Is a Woman’s Heart Different than a Man’s Heart?

-Hannah Raasch, MD, FACC
March 7, 2015
<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gender influences onset of CAD symptoms.</td>
<td>• Diagnostic testing and treatment regimens are the same for men and women.</td>
</tr>
<tr>
<td>• Gender affects treatment response to certain medical technologies (CRT and ICDs).</td>
<td>• In the guidelines there are not specific therapies which are recommended or withheld solely based on gender.</td>
</tr>
</tbody>
</table>
PREVALENCE OF CHD IN WOMEN
• Heart disease is the leading cause of death in women
• Since 1984, the number of deaths due to cardiovascular disease in women has exceeded that in men
• Risk of death due to CHD (coronary heart disease) in women is roughly similar to that of men 10 years younger
• In the Framingham Heart Study, nearly 2/3 of sudden deaths due to CHD in women occurred in those with no previous symptoms, as compared to 50% in men
AHA Statistical Update

Heart Disease and Stroke Statistics—2015 Update
A Report From the American Heart Association

Major Causes of Death for Males and Females, 2010

Source: NCHS.

A indicates cardiovascular disease plus congenital cardiovascular disease (ICD-10 I00-I99, Q20-Q28); B, cancer (C00-C97); C, accidents (V01-X59, Y85-Y86); D, chronic lower respiratory disease (J40-J47); E, diabetes mellitus (E10-E14); F, Alzheimer disease (G30).
CHD RISK FACTORS IN WOMEN
Cigarette smoking remains the leading preventable cause of CHD in women, with more than 50% of MIs among women attributable to tobacco.

The magnitude of excess risk imparted by smoking, which is estimated as 2-4 fold, is similar regardless of gender.

Risks of CHD begin to decline within months of smoking cessation and reach the levels of individuals who have never smoked within 3-5 years.
Diabetes and CHD

• Diabetes is associated with a 3-fold to 7-fold elevation in CHD among women, compared with a 2-3 fold elevation among men.
• The above difference may be attributable to more profound effects of diabetes on lipids and blood pressure in women.
• A higher percentage of men than women have high blood pressure until age 45.
• From 45-64, the prevalence of hypertension is similar between men and women.
• After age 65, more women have hypertension than men.
In 2010…
- 33% of PCI patients were female
- 25% of CABG patients were female

In 2012…
- 30% of heart transplant recipients were female

So… Do Women Have More Trips to the Cath Lab?
CHD SYMPTOMS AND EVALUATION
• Historically, chest pain has not been perceived to be of great prognostic value in women.
• In the Coronary Artery Surgery Study (CASS), half of all women undergoing angiography for suspected CHD did not have significant obstruction.
• Refinement of the diagnosis as definite angina, probable angina, or nonspecific chest pain improved the predictive value of symptoms.
• Women with classic angina pectoris had a 71% probability of angiographic disease compared to 36% with probable angina.
• In the Myocardial Infarction Triage and Intervention (MITI) project, women with MI were significantly more likely to present with abdominal pain, dyspnea, nausea, and fatigue.
Go Red Campaign

• https://www.youtube.com/watch?v=t7wmPWTnDbE
### Table 9. Pretest Likelihood of CAD in Symptomatic Patients According to Age and Sex* (Combined Diamond/Forrester and CASS Data)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Nonanginal Chest Pain</th>
<th>Atypical Angina</th>
<th>Typical Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>30-39</td>
<td>4</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>40-49</td>
<td>13</td>
<td>3</td>
<td>51</td>
</tr>
<tr>
<td>50-59</td>
<td>20</td>
<td>7</td>
<td>65</td>
</tr>
<tr>
<td>60-69</td>
<td>27</td>
<td>14</td>
<td>72</td>
</tr>
</tbody>
</table>

*Each value represents the percent with significant CAD on catheterization.

CAD indicates coronary artery disease; and CASS, Coronary Artery Surgery Study.

Adapted from Forrester and Diamond (52,73).
### Table 1. ACC/AHA Practice Guidelines on Exercise Testing: Pretest Probability of CAD by Age and Symptoms in Women

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Typical/Definite Angina Pectoris</th>
<th>Atypical/Probable Angina Pectoris</th>
<th>Nonanginal Chest Pain</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–39</td>
<td>Intermediate</td>
<td>Very low</td>
<td>Very low</td>
<td>Very low</td>
</tr>
<tr>
<td>40–49</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very low</td>
<td>Very low</td>
</tr>
<tr>
<td>50–59</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>60–69</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td>≥70</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
</tbody>
</table>

High indicates >90%; intermediate, 10–90%; low, <10%; and very low, <5%. Source: American Heart Association, Inc.

