Ischemic Heart disease in Women

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Disclosures

- none
Objectives

- Outline importance of heart disease in women
- Discuss tools for risk stratification of women
- Review guidelines for treatment of women
- Discuss statins in primary prevention
- Review gender differences in treatment of coronary artery disease
- Review female specific cardiac syndromes
Who provides best heart failure care

- A) male physicians
- B) female physicians
B) Female physicians

- A new German study has shown that female doctors appear to provide the best care to heart-failure patients, by being more likely to prescribe guideline-recommended treatment.
- The results also show that female HF patients are less likely to receive optimum care, particularly when male physicians treat them.
How many more women die from cardiovascular disease in Canada than breast cancer?

- A) 2X
- B) 5X
- C) 7X
- D) 16X
7 X more women die of heart disease and stroke each year than breast cancer
True or False?

- More women die of heart disease than men?
- A) True
- B) False
More women die of heart disease than men

Heart Disease Mortality in Women and Men
Absolute Number of Deaths, 1979-2004
At what age do women present with MI

- A) 10yrs younger than men
- B) same as men
- C) 10yr older than men
Answer

- C) 10yrs older than men
  - More DM
  - More HTN
  - More CHF
  - Family history more significant
Cardiovascular disease in women
(AHA update 2007)

- Heart disease claims more women than the next 5 causes combined
- 35% of women believe heart disease and stroke are the greatest health risk
- 64% of women vs 50% of men who die suddenly of CHD had no previous symptoms
What is the best method to risk stratify female patients?

- Framingham risk score
- Reynold’s risk score
- Treadmill testing
- CT angiogram
- etc
Framingham risk score

- 5209 initial participants (2873 women, 2366 men)
- 4522 women in current risk model
- Age 30-74 no CVD
- Enrolled 1948, children 1971
- Primarily caucasian
- CAD, cerebrovascular events, PAD, CHF
Framingham risk score
ATPIII cholesterol panel

Age: [ ] years
Gender: [ ] Female  [ ] Male
Total Cholesterol: [ ] mg/dL
HDL Cholesterol: [ ] mg/dL
Smoker: [ ] No  [ ] Yes
Systolic Blood Pressure: [ ] mm/Hg
Currently on any medication to treat high blood pressure: [ ] No  [ ] Yes

Calculate 10-Year Risk
Framingham risk score

- <10% low risk
- 10-20% intermediate risk
- >20% high risk
- ? Underestimates risk as doesn’t include family history and inflammatory markers
- Valid for 12 years not life-time
Reynold’s risk score

- 24558 healthy women followed over median 10.2 years for incidence of stroke, MI, coronary revascularization, cardiovascular death (766 events)
- Derived from Women’s Health Study
  - >45 yrs, no cardiovascular disease or cancer
Reynold’s risk score

- Monitored age, race, DM, BP treatment, menopausal status, HRT use, height, weight, ETOH use, exercise frequency, parental history of MI <60, multivit use, smoking status, cholesterol treatment.
Reynold’s risk score

- Measured total cholesterol, HDL, LDL, apolipo-B, A, hsCRP, ICAM-1, fibrinogen, Cr, HbA1C, homocysteine
- 2/3 women assigned to model derivation data set
- 1/3 assigned as independent validation data set
Reynold’s Risk score

<table>
<thead>
<tr>
<th>Age</th>
<th>Years (Maximum age must be 80)</th>
</tr>
</thead>
</table>

| Do you currently smoke? | Yes | No |

| Systolic Blood Pressure (SBP) | mm/Hg |
| Total Cholesterol | mg/DL |
| HDL or "Good" Cholesterol | mg/DL |
| High Sensitivity C-Reactive Protein (hsCRP) | mg/L |

| Did your Mother or Father have a heart attack before age 60? | Yes | No |
Reynolds vs Framingham

- Reynolds performed similar to Framingham in classifying high or low risk patients
- Reclassified 20% of intermediate risk patients into high or low risk
- Reynolds includes revascularization as an endpoint
- Neither include coronary artery calcification or treadmill testing
Coronary artery calcification/ CT angiogram

- Studies with women underpowered and women studied at too low a risk
- Limited data to draw conclusions
  - Radiation exposure must be considered
Treadmill testing in women

- Women 61% specificity, 70% sensitivity
- Men 70% specific, 67% sensitive
  - Exertional symptoms are of low predictive value in women
  - Sub-maximal exercise durations affect diagnostic accuracy
What information do we get from EST?
Duke Treadmill score

- Takes into account exercise time, ST changes and chest pain symptoms
- Stratifies into low, mod or high risk
- Performs better in women than men at excluding disease in low risk pts
Outcomes based on performance on EST JAMA 2003

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All-cause mortality (%)</th>
<th>CVD mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High METs, high HRR</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Low METs, high HRR</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>High METs, low HRR</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Low METs, low HRR</td>
<td>27</td>
<td>11</td>
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</table>
What to do once risk level is established.
<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Conditions</th>
</tr>
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<tbody>
<tr>
<td>High risk</td>
<td>Established coronary heart disease, Cerebrovascular disease, Peripheral arterial disease, Abdominal aortic aneurysm, End-stage or chronic renal disease, Diabetes mellitus, 10-year Framingham global risk &gt;20%*</td>
</tr>
<tr>
<td>At risk</td>
<td>Cigarette smoking, Poor diet, Physical inactivity, Obesity, especially central adiposity, Family history of premature CVD**, Hypertension, Dyslipidemia, Evidence of subclinical vascular disease (eg, coronary calcification), Metabolic syndrome, Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise</td>
</tr>
<tr>
<td>(≥1 major risk factors for CVD)</td>
<td></td>
</tr>
<tr>
<td>Optimal risk</td>
<td>Framingham global risk &lt;10% and a healthy lifestyle</td>
</tr>
</tbody>
</table>
Lifestyle interventions

