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Sex and Race Disparities in Presumed Sudden Cardiac Death: One Size Does Not Fit All

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Sudden cardiac death (SCD), the sudden circulatory collapse due to ventricular arrhythmia has underlying various etiologies, ranging from acute and chronic cardiovascular conditions and include both ischemic and nonischemic disease, with an estimated annual incidence between 180,000–450,000 deaths in the United States/year, which corresponds to 7–18% of all deaths in the US.¹ More precise assessment of the true incidence of SCD remains challenging given current sources of case ascertainment. Given the difficulty in establishing the “denominator,” or the true total incidence of SCD in the population, understanding sex and race differences in patient with SCD is even more challenging.

Previous studies have begun to address this issue of sex and race differences in the incidence of SCD, with higher rates found in males and Blacks.^{2,3} Significant sex and racial disparities represent a major public health concern and may potentially be even more pronounced with a more robust data set. A limitation of previous studies is that many of them rely on medical or emergency medical service records and death certificates. This case ascertainment bias cannot and should not be overlooked. Misclassification of non-cardiac and non-arrhythmic

causes cannot be excluded without full autopsy which is influenced by family, providers, and the medical examiner's office.

In the current issue of *Circulation: Arrhythmia and Electrophysiology*, Tseng *et al.* reported a 3-year prospective postmortem study in San Francisco county to determine gender and racial disparities in rates and causes of presumed SCDs over a 37-month period from 2011–2014.⁴ The study took advantage of the multi-ethnic population within San Francisco county and included all incident presumed SCDs, meeting World Health Organization definition. Sudden arrhythmia deaths (SAD) were defined after autopsy evaluation of having no extra-cardiac cause or acute heart failure.

It is critical to consider the validity of all SCD studies since these studies are dependent on the specificity for actual cardiac causes. Therefore, it is important to note that the current study used autopsy findings to define causes for the presumed SCDs as well as a comprehensive toxicology analysis to exclude occult overdose as a cause of non-cardiac sudden death. The study identified 541 presumed SCD of which 97% were autopsy verified with a male:female ratio of 2.2 to 1. Indeed, the subjects were diverse with 21% Asian, 15% Black, 7.6% Hispanic, and 53% White, consistent the urban setting for the study. The very high rate of autopsy-verified causes lends significant credence to the findings of the study.

The current study highlights significant disparities in the race and sex for the presumed SCDs. Remarkably, more than half of presumed SCDs in women and Blacks are misclassified. The significant disparity uncovered provides important mechanistic underpinnings for presumed SCDs in women and minority populations. Specifically, there are significant differences in misclassification in female for presumed SCD with non-cardiac causes compared to male, with sudden neurologic deaths and fatal pulmonary emboli (10 and 8%, respectively of presumed SCDs). Indeed, previous studies have shown that women have more severe cases of massive pulmonary emboli than men,⁵ and likewise more severe strokes than men.^{6,7}

Moreover, within the defined population of SAD, women have a lower proportion of ischemic causes and a greater proportion of primary electrical causes compared to men. The current study also confirms significant racial disparity in presumed SCDs and SADs, with Blacks having the lowest proportion of presumed SCDs due to SAD and the largest proportion from non-cardiac causes that are not rescuable by implantable cardioverter defibrillators (ICD), including glycemic emergencies. Asians had the highest neurologic causes and a higher rate of lethal myocardial infarction without obstructive coronary arteries while Hispanics had the most gastrointestinal causes. Collectively, the findings provide strong evidence for a more targeted approach in the prevention and intervention based on race and sex for presumed SCDs and SADs. We need to focus beyond traditional coronary artery disease risk modification in women and minority populations and strategies need to target non-ischemic causes of SAD that include primary electrical diseases as well as cerebrovascular and thrombo-embolic diseases in women and a more comprehensive glycemic control in Black population.

Future Perspectives

With sex and racial disparities in SCD coming into sharper focus, it is crucial for the field to address this urgent issue. Indeed, understanding the pathophysiology and molecular underpinnings leading to the sex and racial disparities in SCD is critical, not only for designing appropriate and personalized treatments but also for developing effective and targeted prevention strategies. Specifically, understanding the pathophysiology as well as molecular mechanisms underpinning disparity is vital. Healthcare professionals, and cardiac electrophysiologists in particular, need to first recognize the significant burden of sex-race disparity and the possible underlying mechanisms. For example, in Black women, non-ischemic heart disease may represent a more common precursor of SCD.^{8,9} African Americans have higher incidence of hypertension, left ventricular hypertrophy, diabetes, that is associated with increased incidence of SCD.¹⁰ Women who present with myocardial infarctions may have atypical symptoms from men who usually present with chest pain. Based on prior studies, women with ICD have less firings than men and less inducibility,¹¹ and women are less likely to undergo cardiac angiography or revascularization after surviving SCD.¹² Even though the exact mechanisms underlying these differences are not completely understood, it is reasonable to speculate that sex variation in presenting symptoms may be one of the first modifiable factors.

Even though the current study in this issue of *Circulation: Arrhythmia and Electrophysiology* focuses on sex and race disparities,⁴ we need to also consider gender-race disparity within this same context. Beyond genetics and biology, low socioeconomic status is known to be a major contributor of excess SCD in Blacks where income and education are major contributing factors.² Future studies are required to decipher other factors that may contribute towards the known disparity including cultural differences, access to preventive medicine, and environmental factors including air pollution. Ongoing research into gender and racial disparities coupled with community advocacy and patient education are critical in the current healthcare climate.

Emerging technologies including remote access and cardiac wearable devices for preventive cardiology can be used to build bridges in these health disparities. Our collective goal in training the next generation of healthcare providers and cardiac electrophysiologists to embrace the new paradigms in health delivery will be highly impactful. We should all aspire towards precision medicine with the development of targeted clinical practice that takes into account race, sex and gender for risk-stratified prevention and treatment for SCD.

Abbreviations

SCD	Sudden cardiac death
SAD	Sudden arrhythmic death
ICD	Implantable cardiac defibrillator

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