Race, Ethnicity, and Gender Disparities in Acute Myocardial Infarction

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KEYWORDS

• Acute myocardial infarction • Cardiogenic shock • Cardiac arrest • Disparities • Sex • Race

KEY POINTS

- Women and racial minorities continue to have worse outcomes highlighting the need to make health care more accessible and equitable.
- Despite national and societal efforts, clinical trials continue to have under representation of women and minorities, further limiting the full range of benefits from novel therapies for this population.
- An in-depth, comprehensive, and integrated understanding of the gender and racial disparities with particular attention to their social determinants of health to help in cardiovascular disease prevention and appropriate secondary prevention after incident acute myocardial infarction event are the need of the hour.

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INTRODUCTION

Cardiovascular disease (CVD) continues to be the leading cause of morbidity and mortality in the United States and worldwide, with over 17.9 million deaths from CVD in 2019.[1,2] There are persistent racial and gender disparities in the diagnosis, treatment, and prognosis of individuals with CVD, despite multiple advances in this field.[3–5] Women and people from racial and ethnic minority groups (black race, Hispanic ethnicity, Asian and Native Americans) are disproportionately affected by discrepancies in CVD diagnosis, treatment, and outcomes.[6] These racial and gender disparities are further exaggerated in the acute care setting, such as in patients with acute myocardial infarction (AMI), due to the additional time-sensitive nature.[7] Identifying and mitigating these vulnerabilities in conjunction with addressing structural racism and bias and encouraging suitable representation could result in better outcomes.[8] Unlike other reasons for admission to the intensive care unit (ICU) with a critical syndrome (such as sepsis or acute respiratory distress syndrome), AMI constitutes the end-result of failure of both primary and secondary prevention techniques. Further, the impact of lifestyle interventions and the social determinant of health is very pronounced in CVD. Therefore, when faced with these critically ill patients in the ICU, the critical care physician should seek to address both the acute health care disparities and the prevalent long-standing disparities to ensure durability of the ICU interventions.

In this narrative review, the differences in pathophysiology, clinical course, risk profile, and in management and outcomes of AMI patients across gender, racial, and ethnic groups will be discussed (**Table 1**). We also highlight demographic and psychosocial perspectives that might undergird disparities in cardiovascular care and provide recommendations for earlier identification of novel risk factors that increase the risk of adverse outcomes.

BACKGROUND

Extensive scientific literature describing differences in patterns of health care delivered to vulnerable populations dates back many decades. In the mid-19th century, German physician Rudolph Virchow suggested the presence of variations in health care-related outcomes and attributed these differences to several societal factors.[9] In the early to mid-20th century, CVD became one of the leading causes of death worldwide and was described to affect men, women, all races, and age groups equally.[10] In 1927, a study by Stone and Vanzant noted heart disease to be different in the Southern United States compared to the Eastern and Northern United States.[11] They attributed the larger population of black in the Southern United States to be one of the contributing factors and described the incidence of CVD in the black race to be 1.8 times more than the white race. A prospective cohort study done in Northern California that included patients who experienced acute AMI between 1995 and 2002, found the age-adjusted risk of AMI recurrence to be significantly higher in black men, black women, and Asian/Native American women when compared with white men.[12] Age-adjusted all-cause mortality was also significantly higher in black men and women compared with white men. These differences, attributed to gender, race, and ethnicity, were attenuated when certain variables including sociodemographic background were accounted for.[12] Differences in the incidence of AMI or recurrence of AMI were also being attributed to differences in risk factors for the development of CVD. Black and Hispanic Americans in the study population were more likely to be physically inactive, have poorer hypertensive and glycemic control, and were less likely to be informed by their health care professional that they were

Table 1
Summary of health care disparities in acute myocardial infarction and related states

Condition	Disparities Stratification[a]	Epidemiology and Risk Factors	Management	Outcomes
Acute myocardial infarction	Race and Ethnicity	Minority group have higher rates of dyslipidemia, obesity, chronic renal disease, insulin resistance, hypertension, and diabetes mellitus due to social factors	Minority groups are less likely to receive guideline-directed medications overall, and invasive procedures in non-ST-segment-elevation acute myocardial infarction	Minority group have higher readmission rates, increased adverse outcomes and long-term mortality
	Gender	Women are older and have higher prevalence of hypertension, and diabetes mellitus, have delayed time to first medical contact and increased rates of in-hospital and transfer times	Women have lower rates of reperfusion therapies, lower likelihood of receiving optimal medical therapy, longer delay to first medical contact and longer door-to-balloon time	Women have higher mortality
Cardiogenic shock	Race and Ethnicity	Minority groups have lower socio-economic status, higher rate of comorbidity in non-ST-segment-elevation acute myocardial infarction-cardiogenic shock	Minority group have lower rates of guideline-directed therapy and revascularization therapies	Minority group have higher mortality
	Gender	Women are older and with higher comorbidity	Older women have lower rates of invasive hemodynamic monitoring, revascularization therapies, and mechanical circulatory support utilization	Women have higher rates of morbidity, morbidity, and vascular complications
Cardiac arrest	Race and Ethnicity	Lower rates of receiving bystander cardiopulmonary resuscitation in minority group neighborhoods, variable emergency medical services arrival time	Minority groups have lower likelihood of receiving reperfusion therapies in post resuscitation treatment and lower utilization of targeted temperature management strategies	Minority group have higher mortality and poorer neurologic outcomes
	Gender	Women have lower rates of bystander cardiopulmonary resuscitation	Lower likelihood of receiving reperfusion therapies in post resuscitation treatment and lower utilization of targeted temperature management strategies	Variable results on mortality and neurologic outcomes

