Women and Heart Disease: CVD Risk and Assessment

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No disclosures
HEART DISEASE PREVENTION IN THE 1960's

- American Heart Association 1964: First Conference for Women on Heart Disease.
  - Title: “Hearts and Husbands”
  - Objective: Learn how to keep your husbands heart healthy.
- Conference for women only: 10,000 female participants to Portland, OR.

Courtesy: Dr. Nanette Wenger
Women and Heart Disease

• What we know about CVD risk in women
• Assessment of chest pain in women
  – Noninvasive testing
  – When to proceed to invasive testing
• Risk stratification
  – Calculation of risk
  – Prevention of disease
Mortality from CV disease

Source: American Heart Association
Extent of Problem

• CVD leading cause of death in US
  – Accounts for approximately 1/3 of deaths in women
  – Incidence increases dramatically with age

• Vascular disease
  – 1 in 9 women 45 - 65 yrs
  – 1 in 3 women > 65 yrs
Factors Influencing diagnosis of cardiovascular disease in Women

• Risk of heart disease underestimated in women
  – By women themselves
  – By physicians
    • Role of a woman’s demeanor
    • Physician estimate of cardiac risk
• Patterns of angina
  – Angina with exertion occurs similarly to men, but is more frequent with rest, sleep or mental stress
How aware are women in 2010?

Figure. Overall trends in awareness that coronary heart disease is the leading cause of death in women.

Source: American Heart Association
Diagnosis
Presentation in men

- Typical angina SSCP – uncomfortable pressure, fullness or squeezing or pain in the center of the chest
- CP brought on by exertion and is relieved by rest
- CP lasting more than a few minutes
- Radiation to the jaw or left arm.
Presentation in Women

- Typical angina
- Atypical CP
- Shortness of breath
- Neck or jaw pain
- Back, stomach or abdominal pain
- Nausea
- Palpitations
- Weakness
- Fatigue
- Unexplained Anxiety
- Only 30% with prodromal CP
Mechanisms for Ischemia in Women

• Higher prevalence of vasospastic angina and microvascular angina
• Gender differences
  – Plaque components: ↑ cellularity and fibrosis
  – Plaque location: diffuse disease
  – Endothelium: estrogen-dependent vasodilation
  – Hemostasis: ↑ fibrinogen and Factor VII
• Noncoronary syndromes more common
Are There Gender Differences in Non-invasive Diagnostic Tests?
## Pretest Probability of Coronary Heart Disease in Patients with Chest Pain
According to Age, Gender, and Symptoms

<table>
<thead>
<tr>
<th>Age</th>
<th>Nonanginal 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>


The probability values are expressed as the percent of patients with significant coronary artery disease on angiography.
Accuracy of exercise ECG test

<table>
<thead>
<tr>
<th>Clinical history</th>
<th>Gender</th>
<th>Prevalence of CHD (%)</th>
<th>False positive (%)</th>
<th>False negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite angina</td>
<td>Male</td>
<td>89</td>
<td>4</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>63</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>Probable angina</td>
<td>Male</td>
<td>70</td>
<td>13</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>40</td>
<td>46</td>
<td>22</td>
</tr>
<tr>
<td>Nonischemic chest pain</td>
<td>Male</td>
<td>22</td>
<td>91</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>5</td>
<td>94</td>
<td>5</td>
</tr>
</tbody>
</table>
Noninvasive Stress Testing

• Exercise (treadmill/bike) or Pharmacologic stress
• Cardiac monitoring with ECG or additionally with nuclear myocardial perfusion imaging or echocardiography
Exercise ECG stress testing in women

- Inexpensive, easy to perform
- Low sensitivity
  - Low prevalence of multivessel disease
  - Inadequate exercise duration
- Low specificity >> nonspecific ST changes in women
  - MVP
  - LVH with strain
  - Drugs
  - Motion and hyperventilation
  - Possible digitalis-like effect of estrogen
Prognostic Value of Exercise Capacity in Women: Nomogram for Female Populations

Value of the Treadmill Exercise ECG in Women

Still useful
• provides information about functional capacity
• Less accurate for the detection of significant coronary artery disease.
• Useful for women with very good exercise capacity

Sensitivity
- Men: 70%
- Women: 61%

Specificity
- Men: 77%
- Women: 70%

*Sn = Diagnostic Sensitivity (True Pos / CAD)
*Sp = Diagnostic Specificity (True Neg / No CAD)
Estimating 5-Year Survival By Duke Treadmill Score \( (\text{Ex Time} - (5 \times \text{ST Dev}) - (4 \times \text{CP}[1=\text{non-limiting}, \ 2=\text{limiting}]) \) 

