

AHA Scientific Statement

Preventing and Experiencing Ischemic Heart Disease as a Woman: State of the Science

A Scientific Statement from the American Heart Association

Authors



Jean C. McSweeney, PhD, RN, FAHA, Chair; Anne G. Rosenfeld, PhD, RN, FAHA, Vice Chair; Willie M. Abel, PhD, RN, ACNS-BC; Lynne T. Braun, PhD, CNP, FAHA; Lora E. Burke, PhD, MPH; Stacie L. Daugherty, MD, MSPH; Gerald F. Fletcher, MD; Martha Gulati, MD, MS, FAHA; Laxmi S. Mehta, MD, FAHA; Christina Pettey, PhD, APRN, FAHA; Jane F. Reckelhoff, PhD

on behalf of the American Heart Association Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Hypertension, Council on Lifestyle and Cardiometabolic Health, and Council on Quality of Care and Outcomes Research

Slides Prepared by Chair and Vice Chair



Jean C. McSweeney, PhD, RN, FAHA, Chair
Anne G. Rosenfeld, PhD, RN, FAHA, Vice Chair

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II. Purpose



To present the most current research related to IHD in women, including studies that document women's experiences and influential factors that affect their receiving a correct diagnosis and timely treatment for IHD.

III. Epidemiology of IHD in Women



- IHD is multifactorial and includes risk factors such as:
 - Age
 - Race
 - Genomics
 - Ethnicity
 - Culture
 - Social
 - Lifestyle
 - Environmental Influences
- Studies indicate that women have substantially worse outcomes than men after acute IHD events
- Diagnosing and treating IHD in women are costly and contribute to escalating healthcare expenditures

III. Epidemiology of IHD in Women



- IHD affects ≈ 15.5 million Americans ≥ 20 years of age
 - Lower prevalence rates for women (5.0%) compared with men (7.6%)
- The IHD death rate in women 35-44 years of age continues to increase, while decreasing in their male counterparts
- Risk factors in younger women are thought to be the primary culprit in these IHD trends
- Other factors that may contribute to this trend:
 - Lack of recognition of prodromal symptoms
 - Failure to assess for IHD in younger women

III. Epidemiology of IHD in Women



- Black women have higher prevalence rates (7.0%) of IHD compared to Hispanic (5.9%) and White (4.6%) women
- The CDC reports IHD is the leading cause of death for black (23.4%) and white (22.9%) women
- IHD is the second leading cause of death for Hispanic (20.5%), Asian/Pacific Islander (20.8%), and American Indian/Alaska Native (16.9%) women

III. Epidemiology of IHD in Women



Genomics:

- There may be genetic and genomic influences that place some women at increased risk for IHD
- IHD is considered a multifactorial disease because it is influenced by multiple genes and the environment
 - Women may inherit ≥ 1 alleles that increases risk for IHD
 - Environmental factors also influence IHD development and progression
- Inheriting alleles that increase IHD risk does not mean women are destined to develop this multifactorial disease
- A woman who is susceptible to IHD should receive education on how to reduce her risk factors

III. Epidemiology of IHD in Women



- Women are influenced by their ethnicity and cultural background and are not a homogeneous group
- Ethnic or cultural background creates complex norms and expectations that affect all aspects of life, including development of risk factors
- Social and physical environments have also been implicated as major determinants of cardiovascular health
- Healthcare providers must be prepared to address the influence of ethnicity, culture, social and environmental influences on women's health and well being to impact escalating IHD rates

IV. How Women Experience IHD



- Women have notably poorer outcomes than men after initial IHD presentation
 - 1 year after acute myocardial infarction (AMI) 19% of men and 26% of women \geq 45 years of age will die
 - Within 5 years, 47% of women will die as compared to 36% of men
 - Women have higher in-hospital mortality rate with stable angina and acute coronary syndrome (ACS) compared to men
- Women have more complications after a first AMI such as increased bleeding risk after percutaneous coronary intervention
- A greater portion of women than men with angina and ACS have nonobstructive IHD, however women have more adverse outcomes than men