Evaluation for CHD
• ECG stress testing in women has a lower sensitivity and specificity compared with men, but not only because of gender difference in prevalence of disease.
• Women are more likely to have repolarization abnormalities and are less likely to achieve an adequate heart rate response.
• Estrogen may also have a digoxin-like effect on ST segments with exercise.
• In premenopausal women with no CAD the presence of ST depression with exercise varies with the menstrual cycle.
• Postmenopausal women receiving oral estrogen therapy are more likely to have exercise-induced ST depression with normal coronary angiograms than postmenopausal women not on hormone replacement.

Evaluation for CHD
# Exercise in Cardiovascular Disease

**Exercise Stress Testing in Women**  
**Going Back to the Basics**  
Priya Kohli, MD; Martha Gulati, MD, MS, FAHA

## Table 2. Diagnostic Value of Various Stress Testing Modalities in Women

<table>
<thead>
<tr>
<th>Stress Testing Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise ECG</td>
<td>31–71</td>
<td>66–78</td>
<td>78</td>
<td>47</td>
</tr>
<tr>
<td>Exercise echocardiography</td>
<td>80–88</td>
<td>79–86</td>
<td>98</td>
<td>74</td>
</tr>
<tr>
<td>Exercise SPECT</td>
<td>78–88</td>
<td>64–91</td>
<td>92</td>
<td>87</td>
</tr>
<tr>
<td>Pharmacological echocardiography</td>
<td>76–90</td>
<td>85–94</td>
<td>68</td>
<td>94</td>
</tr>
<tr>
<td>Pharmacological SPECT</td>
<td>80–91</td>
<td>65–75</td>
<td>90</td>
<td>68</td>
</tr>
</tbody>
</table>

Values are percentages. PPV indicates positive predictive value.
What do the guidelines say?
• In a cohort of >5000 asymptomatic women in the St. James Women Take Heart Project, there was no relationship between ST segment depression with exercise and mortality.
• ST depression prevalence was the same among women who died and those who survived.
• A relationship between ST depression with exercise and both cardiovascular and all-cause mortality was seen in men.
• Exercise capacity does have strong prognostic implications in women.
• In the same trial, those women unable to achieve 5 METs had a 3-fold increase risk of death compared to those who achieved >8 METS.
• For each additional MET achieved, there was a 17% reduction in mortality, after controlling for traditional cardiac risk factors.

ST Depression vs. Exercise
### Table 3. Non-ECG Exercise Test Variables of Diagnostic and Prognostic Value in Women

<table>
<thead>
<tr>
<th>Exercise Variable</th>
<th>Method of Assessment</th>
<th>High-Risk Values</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise capacity</td>
<td>Estimated by the stress protocol (in METs)</td>
<td>&lt;5 METs; &lt;85% of predicted value (predicted METs = 14.7 – (0.13 × age))</td>
<td>Predictive of mortality and cardiovascular events in both asymptomatic and symptomatic women</td>
</tr>
<tr>
<td>Chronotropic response</td>
<td>Achievement of age-predicted HR</td>
<td>&lt;85% of age-predicted HR</td>
<td>Predictive of survival in symptomatic women</td>
</tr>
<tr>
<td></td>
<td>Chronotropic index: chronotropic index = (HR_{peak} × metabolic reserve; metabolic reserve = (MET_{max} – 1)/MET_{peak} – 1); HR_{max} = (HR_{max} × HRR)/100% age-predicted peak HR</td>
<td>Chronotropic index ≤ 0.80</td>
<td>Predictive of mortality and cardiovascular events in asymptomatic and symptomatic women</td>
</tr>
<tr>
<td>HRR</td>
<td>Difference between HR at peak exercise and HR after 1-minute recovery</td>
<td>≤ 12 bpm after 1-minute recovery (upright cool-down period)</td>
<td>Predictive of mortality in asymptomatic and symptomatic women</td>
</tr>
<tr>
<td>DTS</td>
<td>DTS = exercise time – (5 × ST deviation) – (4 × angina score index)</td>
<td>Low-risk DTS, &gt; 11; moderate-risk DTS, &gt; 11, &lt; 15; high-risk DTS, ≤ 11</td>
<td>Predictive of all-cause mortality and cardiac mortality in asymptomatic and symptomatic women; in symptomatic women, moderate- and high-risk DTS indicate more severe CAD</td>
</tr>
<tr>
<td>ΔST/ΔHR index</td>
<td>Maximum change in ST-segment depression/change in HR</td>
<td>Abnormal, &gt; 1.6 μVbpm</td>
<td>Increases the sensitivity for detection of CAD in asymptomatic women</td>
</tr>
<tr>
<td>ST/HR slope</td>
<td>Greatest statistically significant slope by linear regression relating ST-segment depression to HR during exercise</td>
<td>Abnormal, &gt; 2.4 μVbpm; markedly abnormal, &gt; 6.0 μVbpm</td>
<td>Increases the sensitivity for detection of CAD in asymptomatic women</td>
</tr>
<tr>
<td>BP response</td>
<td>Assessment of BP response to exercise, change in SBP and DBP from rest with maximal stress</td>
<td>Decrease in SBP &gt; 10 mm Hg from baseline</td>
<td>High likelihood of ischemia/detection of CAD in left main coronary artery and/or 3-vessel disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SBP &gt; 190 mm Hg with exercise testing</td>
<td>Increased risk of developing hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exaggerated DBP response to exercise</td>
<td>Increased risk of developing hypertension</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; SBP, systolic blood pressure; and DBP, diastolic blood pressure. Source: American Heart Association, Inc.