Source: Alexander JACC 1998;32:1657
Nuclear stress myocardial perfusion imaging

- Radiation exposure
- Breast tissue attenuation artifact
- Larger and more extensive defects identify women at higher risk for more severe IHD and cardiac events
- Negative scans helpful in excluding ischemic heart disease
Stress Echocardiography

- No radiation exposure
- Functional information about the heart provided
- Difficult in patients with poor echo windows (COPD, obesity)
- Poor sensitivity in single vessel disease
## Noninvasive Diagnosis of CAD in Women

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise ECG</td>
<td>61%</td>
<td>70%</td>
</tr>
<tr>
<td>Exercise Thallium</td>
<td>78%</td>
<td>64%</td>
</tr>
<tr>
<td>Exercise Echo</td>
<td>86%</td>
<td>79%</td>
</tr>
</tbody>
</table>
The WOMEN Study: What’s Optimal Method for Ischemia Evaluation in Women?

“A Multi-Center, Prospective, Randomized Study to Establish the Optimal Method for Detection of CAD Risk in Women at an Intermediate-High Pre-Test Likelihood of CAD” (n=824)

Intermediate - High risk women

DASI questionnaire

> 5 MET equivalent
50 years and older or,
Surgical menopause, or
Diabetic women of any age

Randomize

Exercise ECG
Exercise SPECT

G Heller, R Hendel, J Mieres and L Shaw
WOMEN’s Trial
Kaplan-Meier MACE-Free Survival by Randomized Test Assignment

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**Source:** Shaw et al AHA 2010
Cardiac Catherization

- Direct visualization of coronary arteries
- Gold standard – 100% accuracy
- But…
Cardiac CT angiography

- Looks at the arteries and the chambers
- High spatial resolution
- Radiation exposure
- Best in those without coronary calcium
Cardiac MRI

- Can only identify coronary ostia
- Can identify infarct
- Also views cardiac structures
- No radiation exposure
- Expensive?
The primary objectives of the WISE study were:

- To study the symptom presentation and patho-physiologic mechanisms of CVD in women
- To improve the diagnostic testing of CVD in women
- To evaluate the role of reproductive hormones and menopausal status in CVD
WISE Protocol

Women with chest pain symptoms or suspected ischemia

Inclusion/Exclusion Criteria
- Demographic Data
- Symptom Questionnaires
- Psychosocial Questionnaires
- Blood Sampling

- Resting ECG
- Ambulatory ECG
- Brachial Artery Reactivity Testing

- LV Angiography
- Coronary Angiography

Significant Stenosis

Normal or Minor Stenosis

MR Spectroscopy Testing
- P-31 Study

Site-Specific Invasive and Non-Invasive Protocols

Follow-up for symptom/menstrual status and CV events
- 6 weeks
- Annually
Symptom assessment: Typical symptoms of chest pain, dyspnea, diaphoresis, arm/shoulder pain are accurate in diagnosing myocardial ischemia in women.
WISE Results - Symptoms

• Atypical symptoms such as fatigue, loss of appetite, SOB, and anxiety may be more prominent

• The new onset of symptoms and their relationship to activity has more clinical relevance than location

• Women report symptoms more often during routine daily activities and mental stress than during exercise
WISE Results

• 60% of women who had cardiac catheterization for suspected ischemia had no flow-limiting coronary stenosis

• 20% of these women had phosphocreatinine/ATP ratio on MRI consistent with a shift to anaerobic metabolism and myocardial ischemia

• When followed over time, these women were frequently disabled, consumed tremendous health care resources and experienced adverse cardiovascular events
WISE Results

The graph illustrates the freedom from events over time for two groups: No CAD/Normal MRS (n=60) and No CAD/Abnormal MRS (n=14) compared to CAD (n=352). The x-axis represents months to the first event, while the y-axis represents the freedom from events. The graph shows a decline in freedom from events over time for all groups, with the No CAD/Normal MRS group starting at a higher baseline than the No CAD/Abnormal MRS group.
Key Findings From the WISE Study

• The "typical" presentation of ischemic heart disease (IHD) is more complex and multifactorial in women than in men

• Persistent signs and symptoms of IHD in the setting of nonobstructive coronary disease:
  – A significant health problem for women
  – Appears to be related to vascular dysfunction
Decisive Finding from the WISE study

- Approximately 50% of women referred for evaluation of ischemia do not have obstructive coronary disease.
- Prognosis for these women is intermediate for future adverse cardiac events and persistent symptoms.
- Practitioners should no longer ignore nonobstructive coronary angiograms in women.
- Practitioners should not call evidence of clear ischemia a false positive in this setting (i.e.+ troponin or abnormal stress perfusion).
Where are we with diagnosis of CAD in women