[a] Black race and Hispanic ethnicity are the most studied minority groups, with limited information on other sub-groups (Asian, Native American).

overweight.[13] In an analysis done in 1997, black patients were found to be less likely to undergo coronary revascularization procedures when compared to white patients, and this was not explained by the differences in clinical features of their CVD.[14] They were 13% less likely to receive angioplasty and 32% less likely to undergo coronary artery bypass grafting (CABG).[14] A similar but less significant trend was observed between coronary revascularization procedures between Hispanic and non-Hispanic white patients from 1975 to 1999 by Yarzebski and colleagues[15] This was also noted to be present in 2014, when Albert and colleagues explored the impact of Massachusetts enacted legislation that required all the residents to have health insurance.[16] Compared with white patients in the pre-legislature period, black and Hispanic patients were found to have lower rates of CABG or percutaneous coronary intervention (PCI) while Asians/Native Americans were found to have a higher rate of revascularization.[16] Similarly, during the post-legislature period lower rates of revascularization therapies were observed in black and Hispanic patients with higher rates in Asians/Native Americans when compared to white patients. In this analysis, men were also more likely to receive cardiovascular revascularization procedures when compared to women. Hence, a reduction in barriers to insurance did not eliminate pre-existing disparities in access to cardiovascular procedures.[16] Glance and colleagues in their analysis on effect of Medicaid expansion noted reduction of uninsured black patients as compared to uninsured white patients. However, this was not associated with reduction in disparities in AMI revascularization therapies.[17] The concerns of AMI care disparities on being less sensitive to insurance, was also noted in another similar study on Medicaid expansion.[18]

Apart from racial disparities, differences in outcomes due to gender have been studied extensively. In 1997, Herman and colleagues analyzed the population admitted from 1985 to 1990 and included in World Health Organization multinational monitoring of trends and determinants in CVD-Bremen AMI Registry for 28-day mortality difference among men and women.[19] They noted that even after adjusting for age, women had 20.9% mortality post-AMI versus 16.8% in men (P= .04). After adjusting for cardiac impairment and therapies however no difference was observed. The Minnesota Heart Study also showed higher age-adjusted mortality in women less than 65 years (12.5% of women vs 6.5% of men, P<.01).[20] The increased risk was driven by young women, which has been shown in other studies as well.

Multivariate analysis also showed that among those less than 65 years, female gender was a strong and independent predictor of early death (odds ratio [OR] 2.0; 95% confidence interval [CI] 1.2–3.5; P<.01). Another large database study consisting greater than 15,000 patients noted that female gender was an independent predictor of operative mortality after CABG surgery.[21] Additionally, women and minorities have also historically been underrepresented in human subject research. In a mandate in 1993 through the National Institute of Health (NIH) Revitalization Act, the NIH established guidelines to include minorities and women in clinical research trials.[22] Furthermore, in 2016 NIH enacted a policy to list sex as a biological variable.[23]

Despite the pervasive disparities and the attempt to improve these efforts by NIH guidelines, studies continue to note the under-representation of women and minorities in cardiovascular clinical trials. In an analysis of clinical trials, Gong and colleagues noted that women comprised less than 40% of all subjects (37% non-coronary artery disease vascular, 30% coronary artery disease, 28% heart failure, 28% arrhythmia) during 1986 to 2015.[24] Although the enrollment increased in recent years, it still represented lower than expected disease population proportions. Another analysis of cardiovascular clinical trials in Canada between 1997 and 2009 found that the enrollment rates for women were lower than expected by 5% in coronary artery disease,

13% in heart failure, 9% in arrhythmia, and 3% in primary prevention.[25] A recent 10-year analysis on different cardiometabolic drugs noted that the majority of the trials only had 36% women and they were grossly under-represented compared to their disease burden.[26] Similar disparities have also existed among the minority and non-white population. When stratified by race, there were 81% white subjects enrolled compared to just 4% black subjects in this study. These findings were also observed by Purasana and colleagues who noted that between years 2000 and 2019 among the clinical trials registered in ClinicalTrials.gov only 21% of trials defined a recruitment target for underrepresented groups.[27]

CHARACTERISTICS OF DISPARITIES

In this section, we will seek to address the basis for clinical and health care disparities in the care of AMI patients. While AMI, and certainly cardiogenic shock (CS) and cardiac arrest (CA) complicating AMI, are frequently seen in the ICU, the health care disparities associated with these conditions are grounded in the baseline characteristics. In this section, we will highlight gender disparities in presentation, sex differences in biology, and the interaction of gender, race, and ethnicity.