IV. How Women Experience IHD



- The estimated direct and indirect cost for IHD in 2010 was \$108.9 billion and is projected to more than double by 2030
- The WISE study estimated the average lifetime cost for women with nonobstructive IHD at \$767,288 (95% CI, 708,480–826,097)
- The estimated cost ranged from \$1,001,493 to \$1,051,302 for women with 1-vessel to 3-vessel IHD ($P=0.0003$)

IV. How Women Experience IHD



Results from the 2012 AHA survey of women's awareness of CVD:

- 56% of white women recognized CVD as the leading cause of death
 - lower recognition in black and Hispanic women who are most at risk
- About half of women in 2012 considered themselves very well/well informed about heart disease in women
 - but most had difficulty identifying symptoms of IHD
- Chest pain was less frequently cited as a warning sign of a heart attack in 2012 compared with 1997 (56% versus 67%)
- Awareness of women's less typical IHD symptoms was very low

V. Risk Factors



Traditional Risk Factors:

- Increasing age (women are typically diagnosed 10 years older than men)
- Obesity
- Dyslipidemia
- Diabetes Mellitus
- HTN
- Inactivity
- Family History
- Tobacco Use
- Depression
- Stress

V. Risk Factors



Traditional Risk Factors:

- IHD risk in women increases as the number of co-occurring risk factors increases
- Psychosocial risk factors, such as depression, are more prevalent in women than men
- After menopause, there is redistribution of body fat to the abdominal area
 - Increased abdominal fat is associated with higher incidence of CVD
- Postmenopausal, obesity rates maybe as high as 40%
 - 49.6% of all Black women are obese
- Women with diabetes mellitus have a 6 times higher risk of dying of CHD than women without diabetes mellitus



V. Risk Factors



Traditional Risk Factors:

- Older women tend to be less physically active than male counterparts
 - Contributes to development of co-occurring risk factors-obesity, hypertension, etc.
- Tobacco use imparts 25% greater risk of IHD in women than in males
 - Independent of smoking intensity or other CV risk factors
 - The largest difference in risk for IHD events between smokers and non-smokers was in younger women
- Systolic blood pressure is the most important modifiable risk factor, contributing to the excess IHD risk that occurs with aging
- Loss of estrogen at any age contributes to endothelial dysfunction and may increase risk of IHD
 - Observational studies suggest association between hormone replacement therapy and lower CV risk in postmenopausal women but large clinical trials did not

V. Risk Factors



Emerging Risk Factors:

- Inflammatory Markers
- Autoimmune Disease
- Preeclampsia & Pregnancy-Associated Hypertension
- Gestational Diabetes Mellitus
- Reproductive Hormones
- Postmenopausal Hormone Therapy
- Polycystic Ovarian Syndrome
- Functional Hypothalamic Amenorrhea
- Breast Cancer Therapy
- Sleep Apnea

V. Risk Factors



Emerging Risk Factors:

- Correlation has been shown between inflammation and IHD
- Some biomarkers that have shown correlation with inflammation and IHD include:
 - High-sensitivity C-reactive protein
 - Interleukin-1
 - Interleukin-6
 - Tumor necrosis factor- α
- However, some of these biomarkers are not specific for IHD, which can limit diagnostic usefulness
- Autoimmune diseases, like rheumatoid arthritis and systemic lupus erythematosus, are more common in women and are associated with significantly increased risk for CVD

V. Risk Factors



Emerging Risk Factors:

- Women with a history of preeclampsia have approximately double the risk of subsequent IHD, stroke, and venous thromboembolic events over 5 to 10 years post pregnancy
- Gestational diabetes mellitus doubles the risk of developing diabetes mellitus 4 months post partum and remains a lifelong risk factor
- Polycystic ovarian disease is associated with development of metabolic syndrome and may be an independent risk factor for premature CVD
- Sleep apnea is common in women but its impact on CVD is under recognized
- Breast cancer treatments are associated with:
 - An elevated risk of developing CVD
 - Various degrees of direct cardiovascular injury