1. Chest Pain in women is less likely to be CAD
2. When it is CAD it may present atypically
3. Stress testing is less accurate in women but start with ETT
4. Even normal coronaries on catheterization does not guarantee women will not have coronary events
Prevention
Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

http://www.circ.ahajournals.org
Cardiovascular Disease Prevention in Women: Current Guidelines

- A five-step approach
  - Assess and stratify women into high, intermediate, lower and optimal risk categories
  - Lifestyle approaches recommended for all women
  - Other cardiovascular disease interventions: treatment of HTN, DM, lipid abnormalities
  - Highest priority is for interventions in high risk patients
  - Avoid initiating therapies that have been shown to lack benefit, or where risks outweigh benefits

Source: Adapted from Mosca 2004
Risk Stratification:

- CVD equivalent
  - Diabetes mellitus
  - Established atherosclerotic disease
  - Chronic kidney disease, especially ESRD

- Major Risk Factors:
  - Age ≥ 55 years
  - Smoking
  - Hypertension, whether or not treated with medication
  - HDL cholesterol < 40mg/dL
    (HDL cholesterol ≥ 60mg/dL is a negative risk factor)
  - Family history of premature CVD

Source: Mosca 2004, ATP III 2002
Risk Stratification

- Diabetes
  - Automatically places a patient in a “High Risk” category

- Family History
  - Defined as CVD in a female first degree relative < 65 years old, or a first degree male relative < 55 years old

Source: AHA/NHLBI 2005
Risk Stratification

- Calculate 10 year risk for all patients with two or more risk factors that do not already meet criteria for CHD equivalent

- Use electronic calculator for most precise estimate:

Source: AHA/NHLBI 2005
CHD Risk

Risk Prediction
The Coronary Heart Disease Prevention Iceberg

- High: > 20%, Coronary Heart Disease or Diabetes Mellitus
- Intermediate: 10% - 20%
- Low: < 10%

Estimated 10-Year Risk
Very High Risk Women

- Recent heart attack or known CAD, along with one or more of the following:
  - Multiple major risk factors, particularly in diabetics
  - Severe or poorly controlled risk factors (i.e., continued smoking)
  - Multiple risk factors of the metabolic syndrome, especially TG > 200 mg/dL AND HDL < 40 mg/dL

Source: Grundy 2004
CHD Risk Equivalents

- High Risk > 20% 10-yr risk for CHD events
  - Established coronary artery disease
  - Carotid artery stenosis
  - Peripheral arterial disease
  - Abdominal aortic aneurysm
  - Diabetes
  - Includes many patients with chronic renal disease, especially ESRD

Source: AHA/NHLBI 2005
Risk Stratification

- Intermediate Risk 10-20% 10-yr risk for CHD events
  - May include women with metabolic syndrome, especially women over the age of 60 or with individual factors that are markedly elevated or severe
  - Often includes women with multiple risk factors, a single markedly elevated risk factor, or a 1st degree relative with premature CVD
  - May include women with subclinical cardiovascular disease (elevated coronary calcium score) - this is not included in Framingham risk calculations

Source: AHA/NHLBI 2005
Definition of Metabolic Syndrome in Women

- Abdominal obesity - waist circumference ≥ 35 in.
- High triglycerides ≥ 150mg/dL
- Low HDL cholesterol < 50mg/dL
- Elevated BP ≥ 130/85mm Hg
- Fasting glucose ≥ 100mg/dL

Source: AHA/NHLBI 2005
Risk Stratification

- **Lower Risk** <10% 10-yr risk for CHD events
  - May include women with one or more risk factors
  - May include women with defined metabolic syndrome, if no individual factor is severe or markedly elevated
  - May include women with no risk factors, but non-optimal lifestyle factors, such as lack of regular exercise or a high fat diet

- **Optimal Risk** <10% 10-yr risk for CHD events
  - Optimal levels of risk factors
  - Heart healthy lifestyle

Source: AHA/NHLBI 2005
Modifiable Risk Factors for CV disease

- Tobacco
- Hypertension
- DM
- Dyslipidemia
- Physical Inactivity
- Obesity
- Psychosocial
- Medications
Smoking

- All women should be consistently encouraged to stop smoking and avoid environmental tobacco
  - The same treatments benefit both women and men
  - Women face different barriers to quitting
  Concomitant depression
  Concerns about weight gain

Source: Fiore 2000
**Hypertension**

- Encourage an optimal blood pressure of $< 120/80$ mm Hg through lifestyle approaches.

