CARDIOVASCULAR DISEASE IN WOMEN: THE FACTS

Karla M. Kurrelmeyer

From Methodist OeBakey Heart Center, Houston, Texas

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in women. One of every 2.4 women will die of CVD, and it claims almost 500,000 female lives annually.1 Since women are more likely than men to have sudden death as their initial presenting symptom, early prevention measures are even more important in women to prevent this catastrophic outcome.[2]

Ironically, more than 50% of women who were surveyed did not know CVD was the leading killer of women, and only 5% identified heart disease as their greatest health problem.3 This unawareness likely has contributed to the increase of cardiovascular deaths among women, whereas the number of cardiovascular deaths among men has slowly decreased since 1984.4

PREVENTION OF CVD IN WOMEN

The risk factors for heart disease 'm women are similar to men, though the weighting differs. For example, smoking, hypertension, LDL cholesterol and family history increase risk in women as much as they do in men.5 Diabetes, however, is a stronger risk factor in women, as are elevated triglycerides and low HDL levels.5•[7] Diabetic women are five times more likely co develop CVD than non-diabetic women, whereas diabetic men are only two times more likely co develop CVD than non-diabetic men.[6]

The most prevalent modifiable risk factor in American women is excess weight, and approximately 62% of American women are either overweight or obese.[8] Prospective daca from the Nurses' Healch Study dearly demonstrates that the relative risk of death from CVD increases with body mass index (BMI - defined as weight in kilograms divided by the square of the height in meters) once che BMI exceeds 19, che upper limit of normal; those with BMis greater than 29, defined as obesity, are at greatest risk.9

The second most prevalent modifiable risk factor in women is elevated total and LDL cholesterol.[8] Diet and aerobic exercise have been shown co lower total and LDL cholesterol and raise HDL cholesterol in women if they are performed together, although either in isolation failed to reach statistical significance.10 Unfortunately, the chird most prevalent risk factor in women is physical inactivity. In 2002, 43% of American women reported that chey were phys ically inactive.[8] The good news is their cholesterol abnormalities can be created with medication. In che large scatin trials, women responded similarly co drug therapy as men and benefited from a similar reduction in

Guidelines outline best practices for treating CVD in women

CVD treatment/prevention options for various risk levels

Recommendation Class, by Risk Level	I	IIa	IIb	III
High	• Aspirin therapy • ACE inhibitor therapy • Glycemic control • Treatments for low/ intermediate risk	• Depression evaluation and treatment	• Omega-3 fatty acid supplementation • Folic acid supplementation	• Hormone therapy • Antioxidant supplementation
Intermediate	• BP control • Lipid control • Treatments for low risk	• Aspirin therapy	N/A	• Hormone therapy • Antioxidant supplementation
Low/Optimal	• Smoking cessation • Physical activity • Weight reduction	N/A	N/A	• Aspirin therapy • Hormone therapy • Antioxidant supplementation

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Table 1. Current ACC/AHA guidelines for treating CVD in women

major coronary events.[11] The bad news is they will not benefit from the myriad other effects of aerobic exercise.

The current ACC/AHA guidelines for treating CVD in women are listed in Table 1.[38] Women have been stratified into four groups based on their risk for developing CVD: high risk means > 20% chance of developing CVD in 10 years, intermediate risk means a 10-20% chance of developing CVD in 10 years, and low/optimal risk means < 10% chance of developing CVD in 10 years. For each group there are four different levels of recommendations: Class I describes interventions deemed safe and effective; Class IIa describes treatments favored by clinical evidence; Class IIb describes therapies fur which evidence is less well established; and Class III describes interventions that are not useful and may be harmful.[38] Table 2 demonstrates how to estimate 10-year risk for developing CVD in women.39

DIAGNOSING CORONARY ARTERY DISEASE IN WOMEN

Diagnosing coronary arcery disease (CAD) in women is difficult for several reasons. First, chest pain in women does not accurately predict the presence of CAD, making risk stratification based on chis symptom alone practically useless. However, refining the diagnoses of chest pain into definite angina, probable angina, or nonspecific chest pain may improve the predictive value of symptoms.[18] Like men, nearly 90% of women with myocardial infarction (MI) in the Myocardial Infarction Trial and lnrervemion Project presented with chest pain. However, women with MI were also more likely than men to present with upper abdominal pain, dyspnea, nausea, and fatigue.[12-14] Therefore, both chest pain and atypical symptoms of angina should be pursued in women based on che appropriate clinical context and the underlying probability of disease. Second, for a given age and risk factor profile, the prevalence of CAD in women when compared co men is significantly less.[18] Women develop CAD on average 10 years later than men and therefore have frequendy developed ocher diseases, which affect their ability to exercise.[17] *These* factors decrease the accuracy of all available noninvasive tests, which may partially explain why women are less likely than men to be referred fur diagnostic testing.[15•16] Some earlier studies demonstrated that women with positive test results are *less* likely to undergo coronary angiography and revascularization procedures and therefore are twice as likely as men to experience a cardiac event during follow-up.19 However, these biases appear to be disappearing as physician awareness increases.

The following gender-specific issues should be considered when choosing a noninvasive stress test to evaluate chest pain in women. The sensitivity and specificity of electrocardiography (ECG) stress testing is much lower in women than men.[20] This not only reflects the lower prevalence of CAD in women < 50 years old, higher prevalence of single-vessel disease in women 50-75 years and lower exercise capacity of older women as previously stated, but also the ST-response used co evaluate ECG results is less accurate in women since it varies with the menstrual cycle and estrogen replacement therapy. Mitral valve prolapse, syndrome X, and coronary artery spasm are more prevalent in women and can cause an abnormal ST response in the absence of CAO.[21,22]

The sensitivity and specificity of pharmacologic or exercise testing is enhanced by adding imaging techniques. Myocardial perfusion imaging with gated SPECT has improved sensitivity over conventional treadmill testing, however breast tissue arrifacts may lead to a false-positive test result (decreased specificity).[23•24] Breast tissue artifacts may be reduced and specificity increased wich che use of newer high-energy agents such as technetium-99m sestamibi rather than thallium-201.[25] Application of computerized breast attenuation correction algorithms may also lead to enhanced specificity.

