Ischemic Heart Disease in Women

Lawrence J. Hergott, M.D.
Professor of Medicine
Director of Outpatient Clinical Services
University of Colorado Denver

Historical Perspective Regarding IHD In Women

Method: literature search
Keywords: coronary artery disease/coronary heart disease/ischemic heart disease in women
Timeframe: 1950-1969
Women have been understudied in clinical research over time. Diagnostic tests and treatments have been applied to both men and women equally. 1993: Congressional Caucus for Women's Health Issues forces NIH to include potential differences in outcomes between the genders in all studies it funds.
Ischemic Heart Disease (IHD) in Women: Principles - Epidemiology

-- IHD is the main cause of death in women of all ages:
1 in 2.6 women die of IHD vs. 1 in 4.6 from cancer

In 2007 more women's lives were claimed by CVD than by cancer, chronic lower respiratory disease, Alzheimer disease and accidents combined

- American Heart Association 1997 data regarding causes of death in women:
  - Breast cancer: 41,943
  - Coronary artery disease: 502,938
Ischemic Heart Disease in Women

Principles - Epidemiology

-- More women than men die from IHD in the U.S. annually

After decades of CHD death rate reduction, rates in U.S. women ages 35-54 appear to be increasing
-- Main factor: greater rates of obesity, DM II

-- Each year 55,000 more women than men have a stroke

Ischemic Heart Disease in Women

Principles - Outcomes

-- Mortality in ischemic heart disease, MI, thrombolytic therapy, PCI, CABG higher than in age-matched men
-- Though ejection fraction more preserved in women

IHD in Women

Awareness

• Health workers and women need to be educated re: IHD
  – 78% of women estimated their risk of developing CAD by age 70 at:
    - < 1%

  – Percent of women in AHA survey who said the first thing they would do if they thought they were having an acute MI is call 911:
    • 53%

Ischemic Heart Disease in Women

Pathophysiology

-- Even with documented ischemia, women have less anatomically obstructive disease than men

Ischemic Heart Disease in Women

Principles

• Women are undertreated regarding IHD
  – Less often received guideline-directed therapy for IHD
  • When they do outcomes are similar
  – Fewer undergo coronary angiography
  – Fewer receive statins
  – Etc.
Ischemic Heart Disease in Women
Principles - Pathophysiology

Even with documented ischemia, women have less anatomically obstructive disease than men.

Mechanism: Microvascular Dysfunction
- Non-epicardial, intra-myocardial vessels
- Causes:
  - Risk factor clustering
  - Vascular inflammation and remodeling
  - Hormonal alterations

Term ischemic heart disease preferred in women vs. coronary artery disease.

Treadmill Stress Testing

Greater tendency toward plaque erosion, rupture in women vs. men.

Probability of Those With 1.0-1.49 mm ST Depression On Exercise Testing Having Important Coronary Disease

Greater tendency toward plaque erosion, rupture in women vs. men.

Even in non-obstructed vessels, can cause:
- Unstable angina
- Non-STEMI
- Coronary spasm
Risk Factors

- Traditional
  - Hypertension
  - Tobacco use
  - Dyslipidemia
  - Family history
  - Diabetes
  - Obesity
  - Postmenopausal state

Female-specific variants
- Smoking & Diabetes
  - Negate premenopausal protective effect
- Dyslipidemia
  - High triglycerides impose greater risk vs. men
- Inflammatory biomarkers
  - Inflammatory-mediated autoimmune diseases increased
    - Suggests prominent role for inflammation in IHD in women
**Risk Factors**

- **Female-specific variants**
  - Altered Fibrinolysis
    - Impaired in: CVD, hypertension, obesity, Type 2 DM
    - Can be a cause of coronary thrombosis with even *normal* coronary arteries

- **Cardiometabolic Syndrome**
  - Associated with estrogen, androgen alterations
  - Polycystic Ovary Syndrome
    - Higher incidence of DM
    - Clustering of risk factors
    - Impaired exercise tolerance
    - Sedentary lifestyle

- **Pregnancy**
  - A state of unique cardiovascular and metabolic stress
  - Preeclampsia doubles risk of IHD, CVA, venous TE events over 5-15 years after pregnancy
  - "Metabolic Syndrome of Pregnancy"
    - May unmask endothelial dysfunction, vascular or metabolic disease
    - May be associated with gestational DM, preterm birth, birth of an infant small for gestational age
    - Considered an indication for OB referral to PCP or cardiologist for preventive care
    - Practitioners who meet women later in their lives should ask about complications of pregnancy

**Classification of Cardiovascular Disease Risk for Women**

Risk for CVA & heart failure exceeds even IHD risk in middle and older age women vs. men

**Presentation of IHD in Women**

- **Symptoms**
  - Myth?
    - Women with IHD do not present with angina
      - Framingham, CASS, acute coronary occlusion study, etc. show the same or higher rates of angina with CAD