- Pharmacologic therapy is indicated when blood pressure is $\geq 140/90$ mm Hg or an even lower blood pressure in the setting of diabetes or target-organ damage ($\geq 130/80$ mm Hg).

- Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated.
Diabetes increases coronary mortality with and without a prior MI

In a seven-year follow-up of 1059 subjects with type 2 diabetes and 1378 nondiabetics, diabetics with or without a prior myocardial infarction (MI) had a greater mortality from coronary disease compared to nondiabetics (42 versus 16 percent for those with a prior MI and 15 versus 2 percent for those without a prior MI). The rate of coronary death and fatal and nonfatal MI in diabetics without a prior MI was the same as in nondiabetics with a prior MI, providing part of the rationale for considering type 2 diabetes a coronary equivalent.

Hyperlipidemia: LDL goals

- **LDL goal**
  - <70
  - <100
  - <100
  - <160
Physical Activity

- Consistently encourage women to accumulate a minimum of 30 minutes of moderate intensity physical activity on most, or preferably all, days of the week

Source: Mosca 2004
Body Weight and CHD Mortality Among Women

- **Relative Risk of CHD Mortality**
  - Weight Gain 10-19kg: 2.6
  - Weight Gain ≥ 20kg: 7.4

- **P for trend < 0.001**

**Source:** Adapted from Manson 1995
Weight Maintenance/Reduction Goals

- BMI between 18.5 and 24.9
- Waist circumference < 35 inches
- Weight loss goals
  - 10% of body weight over six months or 1-2 pounds weight loss/week
  - Reduce calories by 500-1,000 per day

Source: Mosca 2004, ATP III 2002
Psychosocial Stressors in Women with CHD: The Stockholm Female Coronary Risk Study

- Among women who were married or cohabitating with a male partner, marital stress was associated with nearly 3-fold increased risk of recurrent CHD events.

- Living alone and work stress did not significantly increase recurrent CHD events.

Source: Orth-Gomer 2000
Depression and CHD: Results from the Women’s Health Initiative Study

- Depression is an independent predictor of CHD death among women with no history of CHD

Source: Wassertheil-Smoller 2004
Primary Preventive Drug Interventions

- Aspirin – High risk women
  - 75-162 mg, or clopidogrel if patient intolerant to aspirin; should be used in high-risk women unless contraindicated

- Aspirin – Intermediate risk women
  - Women over age 65 may benefit from taking low-dose aspirin to reduce major cardiovascular events

- Aspirin - Lower risk women
  - Consider aspirin therapy (75-162 mg) in intermediate-risk women as long as blood pressure is controlled and benefit is likely to outweigh risk of GI side effects

Source: Mosca 2004
Interventions that are not useful/effective and may be harmful for the prevention of heart disease

- **Hormone Therapy**
  - Combined estrogen and progesterone hormone therapy should not be initiated or continued to prevent CVD in post-menopausal women. Alternative forms of HT should not be used to prevent CVD, pending results of ongoing trials.

*Source: Mosca 2004*
Interventions that are not useful/effective and may be harmful for the prevention of heart disease

- Antioxidant supplements
  - No cardiovascular benefit in randomized trials of primary and secondary prevention

Source: Mosca 2004
Must reduce comorbidities in women

- Education takes time!
- Use free resources available to you:
- Phillips Women’s Heart Program at Saint Francis:
- (860) 714-6389
Phillips Women’s Heart Program at Saint Francis

- Claire L. Karwacki-Marugg, M.S., Certified Exercise Specialist
- Kathleen Marrero R.N.
- Beth Morse, M.S., R.D., Dietitian
- Beverley Vassell, Administrative Assistant
Since the Grant Funded in 2003

- Assessed and educated >7000 women
- In recent follow up 75% have increased exercise, 39% have met recommended goal of exercise 30 minutes at least 5 times per week!
- Average follow up systolic BP reductions of 5 mmHg
- Average weight loss 2 lbs and 1 inch decrease in waist
Summary

• We are just learning about the pathophysiology of ischemic heart disease in women and it is not as simple as coronary artery disease
  – Atypical presentations
  – More nonobstructive coronary disease with bad outcomes
  – CP likely represents ischemic heart disease

• Diagnosis tests are more complicated in women

• 80% of IHD can be prevented: Lifestyle changes & Risk factor modification
Conclusions:

- Don’t ignore symptoms in women – do additional testing
- If stress test is negative by imaging and DTS is low, proceed to cardiac catheterization
- If stress test positive by imaging and cath is “negative” treat aggressively (ASA, Beta blocker, ACE Inhibitors, Exercise Training)
- Risk stratify women and aggressively reduce their risk!