Misclassification and Misdiagnosis Associated with Gender

The major misclassification and misdiagnosis biases stem from the prevalence of symptoms considered atypical of AMI in women. Women present less frequently with classical sub-sternal chest discomfort with radiation to the jaw and shoulder. A recent study by Milner and colleagues noted that only 54% of women had chest pain as their chief complaint when they had an AMI compared to 69% of men ($P<.001$).[28] These differences are more marked in the younger population, where women significantly were less likely to report chest pain. The same study reported that respiratory symptoms like shortness of breath seemed to be the chief complaint of AMI among younger women. Brush and colleagues elucidated how women have a broader and more heterogeneous phenotype of symptoms across the spectrum of AMI that further confounds the initial diagnosis.[29] They showed that women had 426 interview-symptom phenotypes as compared to 280 phenotypes in men. Women were also more broadly distributed in interview-symptoms phenotype.[29] Shin and colleagues investigated the interview styles when assessing for symptoms of AMI and found that if questions were open-ended then women and men had similar reporting of chest pain but if a narrowed line of questioning was adopted, then men reported more chest pain.[30] Recently the role of prodromal symptoms has been explored prior to an AMI. A study in Germany observed that more than 50% of women had prodromal symptoms of sleep disturbance versus 32% of men before an AMI.[31]

Often misclassification of the pathology leads to a domino effect. In an Australian STEMI registry, Stehli and colleagues noted that women had longer delays to primary reperfusion and higher 30-day mortality than their men counterparts (OR 1.38; 95% CI 1.06–1.79; $P=.02$).[32] In a similar analysis, Coventry and colleagues also reported that women who had less chest pain than their men counterparts were less likely to be allocated a priority one ambulance response (men 98.3% vs women 95.5%).[33] A study from New York City noted that 62% of women did not complain of chest pain while having an STEMI as compared to 36% of men ($P=.01$).[34] This eventually led to 72% of women having an estimated time gap of more than 90 minutes between symptom onset and hospital presentation versus 54% of men ($P=.03$).[34] All these studies further consolidate the fact that women present with more nonspecific and atypical symptoms that can often lead to overlooking the diagnosis of acute AMI

in women. This ultimately can lead to delays in presentation to the hospital and receiving timely care.

Pathophysiologic Variations by Sex

In addition to differences in clinical care, certain nuances in pathophysiology differ in biological males and females that may account for variations in outcomes of acute cardiovascular conditions. Studies have reported that women's hearts have increased pro-inflammatory markers compared to men.[35] Fietcher and colleagues used vertebral bone marrow metabolism as a surrogate marker of inflammation and noted that females had increased 18-fluerodexoy glucose bone marrow uptake.[36] They found a significant association between increased bone marrow metabolism and impaired myocardial function (P=.04) and perfusion (P=.014) in females.[36] This association was non-existent in males (P=.28). The role of vascular dysfunction and its higher prevalence in biological females with obstructive coronary artery disease may contribute to the differences in outcomes.[37] Merz and colleagues proposed that myocardial ischemia might result when symptoms occur in an acute stress state in the setting of impaired blood flow reserve and endothelial dysfunction among small arterial lumen vessels.[37]

Multiple analyses have observed that females have less atherosclerotic burden than males when presenting with AMI. Berger and colleagues noted that biological females had more nonobstructive coronary artery disease (14% vs 8%) along with reduced 2-vessel (25% vs 28%) and 3-vessel coronary artery disease (23% vs 26%).[38] Another study done on young people with fatal ischemic heart disease noted that females who died of ischemic heart disease had only a 63% chance of having obstructive disease compared to 77% in biological males (P=.002).[39] Females also tend to have a higher incidence of plaque erosion compared to males, who have more plaque rupture that contributes to increased mortality.[40] Han and colleagues also noted that females have more disease of microcirculation, although males have a higher atherosclerotic burden.[41] In light of these findings and worse outcomes in females, the role of microvascular and endothelial dysfunction has been increasingly studied and recognized in females, especially in myocardial infarction with no obstructive coronary arteries (MINOCA). MINOCA prevalence has been noted to be about 5% to 6%.[42] Up to 50% of MINOCA patients are females. This is a considerable difference form the AMI with coronary artery disease population proportion where females make up only 25% of the population.[43] It is also more likely to be seen in black, Pacific Islander, or Hispanic populations.[43] Although, the pathophysiology remains poorly understood at present.

Intersection of Age, Race, and Gender

Health disparities are mostly caused by the distribution of CVD and associated risk factors, which differ among racial, ethnic, and gender groups. While men tend to have a higher prevalence of CVD risk factors at earlier ages, postmenopausal women have higher blood pressure, cholesterol, and weight compared to men of similar age.[44] Variable concentrations of endogenous estrogens, which have a protective but pleiotropic impact on the cardiovascular system, especially before menopause, are partly responsible for better cardiovascular health in biological females compared to males among white adults.[45] However, black adults do not follow similar trends which argues that the intersectionality framework–a social stratification which includes age, gender, and race and ethnicity–forms an interconnected system of oppression that restricts opportunities for people with underprivileged social status due to structural racism.[46] Therefore, more than just 1 inferior position, having several subordinate