VI. Assessing Women's IHD Risk



- A gap in racial/ethnic awareness of IHD as the number 1 cause of death in women was noted in 1997 and again in 2012, with white women's awareness (65%) superseding that of black (36%) and Hispanic (34%) women
- Because IHD is the leading cause of mortality, morbidity, and disability among women in the United States, it is vital that women have an accurate perception of their risk for IHD
- Risk factors commonly occur together that exacerbates the disease burden. Therefore, treatment should be holistic and not focused on one single individual risk factor

VI. Assessing Women's IHD Risk



- It is vital that healthcare providers accurately use cardiovascular risk assessment tools and effectively treat cardiac risk using recommended guidelines
- Currently, risk assessment tools are available for 5-year, 10-year, or lifetime risk estimate of coronary disease electronically, and the risk estimate is relevant for vulnerable populations such as women and blacks
- However, modifications to current risk assessment tools are needed because most underestimate or overestimate risk for nonwhite racial/ethnic groups

VII. The Diagnostic Experience



- Recognizing IHD in women is a long-standing, 2-pronged problem for both women and health professionals
 - **Women:**
 - ◆ Have to recognize symptoms as indicative of potential disease and seek treatment
 - **Health Professionals:**
 - ◆ Must recognize symptoms as potential prodromes of heart disease or acute symptoms indicative of impending AMI and respond appropriately
- Prodromal symptoms are defined as symptoms that are new and intermittent before an acute cardiac event and resolve after the event
- This lack of recognition of symptoms leads to delays in seeking treatment and contributes to women's disability and mortality rates

VII. The Diagnostic Experience



Women's Viewpoint:

- Often recognize symptoms as not normal, but do not attribute to potential IHD
- Elusive and vague intermittent prodromal symptoms often make it difficult for women to recognize these symptoms as indicative of IHD
- Despite efforts increase women's awareness of heart disease through campaigns from the AHA such as, *Go Red for Women*, studies continue to report that many women frequently attribute symptoms to:
 - Noncardiac reasons
 - Minimize the importance of symptoms
 - Put meeting social & role responsibilities ahead of seeking medical attention

VII. The Diagnostic Experience



Healthcare Providers' Viewpoint:

- Many healthcare providers still have difficulty recognizing IHD in women
- Lack of recognition often results in less aggressive or less timely treatment for women with possible IHD
- Among women who present with “chest symptoms,” only $\approx 50\%$ have obstructive IHD
 - Most women with IHD have non-obstructive disease, resulting in reluctance to order coronary angiography
 - However, the diagnosis of IHD may be missed or delayed when coronary angiography is not performed

VIII. Women's Symptoms/Presentation

- Women's decision to seek care for possible IHD is directly related to their symptoms
 - Multiple studies have shown that women have trouble recognizing their symptoms as cardiac related especially, when symptoms are atypical
- Women are less likely to experience chest pain than men, but the majority experience prodromal symptoms for weeks or even months before an acute cardiac event
 - Women may be reluctant to attribute symptoms to heart disease even when they experience typical chest pain
- Recognition of these prodromal symptoms by women and healthcare providers could improve the diagnosis of IHD and promote timely treatment to prevent/delay progression to AMI

VIII. Women's Symptoms/Presentation

- A prospective, longitudinal study conducted in the United States with 1097 women indicated 4 prodromal symptoms that were significantly associated with an increased risk of experiencing a cardiac event:
 - Discomfort in the jaw/teeth
 - Unusual fatigue
 - Discomfort in the arms
 - Shortness of breath
- Women reporting ≥ 1 of these prodromal symptoms were 4 times more likely to experience a cardiac event within the 2-year follow-up