Likewise, echocardiography has improved sensitivity and specificity over conventional treadmill testing and is considered che most cost-effective approach to diagnosing CAD in women.[26] However, test accuracy is highly dependent on the image quality and the cechnician's and imerprecer's skills. Inadequate imaging occurs in approximately 10% of cases secondary to obesity, severe lung disease, chest wall deformities and inexperience. Using newer techniques such as harmonic imaging and echocardiography contrast agents improves image quality.[27]

PROGNOSIS AFTER REYASCULARIZATION

Several studies have demonstrated a worse prognosis for women than men with ST elevation myocardial infarccion, which may reflect increased severity of illness at presentation, increased age, more comorbidities in women when compared to men, and lower referral rates for coronary angiography and revascularization procedures. For example, the Framingham Study demonstrated char women were more likely than men to die in the hospital and within one year after infarccionP The International Study of Infarct Survival (ISIS-l) examined the effects of atenolol post-Ml and demonstrated greater one-week mortalicy for women compared wich men.36 ISIS-4 examined the effects of captopril after thrombolysis for acute MI and also suggested an increased short and long-cerm mortality in women.35 Finally, the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries trial demonstrated higher 30-day morcalicy in women and higher rates of intracerebral hemorrhage, possibly due to smaller body size and lack of chrombolytic dose adjustments.33

Meta-analysis of 10 randomized trials of primary angioplasty versus thrombolytic therapy demonstrated that primary angioplasty results in lower rares of

Estimating the 10-Year Risk of CVD in Women

Step 1. **Age**										
Age, y	20-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
Points	-7	-3	0	3	6	8	10	12	14	16

Step 2. **Total Cholesterol**					
TC, mg/dl	Age, y 20-39	Age, y 40-49	Age, y 50-59	Age,y 60-69	Age, y 70-79
< 160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
?.280	13	10	7	4	2

Step 3. **Smoking Status**					
	Age, y 20-39	Age, y 40-49	Age, y 50-59	Age, y 60-69	Age, y 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

Step 4. **HDL**				
HDL, mg/dl	?.60	50-59	40-49	<40
Points	-1	0	1	2

Step 5. **Blood Pressure**		
Systolic BP, mm Hg	Untreated	Treated
< 120	0	0
120-149	1	3
130-139	2	4
140-159	3	5
? 160	4	6

Step 6. **Add Up the Points**																		
Point Total	<9	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	?.25
10-y Risk,%	<1	1	1	1	1	2	2	3	4	5	6	8	11	14	17	22	27	?.30

Table 2. Steps 1-6 demonstrate how to estimate the 10-year risk for CVD in women.

death and MI at 30 days in women presenting with acute ST elevation MI.34 The CADILLAC trial examined the benefit of stent and abciximab in patients presenting within 12 hours of ST elevation MI and found a higher one-year mortali$_{ty}$ in women, possibly due co a longer time from symptom onset to percucaneous coronary intervention (PCI). Women who received a stem demonstrated no difference in morcality when compared co angioplasty alone, however they had less major adverse cardiac events at one year.31

The outcome of women and men with unstable angina and non-Q-wave MI (NQWMI) was found co be similar in the Thrombolysis in Myocardial Ischemia {TIMI) IIIB Regiscry.28 TACTICS: TIMI 18 demonstrated that, like men, women with NQWMI receiving both aspirin and tirofiban benefited from early invasive treatment.29 Likewise, women and men have similar prognoses after successful high-risk PCI. EPIC, EPILOGUE and

EPISTENT demonstrated that the clinical benefit of abciximab in high-risk PC! is independent of gender, although women experience more minor bleeding.30 The Taxus-IV trial demonstrated that women benefit equally from the Taxus drug-eluting stent-37

The Coronary Artery Surgery Study demonstrated increased operative mortality for women, which may be secondary to differences in functional class, age, size of coronary arteries and greater likelihood of emergent surgery. However, coronary artery bypass surgery provides excellent relief of symptoms and comparable long-term survival in women. [18,32]

CONCLUSION

With respect co coronary artery disease, women are not "small men." Differences in prevention, diagnosis, prognosis, and response to treatment have been identified. The reasons for these differences and the optimal management of coronary artery disease in women will hopefully be elucidated as more and more women are included in large, mulricenter, randomized cardiovascular research trials.

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Recently, the National Heart, Lung, and Blood Institute (NHLBI), the American Heart Association (AHA}, the Sister to Sister: Everyone Has a Heart Foundation and the American College of Cardiology {ACC) have partnered to increase public awareness. The Red Dress - promoted by the NHLBI's «rhe Heart Truth" campaign and the recognized symbol of heart disease awareness in women - cautions women to heed the threat of heart disease and take care of themselves. The AHA s "Go Red for Women" campai$_{gn}$ desi$_{gn}$ated a National Wear Red Day to increase awareness and help stimulate donations for research and education. The Sister to Sister Foundation, dedicated to bringing free screening to ulomen, desi$_{gn}$ated February 17 as National Womans Heart Day and offered free screenings and counseling in Dallas, Philadelphia, Miami, San Diego and Chi$_{cago}$.