. This finding is not entirely surprising, given that the MI case fatality rate has been declining for decades in both women and men of all ages and was quite low in this sample.<sup>2,3,13</sup>

The increasing incidence of hospitalized MI in young women, together with the similar case fatality in women and men in this study, points to primary prevention as pivotal to improve cardiovascular health in women and curb these adverse disease trends. Although we do not know whether there were sex-related differences in risk factor levels and risk factor control before the MI, the treatment differences observed during the MI hospitalization suggest a tendency toward underutilization of

cardiovascular prevention strategies among women, which might have extended to the preinfarction phase and contributed to their risk. A related problem is that prevention guidelines may underestimate risk in the young population, especially in women, because of their lower level of traditional risk factors.<sup>14</sup> Furthermore, in addition to traditional risk factors, there could be risk conditions for this population that are not accounted for in current risk estimation equations. For example, social determinants of health and mental health factors can contribute substantially to the cardiovascular risk of young women but are not routinely evaluated or managed. Young women in general, and especially those who have developed an MI, have a more adverse sociodemographic and psychosocial profile than similarly aged men, including lower income and education, more life adversities, and higher symptom levels of depression, posttraumatic stress disorder, and perceived stress.<sup>9,15</sup> These factors have been associated with MI incidence and mortality, which might help explain why they are disproportionately prevalent in young women with MI. In addition to having a more adverse psychosocial profile, young women are more likely to develop myocardial ischemia with mental stress than men or older subjects,<sup>9</sup> which further illustrates the importance of the psychosocial milieu for cardiovascular health among young women. Female-specific risk factors, such as polycystic ovary syndrome, premature menopause, or a history of pre-eclampsia, are similarly overlooked when risk is estimated in women.

The ARIC surveillance study is the first to report contemporary incidence data of adjudicated MI events in a representative sample of the young US population. However, only hospitalized MI was evaluated. A large portion of MI events, including sudden/unexpected cardiac deaths, occur out of the hospital, and this was not captured through the ARIC hospitalization surveillance. There is evidence that women have experienced smaller improvements in the prehospital case fatality of MI than men,<sup>5</sup> and thus, more data are needed for a complete picture. Nonetheless, the upward incidence trends of hospitalized MI in young women are concerning and deserve an explanation. Younger adults, and women in particular, have been inadequately studied in cardiovascular research. It is now time to pay attention to this group to optimize prevention strategies and promote cardiovascular health among women. Prevention efforts should start at a young age and should take into account currently overlooked risk factors that are relevant for women.

## ARTICLE INFORMATION

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## Disclosures

None.

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