VIII. Women's Symptoms/Presentation



Recognition of Symptoms as Cardiac:

- Women may have difficulty identifying prodromal symptoms as cardiac because they may not experience chest pain
- Women with AMI have lower odds of presenting with chest pain than men
- Women are more likely to present with:
 - Fatigue
 - Nausea
 - Neck Pain
 - Right Arm Pain
 - Jaw Pain
 - Dizziness
 - Syncope

VIII. Women's Symptoms/Presentation



Delay in Seeking Treatment:

- Timely treatment for AMI is crucial, yet women continue to delay longer than men
- Women underestimate their risk of IHD, which can influence their decision to seek care
- Women's treatment-seeking delay is attributed to:
 - Difference in symptoms compared to men
 - Women's interpretation of symptoms compared to men
- Treatment-seeking delay is associated with worse outcomes

VIII. Women's Symptoms/Presentation



Differences in IHD Pattern:

- The current definition of angina is based largely in data on men and generalized to women
- Sex differences exist in terms of type, pattern and quality of symptoms
- Despite lower rates of obstructive disease, less extensive IHD, and decreased incidence of AMI compared with men, women tend to have increased prevalence of angina, higher rates of myocardial ischemia, and more adverse cardiac events (re-hospitalization and death)

IX. Disparities in Guideline Based Diagnosis of IHD



- Women are less likely to be assessed for cardiac symptoms, but when assessment is performed, sex-based differences exist
- Exercise ECG is the first-line diagnostic tool to evaluate for IHD in symptomatic women who have a normal resting ECG, an intermediate pretest probability, and an ability to perform minimal exercise
- Sensitivity and specificity for the detection of obstructive IHD with exercise ECG are lower in women than in men, but the negative predictive value of the exercise ECG is very high
 - Reduced accuracy in women is due to lower exercise capacity, lower QRS voltage, and hormonal factors
 - Duke treadmill score provides additional diagnostic and prognostic information in women

IX. Disparities in Guideline Based Diagnosis of IHD



- The addition of cardiac imaging to assess for stress-induced wall motion or myocardial perfusion abnormalities supports the evaluation of IHD in women with an abnormal resting ECG, diabetes mellitus, questionable functional capacity, or intermediate-risk treadmill findings
- In women, stress echocardiography provides better specificity and diagnostic accuracy than standard exercise electrocardiography
- Diagnostic accuracy of exercise and dobutamine echocardiography appears to be comparable in women and men
- Prognostic information with stress echocardiography is also similar between sexes

IX. Disparities in Guideline Based Diagnosis of IHD



- Stress gated myocardial perfusion single-photon emission computed tomography with contemporary nuclear imaging agents provides high specificity and diagnostic accuracy and high prognostic accuracy regardless of sex
- Challenges of single-photon emission computed tomography imaging in women include breast attenuation artifact and possible unobserved minor perfusion defects in women with smaller hearts, in addition to radiation exposure
- Stress magnetic resonance demonstrated diffuse subendocardial perfusion defects in patient with cardiac syndrome X
 - Syndrome X is triad pattern of chest pain, abnormal stress test consistent with IHD, and absence of significant IHD on angiography
 - Female predominance of Syndrome X is approximately 70%



IX. Disparities in Guideline Based Diagnosis of IHD



- Disparities also exist in regard to physician adherence to evidence-based guidelines in the treatment of CVD at the time of hospital discharge
- Prescribing patterns have shown that women are less likely to be prescribed lipid-lowering medications, antiplatelet agents, and β -blockers at the time of hospital discharge than men
- Even after an appropriate diagnosis of IHD, disparities exist in the treatment of IHD in women despite guidelines for CVD prevention designed specifically for women