**Acute Coronary Occlusion During PTCA**

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>49 (70%)</td>
<td>63 (85%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shortness</td>
<td>2.5 (2.0)</td>
<td>2.6 (2.1)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T wave changes</td>
<td>42 (50%)</td>
<td>59 (42%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Body weight</td>
<td>20 (50%)</td>
<td>30 (70%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Severe</td>
<td>14 (20%)</td>
<td>7.0 (7.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HD systolic</td>
<td>46 (60%)</td>
<td>95 (70%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>12 (10%)</td>
<td>13 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Severe</td>
<td>4.0 (6.0)</td>
<td>2.0 (4.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HR variability</td>
<td>14 (10%)</td>
<td>14 (10%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Decrease</td>
<td>5 (15%)</td>
<td>7 (5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (20%)</td>
<td>55 (15%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Severe</td>
<td>10 (17%)</td>
<td>6.0 (45%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>YST</td>
<td>5 (10%)</td>
<td>8 (15%)</td>
<td>NS</td>
</tr>
</tbody>
</table>
**Presentation of IHD in Women**

**Symptoms**

- **Myth?** Women with IHD do not present with angina.
- **Fact:** Women develop IHD at a later age than men and thus have more co-morbidities when diagnosed.
- **Fact:** The elderly & diabetics do have unusual presentations with CAD (nausea, fatigue, dyspnea, etc.) – is this the source of the "myth", reflecting age bias rather than gender bias?

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**IHD In Women**

**Testing**

- **Class I indication in asymptomatic patients only for:**
  - Taking a family history
  - Performing global risk score
    - Framingham, PROCAM, Reynolds (requires CRP, HbA1c, not recommended for screening in guidelines), etc.
    - Mainly assess CAD risk, not CVD risk
      - Typically underestimate even coronary risk in women
    - Framingham equations now available for 10- and 30-year CVD risk (IHD, CVA, HF, claudication)

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**Risk Estimation Systems**

- Framingham: nhlbi.nih.gov/guidelines/cholesterol/index.htm
- PROCAM: chd-taskforce.com/calculator
- SCORE: heartscore.org
- ASSIGN-SCORE: assign-score.com
- QRISK1, QRISK2: qrisk.co.uk
- WHO/ISH: who.int/cardiovascular_diseases/guidelines
- Reynolds Risk Score: reynoldsriskscore.com

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**IHD In Women**

**Testing**

- **Stress testing:**
  - Not indicated as screen in asymptomatic patients
  - Standard GXT – treadmill – preferred
    - Lower specificity for CAD women vs. men
  - Focus on non-ST results as well as ST results
    - Functional capacity
    - Heart rate recovery
    - Duke Treadmill Score

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**Duke Treadmill Score**

(Exercise duration in minutes-5X ST deviation*-4X angina index**)

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>(Score)</th>
<th>Annual Mortality, %</th>
<th>4-Year Survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low; (&gt;5)</td>
<td>0.25%</td>
<td>99%</td>
<td></td>
</tr>
<tr>
<td>Intermediate; (4 to 4)</td>
<td>1.25%</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>High; (0 to -1)</td>
<td>5%</td>
<td>79%</td>
<td></td>
</tr>
</tbody>
</table>

* ST up or down    **0= no angina, 1=non-limiting angina, 2=limiting angina

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**IHD In Women**

**Testing**

- Stress echo and stress nuclear studies are as predictive in women as in men
  - Stress echo preferred (depends on institutional experience)
    - No radiation
    - Higher specificity
**IHD In Women**

**Treatment**

- Standard treatments for obstructive lesions effective
  - Guideline indicated therapy for ACS abolishes adverse mortality gap
- Invasive strategy for ACS with positive biomarkers: greater benefit
- Conservative strategy for ACS with negative biomarkers: greater risk

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**Prevention**

“Evolving science suggests that the overwhelming majority of recommendations to prevent CVD are similar for women and men, with few exceptions.”

Mosca, et al.

**IHD In Women**

**Prevention Guideline Highlights**

- **Aspirin recommendations** (75-325 mg/d)
  - High-risk women
    - In presence of CHD unless contraindicated
    - Reasonable in women with DM unless contraindicated
    - If ASA intolerance, substitute clopidogrel

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**Prevention Guideline Highlights**

- **Aspirin recommendations**
  - Other at-risk or healthy women
    - Low dose (81-100 mg/d) useful age ≥ 65 if:
      - BP controlled
      - Benefit for ischemic CVA and MI prevention likely exceeds risk of GI bleeding and hemorrhagic stroke

- **Physical activity**
  - 150 min/week moderate activity, or
  - 75 min/week vigorous exercise, or
  - Equivalent combination
  - Additional CV benefits by increasing time to 300 min/week, 150 min/week, respectively
  - For weight loss, 60-90 minutes of moderate activity on most/all days
  - Major muscle group strengthening ≥ 2 days/week
References