positions may be linked to worse health ramifications. An intersectionality framework stresses that being a black woman is more than simply the sum of being black and a woman in terms of CVD risk, challenging a belief that women are a homogenous group with similar life experiences and outcomes. Black women may encounter greater challenges than other intersectional groups in accomplishing ideal cardiovascular health because they may be more likely to encounter a series of life hardships and social or material challenges, and may have fewer available resources to deal with these obstacles.[47] The specific causes of varying racial and gender trends probably involve various environmental risks encountered during an individual's lifetime. There is increasing recognition that social determinants of general health which include health care access and quality, education access and quality, social and community context, economic stability, and neighborhood and built environment play an important role too.[48–50] Black adults are more likely to suffer the negative impacts of bias, such as restricted access to higher paying jobs, education, and health care, according to studies on the impact of communities.[51] In addition to offering fewer options for safe areas to exercise and less healthy food and drink options, low-income communities may also be responsible for obesity and a higher risk of CVD.[52] The intersectionality paradigm also illustrates how a person may be privileged in certain social systems of inequality while experiencing oppression in others. The multiplicative, additive, and amplified interaction between gender, race and ethnicity, and age described above has been demonstrated in a recent study by Kanchi and colleagues who found that the combined effects of gender and race and ethnicity on overweight/obesity and hypertension were greater than the sum of individual gender, race and ethnicity effects.[53] The group also found that white women had the lowest prevalence of CVD risk factors among the groups studied, while black women had the greatest prevalence.[53] These points highlight the significance of looking at gender and race concurrently, and they are consistent with a sizable but inconsistent body of research on social and environmental variations in CVD risk by race and gender as well as on hormonal variations by biological sex.[54] Recognizing the collective gender, racial, and ethnic differences across several CVD risk factors may lead to novel interesting etiologic questions, direct preventative initiatives, and emphasize the relative significance of racial, ethnic, and age differentiation within the same gender for CVD investigations.

ACUTE MYOCARDIAL INFARCTION AND RELATED STATES

ST and Non-ST-Segment Elevation Acute Myocardial Infarction

Disparities in management

Black patients continue to have a higher incidence of AMI including both ST-segment-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI).[55,56] Furthermore, black patients have higher rates of dyslipidemia, obesity, chronic renal disease, insulin resistance, hypertension, and diabetes mellitus, among other cardiovascular system-related comorbidities.[55] Hospital surveillance of NSTEMI in 4 United States areas over 15 years was evaluated by Arora and colleagues as part of the Atherosclerosis Risk in Communities surveillance investigation.[56] They noted that black patients had a 24% lower probability of receiving non aspirin anti-platelet therapies, 29% lower probability of coronary angiography and 45% lower probability of revascularization therapies. Previous studies found race associated with differential NSTEMI management, with black patients less likely than white patients to receive guideline-directed medications and invasive procedures.[55,57–60] According to studies like the Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With The Guidelines database, even in risk-adjusted cases, black patients hospitalized with NSTEMI were

younger, less insured, and had a greater prevalence of comorbidities along with considerably lower likelihood of receiving invasive angiography (45% vs 61%) or revascularization (25% vs 45%) than white patients.[61]

Independent of race, compared to men, women are more likely to be placed in a lower risk category for CVD and to receive less intense medical care for the condition overall, including less invasive and pharmacologic treatments as well as lifestyle counseling.[62,63] Numerous studies have noted that women have lower treatment rates of traditional cardiovascular risk factors such as hypercholesterolemia and hypertension.[64,65] Women from racial and ethnic minority group backgrounds have reduced rates of statin utilization (primary and secondary prevention) and cholesterol goals compared to white women.[66,67] There has been a correlation found between being a women receiving invasive therapy for coronary obstruction and delay in care.[59,68] In the National Heart, Lung, and Blood Institute Dynamic Registry, compared to older women, young women less than 50 years, were more likely to experience adverse outcomes including target vessel and target lesion failure at 1 year, despite having less severe coronary artery disease by angiography.[69] The Variation in Recovery: Role of Gender on Outcomes of Young AMI patients study found that among young patients with STEMI, women experienced delay in reperfusion.[70]

Overall, disparities in treatment have been associated with lower education levels, single-marital status, and care interruptions.[65] Socioeconomic factors, such as lower income and lack of health insurance, physician prescribing tendencies, lower rates of specialist referrals, inadequate risk assessment, and poor patient-physician communication, are other potential explanations for the differences in cardiovascular treatment among women of racial and ethnic minorities.[71,72]

Disparities in outcomes

There have been conflicting data on significant differences in short term mortality rates among different racial and ethnic groups. In a recent observational study on patient with AMI post-PCI it was noted that black and women patients had increased risk of angina at 6 week and 1 year mark.[73] Similarly other analysis have noted that black individuals had increased rates of bleeding post-PCI/thrombolysis after an STEMI and also had increased risk of stent thrombosis.[74,75]

AMI has been associated with higher mortality in women, particularly in younger women with STEMI.[38,76] In 2016, women's overall CVD mortality (49%) was comparable to men's (51%).[6] However, there are still notable differences in subjective outcomes: women with ASCVD of all racial and ethnic origins report worse patient experiences, a worse self-reported perception of their health, and a lower quality of life.[77]