X. Emotional/Affective Responses



- When women receive a diagnosis of IHD or AMI, they often express disbelief
- Even when women are able to identify common CVD risk factors:
 - They often do not personalize this information
 - They do not perceive themselves at risk even though they have multiple risk factors
- Women often report that communication with physicians is less than therapeutic
 - Women do not feel physicians listen or take their self-reported symptoms seriously
 - This can influence women's decision making processes related to making healthy behavior changes and seeking health care
 - Physicians often do not discuss risk behavior modification with women

X. Emotional/Affective Responses



Women's Response to Treatment:

- Women tend to develop IHD 10 years later than men and may be more likely to have limited income
 - Adherence is a multifactorial concern that requires assessment of the patient's financial condition, abilities, and willingness to participate in the plan of care
 - This has implications for both primary and secondary prevention of IHD including medication adherence, particularly for the control of hypertension and dyslipidemia
 - Contributing factors to nonadherence are frequency of medications and perceived and actual side effects
- Increased income and education levels have been well established as associated with increased compliance rates

XI. Explanations for the Unique Experience: The Role of Sex

Determinants of residual gender/sex disparities stem from the health system and providers

- Clinical Perspective contributing to health disparity:
 - Greater clinical uncertainty when interacting with female patients reporting prodromal symptoms that may or may not be indicative of IHD
 - Beliefs or stereotypes about the behavior or health of female patients
 - Bias or prejudice toward women
 - Interpretation of symptoms is influenced by patient demographic factors including sex/gender
- Providers are not immune to bias; levels of implicit bias among clinicians toward different groups have been shown to be similar to those seen in the general population

XI. Explanations for the Unique Experience: The Role of Sex

- **Many other factors may make it more difficult to diagnose IHD in women:**
 - Lack of appropriate risk assessment tools that do not incorporate women's novel risk factors and prodromal symptoms
 - Women's terms to describe symptoms may not match the provider's expectations of IHD symptoms
 - Because women are often older at the time of initial IHD diagnosis, they frequently have other comorbid conditions, confounding the diagnosis
 - Even when providers suspect IHD in women, many diagnostic tools are not as sensitive and specific in women

XII. Gaps in Science



Despite advances, significant gaps in scientific knowledge regarding risks, mechanisms, assessment, interventions, and symptoms for women with IHD remain

- Risks and assessment
 - Inadequate information available about hypertension across the lifespan in women
 - The role of estrogen in IHD is unclear
 - Lack of more precise biomarkers and failure to assess impact of novel risk factors in women
 - Inadequate sensitivity of existing risk scores
- Mechanisms
 - Pathophysiology of microvascular angina is not well understood

XII. Gaps in Science



- **Interventions**

- Intervention tailored to women with IHD, and in particular, to women of ethnic and racial groups are needed
- How to achieve equitable delivery of evidence-based care needs to be studied

- **Symptoms**

- Mechanisms underlying symptoms are not fully understood
- Symptom phenotypes still need to be developed

XII. Future Directions: Practice



- Increased education for providers and women on emerging risks for IHD and routine assessment of individual risk of IHD
- Routine assessment of sex-specific risks for IHD in screening, history and physical examination by all primary care providers and gynecologists
- Population health approaches to decreasing women and girls' risks
- Assessment of risk factors for IHD and ways to reduce risk as part of every clinic visit for women

XII. Future Directions: Research



- Powering of clinical trials to allow for analysis by sex and reporting of sex-specific differences
- Encourage the use of common data elements to allow for data sharing across studies and analysis of treatment effects by sex with big data sets
- Broadening of inclusion criteria that focus on IHD symptoms to include more than chest pain
- Testing of interventions tailored for women and women of different ethnicities; in particular, cardiac rehabilitation programs

XIII. Future Directions: Policy



- Research funding targeted to improving the evidence for guidelines for prevention of IHD in women
- Interventions to identify and eliminate sex bias in treatment and use of clinical guidelines
- Devise measures to assess the effectiveness of guidelines for prevention, diagnosis and treatment of women with or at risk for IHD



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