* Using peak age-predicted HR = 206 – 0.88 (age) in asymptomatic women for chronotropic index calculation.
DEVICE THERAPY IN WOMEN
Sex Differences in Implantable Cardioverter-Defibrillator Outcomes: Findings From a Prospective Defibrillator Database

Derek R. MacFadden, MD; Eugene Crystal, MD; Andrew D. Krahn, MD; Iqwal Mangat, MD; Jeffrey S. Healey, MD, MSc; Paul Dorian, MD; David Birnie, MBChB; Christopher S. Simpson, MD; Yaariv Khaykin, MD; Arnold Pinter, MD; Kumaraswamy Nanthakumar, MD; Andrew J. Calzavara, MSc; Peter C. Austin, PhD; Jack V. Tu, MD, PhD; and Douglas S. Lee, MD, PhD

Annals of Internal Medicine, 2012

2007-2010; 1,288 women and 4,733 men
FIGURE 1.
Time to first appropriate and inappropriate shock, by sex

![Graph showing the time to first appropriate and inappropriate shock by sex.](image-url)
Women who receive ICDs were 31% less likely than men to receive an appropriate shock and 27% less likely to receive appropriate antitachycardia therapy.

Inappropriate shocks were similar regardless of gender.

The most common major early complications were due to lead replacement (5.4% of women and 3.3% of men).

This does not mean that ICDs are not effective in women, simply that the number needed to treat is higher.
Cardiac Resynchronization Therapy
Is More Effective in Women Than in Men

The MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) Trial

Aysha Arshad, MD,* Arthur J. Moss, MD,† Elyse Foster, MD,‡ Luigi Padeletti, MD,§ Alon Barsheshet, MD,† Ilan Goldenberg, MD,† Henry Greenberg, MD,* W. Jackson Hall, PhD,† Scott McNitt, MS,† Wojciech Zareba, MD, PhD,† Scott Solomon, MD,|| Jonathan S. Steinberg, MD,* on behalf of the MADIT-CRT Executive Committee

New York and Rochester, New York; San Francisco, California; Florence, Italy; and Boston, Massachusetts
MADIT CRT Trial demonstrated that CRT treated patients with NYHA class I and II heart failure symptoms, LVEF ≤30% and QRS≥130ms had a 34% reduction in the risk of heart failure or death than those with ICD alone.

Women were 25% of the study population (453 total).

Women had a 72% reduction in all-cause mortality and, for those women with QRS≥150ms or with LBBB, mortality reduction was even greater.

**CRT in Women**
Figure 1

Kaplan-Meier Estimates of Cumulative Probability of Heart Failure or Death Stratified by Sex and ICD or CRT-D Therapy

The 4 curves reflect the probability of heart failure or death, whichever comes first, over time in women and men having the device therapy—Implanted cardioverter-defibrillator (ICD) or cardiac resynchronization therapy with defibrillator (CRT-D)—to which they were randomized. Women randomly assigned to CRT-D therapy (blue line) had the best result. The purple line indicates female ICD therapy; the black line indicates male ICD therapy; and the red line indicates male CRT-D therapy.
**Figure 2** Kaplan-Meier Estimates of the Cumulative Probability of Death in Women and Men by Device Therapy

(A) Women had a significantly lower probability of death over time with CRT-D (red line) than with ICD (black line). (B) Men had similar probability of death over time with CRT-D therapy (red line) or with ICD therapy (black line). Abbreviations as in Figure 1.
• In subjects without heart disease women have, on average, a 10ms shorter QRS duration than men.
• Thus, for any given QRS≥130ms women might have, on a relative basis, more conduction disturbance and greater cardiac dysynchrony than men.
• When analyzing prior CRT trials in patients with more severe heart failure (MIRACLE, COMPANION, and CARE-HF), women, specifically, also seemed to benefit from CRT.
• CHD is evaluated and treated the same in men and women.
• Women are more likely to experience CHD later in life.
• Certain risk factors may pose a greater threat to females.
• Stress testing EKG interpretation has limitations in women.
• Exercise capacity has significant prognostic implications.
• Women may be less likely to receive appropriate ICD therapy.
• CRT is very effective in women.

Conclusions