Analysis of cardiovascular outcomes over time has revealed long-lasting differences among women from racial and ethnic minority groups backgrounds. Compared to men or white women, the in-hospital mortality rate for acute AMI is considerably greater in black and Hispanic women, despite continuous efforts by various government organizations like the National Institute of Minority Health.[6,68] For instance, after controlling for age and comorbidities, a study discovered significantly higher odds of in-hospital mortality among younger Hispanic women compared to younger white men.[68] 1-year event rates for women in the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications trial included higher rates of major adverse cardiac events (23.9% vs 15.3%), ischemic target-vessel revascularization (16.7% vs 12.1%), and mortality (7.6% vs 3.0%). Being a woman was an independent predictor of major adverse cardiovascular events and bleeding complications.[78] It has been repeatedly observed that after PCI, women and racial minorities experience

greater rates of bleeding and vascular complications. Although rates of bleeding and vascular complications in this vulnerable population have decreased over time, data from the Northern New England PCI registry showed that being a woman was still a significant predictor of increased risk of bleeding and vascular complications even after baseline differences were considered.[79] A prospective study by Cai and colleagues, revealed that the incidence of major bleeding following PCI was higher in black patients compared to their white counterparts.[80] The disparate outcomes in women and racial and ethnic minority group backgrounds following AMI may be linked to biases in the provision of diagnosis, treatment (as discussed above), patient education, and an elevated burden of cardiovascular risk factors in certain groups.[81,82]

Cardiogenic Shock

Despite the significant therapeutic advances in management, AMI-CS accounts for significant morbidity and mortality.[4,83] CS accounts for one of the most common causes of death in patients with acute AMI with mortality approaching 50% within the first 48 hours after presentation[83] Despite significant research in the domain of acute cardiovascular care, there exist significant disparities in the management and outcomes of AMI-CS.[84] Studies have shown that patients of racial and ethnic minority group have higher mortality and lower rates of guideline-directed therapy and revascularization when compared to their white counterparts.[85–87] Also, women with acute AMI-CS have been found to have increased morbidity and mortality when compared to men.[88]

Koeth and colleagues evaluated 36,643 patients consisting of 66.8% men and 33.2% women with CS complicating STEMI. STEMI-CS was more frequently found in women when compared to men (adjusted OR 1.19; 95% CI 1.09–1.30).[89] Prior studies from our group have demonstrated gender-based health care disparities in the management and outcome of AMI-CS.[90–93] In one of the National Inpatient Sample analyses, being a woman was found to be a predictor of worse in-hospital outcomes including higher in-hospital mortality (adjusted OR, 1.05; 95% CI 1.02–1.08) and more frequent discharge to a skilled nursing facility.[90] Women with AMI-CS were noted to be older and of the Hispanic or non-white race. Older women had lower rates of PCI, CABG, invasive hemodynamic monitoring, and mechanical circulatory support utilization compared to men. Despite a higher risk of mortality and revascularization failure rate, Joseph and colleagues described a greater survival benefit to hospital discharge in women when compared to men with early initiation of hemodynamic support.[94] Similarly, early use of PCI was demonstrated to be an independent predictor of 1-year survival in women (hazards ratio 0.55; 95% CI 0.37–0.81), and no similar trend in men was noted.[95]

In a study by Ya'Qoub and colleagues in patients with AMI-CS, women of all races had higher in-hospital mortality when compared to men. Men who were of white, black, and Hispanic race and ethnicity had a mortality rate of 33.3%, 33.6%, and 34.7%, respectively.[96] In contrast, women who were of white, black, and Hispanic race and ethnicity had a higher mortality rate of 40.9%, 40%, and 45.4% even after adjusting for confounding factors (adjusted OR 1.11; 95% CI:1.06–1.16).[96] Similarly, men who were black and Hispanic had significantly higher in-hospital mortality compared to white men (black men: adjusted OR 1.18, 95% CI 1.04 to 1.34; Hispanic men: adjusted OR 1.19; 95% CI 1.06 to 1.33).[96] In a National Inpatient Sample analysis by Raheja and colleagues, mechanical circulatory support was utilized in 11.4% of the total 1,021,274 included patients.[97] White patients had significantly higher odds of getting mechanical circulatory support inserted (OR 1.18, 95% CI: 1.13–1.23) with significantly lower odds in black (OR: 0.65, 95% CI:0.61–0.69) and Hispanic (OR: 0.89; CI: 0.83–0.97)

patients.[97,98] In a study demonstrating the utilization of extracorporeal life support for CS, Wang and colleagues noted women were more likely to be centrally cannulated.[99] They also noted women patients experienced more limb ischemia (7.5% vs 4.1%, $P<.001$) whereas men were more likely to receive renal replacement therapy (25.6% vs 31.3%, $P<.001$) and had longer hospital stays.[99] Women also had worse vascular compilations (8.8% vs 5.7%; $P<.001$), bleeding (7.1% vs 5.2%; $P=.01$), and limb ischemia (6.8% vs 4.5%; $P=.001$) per a recent Cardiogenic Shock Working Group report.[88]

Several studies have shown that being a woman and being from racial and ethnic minority groups to be independently associated with increased mortality. Trials adequately powered for pre-defined subgroup analysis based on gender and race should be promoted.[85] In addition, implementing STEMI and CS protocols will also aid in contributing to a reduction in health care disparities. Other potential solutions involve implicit bias training, social and familial support in patients with AMI-CS. The 6-point actionable framework by Sukhera and colleagues can help in better integration on implicit bias recognition and management to help improve racial and gender disparities.[100] In a recent analysis it was seen that black patients were less likely to be discharged home and more likely discharged to a skilled nursing facility.[101] Black patients in skilled nursing facility were more likely to be hospitalized than their white counterparts. Thus, addressing gaps in social support as part of post hospitalization care may be essential to addressing these disparities.[102]

Cardiac Arrest

It is estimated that every year, about 250,000 Americans suffer from out-of-hospital cardiac arrest (OHCA).[103] However, there are significant gender and racial differences in the incidence of witnessed arrests, resuscitation efforts, shockable rhythms, PCIs, and survival rates of cardiac arrest. Patients suffering from OHCA rely on lay rescuers to identify them, phone for assistance, start cardiopulmonary resuscitation (CPR), and perform early defibrillation.

Disparities in recipients of bystander cardiopulmonary resuscitation in out-of-hospital cardiac arrest

The most vital elements in the chain of survival for CA resuscitation are the identification of CA and provision of bystander CPR.[104] There is a difference in bystander CPR performance between genders.[105,106] Compared to women, men were more likely to get bystander CPR. This difference was not present in the home environment, but it was more notable in public settings.[107,108] Lower rates of women bystander CPR are caused by a variety of factors, including bias in instructional programs, modesty and social conventions surrounding touching or exposing a woman's chest, and a lack of awareness of cardiac disease in women.[105,106] Responders might be more motivated and less concerned about the legal ramifications of their acts while they are at home.[107] By using more realistic women patient simulators in CPR training, prejudice in training can be addressed, which could assist in overcoming social stigma related to the physical characteristics of patient gender or biological sex and lessen resistance to bystander CPR.[105] According to an Austrian study by Krammel and colleagues, women were less likely to administer an automated external defibrillator or do standby CPR on a person with CA.[109] This discrepancy may be lessened if women are encouraged, empowered, and trained to provide bystander CPR.[110]

Additionally, race and socio-economic status have an additive effect on the likelihood of receiving CPR. In a study by Sasson and colleagues, out of 14,225 adult CA patients, those from low-income, predominately black neighborhoods had a

roughly 50% lower chance of receiving bystander CPR than those from high-income, predominately white communities. Higher income, on the other hand, attenuated the disparity in CPR provision for patients from integrated communities, but it only increased the likelihood of receiving CPR for a patient from a black community by 25%. Patients who were given bystander CPR had higher odds of being discovered in a shockable rhythm, requiring defibrillator treatment, and surviving to be admitted to and released from the hospital.[111] Similar findings were discovered for black patients in a different study that looked at 22,487 patients from the 2011 National Emergency Medical Services Information System. This study also found a curvilinear association between county socioeconomic status and bystander assistance.[112] A study by Naim and colleagues showed that black children were 50% less likely to receive bystander CPR if they lived in a neighborhood with the worst socioeconomic index than white children living in a community with the best index (based on a percentage of black race, employment rates, level of education until high school, and median income). Nonetheless, white children, irrespective of their residential neighborhood, were administered CPR at comparable rates.[113]

Being ethnically Hispanic may be associated with one's likelihood of receiving CPR in addition to race. Compared to non-Hispanic patients, a considerable number of studies have shown that Hispanic patients receive bystander CPR less frequently.[114,115] Moon and colleagues, found that in the state of Arizona, bystander CPR was given less frequently in Hispanic neighborhoods specifically and that an initial shockable rhythm during arrest was also less common within Hispanic neighborhoods when comparing CA by Hispanic versus. non-Hispanic neighborhoods. In Hispanic communities, there was also a significant decrease in survival to hospital discharge.[114]

Overall, the hypothesis that race, ethnicity, and socioeconomic factors like work and wages will collectively exacerbate gaps in OHCA bystander care and automated external defibrillator use is supported by both regional and national data. The least likely patients to obtain bystander help are black and Hispanic patients in the most socioeconomically challenged neighborhoods.

Baseline characteristics and prehospital care

In comparison to men, women patients with OHCA are often older, have a larger number of comorbidities, are more likely to be in private settings, have witnessed fewer arrests, and are more likely to have a non-shockable rhythm.[116] For both men and women, the time between collapsing and the ambulance arriving was comparable.[117] One possible explanation for women presenting with non-shockable rhythms more frequently than men could be the frequency of non-ASCVD as the cause of CA.[116] Compared to males, biological females have higher chest wall compliance, which facilitates and improves the effectiveness of chest compressions and resuscitation techniques.[108] Prior data suggest that females who are or will become pregnant have a higher chance of surviving a CA event even though they are more likely to have arrest features that are linked to worse outcomes.[118]

Regarding racial differences, black and Hispanic people with CA were younger, more frequently women, and were more likely to have an arrest in a low-income and black or Hispanic neighborhood. Different results on emergency medical services (EMS) arrival times for patients from low-income and minority group backgrounds have been reported in studies specifically examining variations in EMS response based on neighborhood socio-economic status and race. One study found that EMS arrival times for black neighborhoods were similar to or shorter than those for white neighborhoods, while another study found that EMS arrival times in the poorest neighborhoods were longer than national benchmarks.[119] Starks and colleagues,

discovered that the duration of EMS treatments was longer in communities with a high concentration of black residents, but so did the duration to the first defibrillation. If cardiac arrests are happening in cities with high-rise buildings, it could take longer to defibrillate the patient because of the longer travel time.[120] A retrospective cohort study involving over 850,000 Medicare enrollees also revealed that, in comparison to black or Hispanic patients, a greater percentage of white patients were taken to the reference emergency department for the zip code following an acute event, such as CA. According to the American College of Emergency Medicine, EMS providers should provide transfer to the nearest suitable facility as a top priority. But compared to white patients, black and Hispanic patients in large United States cities were more likely to be sent to safety-net emergency rooms, that is, not to the closest referent emergency room for the zip code.[121] Such procedures could delay necessary post-resuscitation care, lowering overall odds of survival after OHCA, even if they might also be influenced by other variables, such as the facility where a patient has previously received care.

In-hospital management

In CA with STEMI, immediate coronary angiography and PCI lead to better results.[122] Therefore, emergent coronary angiography is advised for patients with OHCA who have STEMI, as well as for patients who have CS or recurrent ventricular arrhythmias.[123] In a recent multi-year national database analysis it was noted that women with CA post AMI, received less frequent coronary angiography (56.0% vs 66.2%), PCI (40.4% vs 49.7%), mechanical circulatory devices support (17.6% vs 22.0%), and CABG (8.3% vs 10.8%), with a longer median time to angiography.[124] Other studies in women with OHCA have also noted similar finding of less frequent coronary angiography (28% vs 50%), PCI (17% vs 30%), and CABG (0.4% vs 30%) in post-resuscitation treatment.[116,122,125] While limited, there appear to be gender differences in targeted temperature management (TTM) use.[126] TTM was employed less frequently in women in both non-shockable and non-shockable rhythms, according to a national database study conducted in the United States.[116] Compared to men, TTM was utilized less frequently in women (47% vs 61% $P<.01$), as shown by Winther-Jensen and colleagues.[125]

A retrospective analysis of hospitalizations following OHCA in California revealed that, while more life-sustaining treatments like percutaneous endoscopic gastrostomy tubes, tracheostomies, and, dialysis were administered to black and Hispanic patients, they received significantly fewer guideline-directed post resuscitation therapies (cardiac catheterization after ventricular fibrillation/tachycardia, therapeutic hypothermia). Also, black patients were more likely to be women with higher comorbidities and increased rates of neurologic and renal failure. Black patients underwent less coronary angiography and PCI.[127] Furthermore, it has been demonstrated that many hospitals treating the Hispanic/Latino community offer a lower level of guideline-directed TTM after OHCA.[128]

Outcomes

There are conflicting data on the impact of gender on survival after OHCA.[108,118,129] Women had lower unadjusted odds of survival, according to prior registry studies; however, on multivariate analysis, after controlling for therapy and baseline variables, women were linked to higher odds of survival.[118,129] The differences in baseline characteristics and interventions seen in the studies provide the most compelling explanation for the higher survival on multivariate analysis. In particular, women had lower rates of coronary angiography, PCI, and TTM; they were also older, less likely to have an

OHCA outside the home, and less frequently received bystander CPR, therefore, diminishing the sign of higher mortality in women.[130] It is possible that geographic difference in gender outcomes might exist in those experiencing AMI-CA. A Swedish study found that women had greater survival rates, and a Canadian study found no gender-specific variance in survival.[108,131] Disparities in prehospital care, risk factors, demography, and health care systems across different nations may account for the contradictory survival outcomes.

In the Cardiac Arrest Registry to Enhance Survival registry (2013–2017), of 250,000 patients, residents in census tracts with a preponderance of black people or those with low-to-middle-class incomes had a lower chance of surviving the OHCA after being released from the hospital or of surviving without suffering from a serious neurologic impairment. In these data they performed as well as their white, wealthier peers when it came to surviving until hospital admittance. The authors challenge the belief that poor survival rates in low-income and minority group areas are primarily caused by subpar CPR performance in the field.[113] According to Chan and colleagues hypothesis, survival differences based on race, ethnicity, and income might be connected to other, sporadically studied aspects of resuscitation care, like hospital post-resuscitation efforts and EMS procedures.[132]

To tackle the barriers in cardiac arrest disparities, it is important to implement public health initiatives to increase the number of women performing CPR as bystanders and to promptly send eligible women for internal defibrillator placement.[108] The lack of authentic women patient simulators could skew research and training in patient care.[105] The observed racial differences in CA outcomes may be reduced by optimizing baseline outpatient medical comorbidities and facilitating quick access to medical care during cardiac arrest. Regardless of gender and race, aggressive post-resuscitation care, which includes TTM and emergency coronary angiography, should be prioritized as it is likely to have positive effects.

FUTURE DIRECTIONS

There is a pressing need for future acute cardiovascular care research to develop strategies to modify social determinants of health. Social determinants of health are described as the conditions in an individual's environment that may affect health, quality of life, outcomes, and risks. This includes but is not limited to the individual's race, ethnicity, income, and health care access.[133] In recent literature, multiple studies have shown the effect of different components of social determinants of health on the outcomes of acute cardiovascular conditions.[48–50] Dupre and colleagues in their analysis noted AMI to be significantly higher among the unemployed (hazard ratio 1.35, 95% CI 1.10–1.66), and the risk increased incrementally with job losses highest being with 4 job losses when compared to no job loss.[134] This was further complemented by a large study in the Netherlands that observed a higher rate of mortality in the lowest income quartile as compared to the highest income quartile (hazard ratio 1.17, 95% CI 1.11–1.25).[135] They also were less likely to receive appropriate reperfusion strategies within the first 24 hours.[135] As described earlier, studies have noted racial disparities, especially among the non-white population who often have worse outcomes as compared to their counterparts. In summary, the current literature has repeatedly noted low economic status, less social support, reduced health care literacy, and limited health care access to be associated with increased CVDs and worse outcomes. Building upon this the American College of Cardiology/American Heart Association guidelines in 2019, published guidelines that recommended clinical evaluation of these determinants to help in the prevention of CVDs[136] (**Fig. 1**).

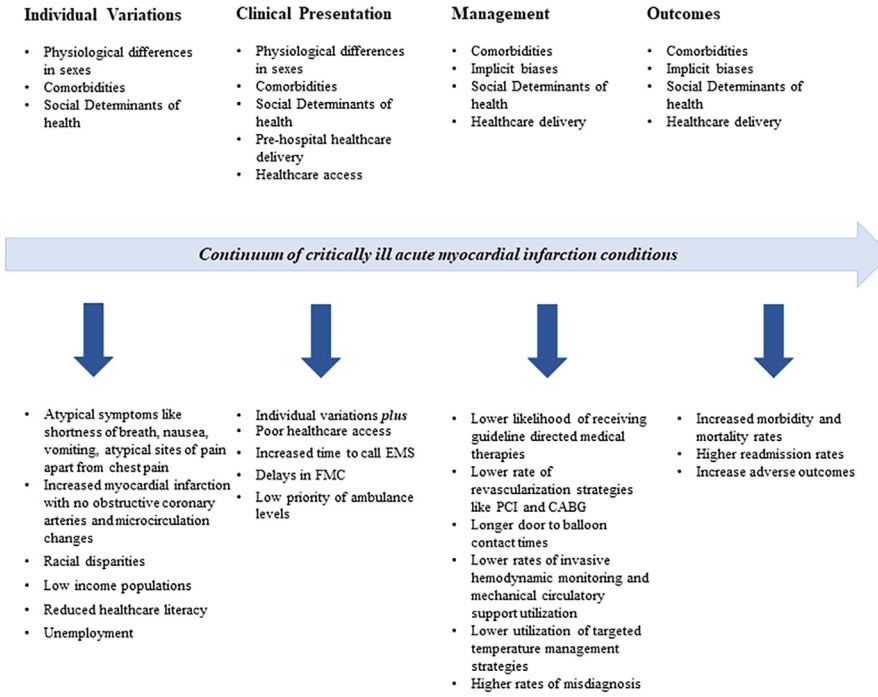

Fig. 1. Health care disparities in the continuum of care for patients with acute myocardial infarction. CABG, coronary artery bypass grafting; EMS, emergency medical services; FMC, first medical contact; PCI, percutaneous coronary intervention.

Recently there also has been focus on the utility and application of standardized AMI protocols to reduce gender gaps.[137] In one such analysis, researchers at the Cleveland Clinic developed a comprehensive 4-step STEMI protocol that used standardized approach to treat patients with STEMI. They observed reduction in variations of care delivered to men and women along with improved outcomes for women.[138] Additional multidisciplinary teams for cardiogenic shock and cardiac arrest may aid in standardization of health care delivery to women and minority populations.[139,140] In addition, there remains a significant under-representation of women and racial minorities in the cardiovascular clinical trials as described above. This lack of diversity presents a dominant clinical concern apart from being a social issue as it limits generalizability and evaluation of various therapies for these vulnerable subpopulations. There are multiple steps to alleviate these issues ranging from strengthening community engagement with pragmatic trial designs, having diverse clinical investigators and staff to stratification of efficacy and adverse events outcomes into different subgroups. Although the NIH and the United States Food and Drug Administration have established guidelines to increase diversity of participants significant work remains to be done.

SUMMARY

In the contemporary era, there remain disparities in management and outcomes of patients with AMI. Women and racial minorities continue to have worse outcomes highlighting the need to make health care more accessible and equitable. Despite national

and societal efforts, clinical trials continue to have under representation of women and minorities, further limiting the full range of benefits from novel therapies for this population. An in-depth, comprehensive, and integrated understanding of the gender and racial disparities with particular attention to their social determinants of health to help in CVD prevention and appropriate secondary prevention after incident AMI event are the need of the hour.[141]

CLINICS CARE POINTS

- Clinicians need to carefully evaluate implicit and explicit biases in the care of women and racial minorities.
- Attention to recruitment of women and racial minorities into clinical trials and studies is urgently needed.

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