- Quit smoking (counseling, nicotine replacement, pharmacotherapy)
- Exercise 30 min every day or 60-90 min if wt loss required
- <10% calories from saturated fat/d, <300mg/d cholesterol, minimize trans fats, Na < 2.3g/d
- Oily fish 2X/week
- Maintain healthy BMI (18-25)
- Omega-3 fatty acids 1mg if CHD or 2-4mg if high Trg
True or False:

- ASA is recommended in primary prevention of cardiovascular disease for women under 65

A) True

B) False
Answer

- A) false
Women’s Health Study

NEJM 2005

- 39876 healthy women > 45 yr, mean age 54
- Randomized 100mg ASA EOD vs placebo
- 10 yr F/up cardiovascular end-points
- No benefit if <65 in reducing MI
- >65 benefit across all cardiovascular end-points
- Reduction in stroke (NNT 400)
79439 healthy women mean age 58
Observational trial 1980-2004
2yr questionnaire re meds
End-point mortality form CV disease and cancer
15-18% decrease in cardiovascular mortality vs controls (significant)
Decrease in mortality increased with age and number of risk factors
ASA: one size does not fit all

- 75-325mg/d in high risk women
  - Clopidogrel if ASA not tolerated
- In healthy or at-risk women ≥65 yrs
  81mg/d or 100mg EOD and women < 65 where benefit for stroke prevention outweighs risk bleed
- Not recommended in healthy women <65 to prevent MI
Not recommended

- HRT to prevent CVD
- Folic acid
- Antioxidant supplements (Vit C, E and beta-carotene)
Evaluation of Cardiovascular Disease Risk:

- Medical/family history
- Symptoms of cardiovascular disease
- Physical examination including BP, body mass index, waist size
- Labs including fasting lipoproteins and glucose
- Framingham risk assessment if no cardiovascular disease or diabetes
- Depression screening in women with cardiovascular disease

Implement Class I Lifestyle Recommendations (Implement in Women at All Risk Levels):

- Smoking cessation
- Heart-healthy eating pattern
- Regular physical activity
- Weight management
Is Woman at High Risk of Cardiovascular Disease?

- Established coronary heart disease
- Cerebrovascular disease
- Peripheral arterial disease
- Abdominal aortic aneurysm
- Diabetes mellitus
- Chronic renal disease
- Global 10-year risk >20%

Yes

No
Recent cardiovascular event, procedure, or congestive heart failure symptoms?

Yes

Refer to rehabilitation

No

Implement Class I Recommendations:
- BP control
- LDL therapy (goal <100 mg/dL)
- Aspirin/antiplatelet agents
- β-Blocker
- Angiotensin-converting enzyme/angiotensin receptor blocker
- Glycemic control in diabetic women
- Aldosterone blocker in select women

Consider Class II Recommendations:
- LDL <70 mg/dL in very high-risk women
- HDL/non-HDL therapy
- Omega-3 fatty acids
- Depression referral/treatment
Implement Class I Recommendations:
- BP control
- LDL therapy in select women

Consider Class II Recommendations:
- HDL, non-HDL, and triglyceride therapy in select women
- Aspirin
What’s new with statins in women

- Should statins be used in primary prevention?
  - Historically controversial
  - Data in women insufficient
Jupiter Trial NEJM 2008

- A randomized trial of Rosuvastatin in the Prevention of Cardiovascular Events Among 17,802 apparently healthy men and women with elevated levels of hs CRP
JUPITER – Trial Design
Multi-National, Randomized, Double-Blind, Placebo-Controlled Trial of Rosuvastatin in the Prevention of Cardiovascular Events Among Individuals With Low LDL and Elevated hs-CRP

No Prior CVD or DM
Men ≥ 50, Women ≥ 60
LDL < 130 mg/dL
hs-CRP ≥ 2 mg/L

4-week run-in

Rosuvastatin 20 mg (N = 8901)
Placebo (N = 8901)

MI Stroke Unstable angina
CVD death CABG/PTCA

Argentina, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Costa Rica, Denmark, El Salvador, Estonia, Germany, Israel, Mexico, Netherlands, Norway, Panama, Poland, Romania, Russia, South Africa, Switzerland, United Kingdom, Uruguay, United States, Venezuela
# JUPITER - Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Rosuvastatin n = 8901</th>
<th>Placebo n = 8901</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years (IQR)</strong></td>
<td>66.0 (60.0-71.0)</td>
<td>66.0 (60.0-71.0)</td>
</tr>
<tr>
<td><strong>Female, N (%)</strong></td>
<td>3426 (38.5)</td>
<td>3375 (37.9)</td>
</tr>
<tr>
<td><strong>Ethnicity, N (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>6315 (71.4)</td>
<td>6325 (71.1)</td>
</tr>
<tr>
<td>Black</td>
<td>1122 (12.6)</td>
<td>1124 (12.6)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1154 (12.6)</td>
<td>1140 (12.8)</td>
</tr>
<tr>
<td><strong>Blood pressure, mm (IQR)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>134 (124-145)</td>
<td>134 (124-145)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80 (75-87)</td>
<td>80 (75-87)</td>
</tr>
<tr>
<td><strong>Smoker, N (%)</strong></td>
<td>1400 (15.7)</td>
<td>1420 (16.0)</td>
</tr>
<tr>
<td><strong>Family history, N (%)</strong></td>
<td>997 (11.2)</td>
<td>1048 (11.8)</td>
</tr>
<tr>
<td><strong>Metabolic syndrome, N (%)</strong></td>
<td>3652 (41.0)</td>
<td>3723 (41.8)</td>
</tr>
<tr>
<td><strong>Aspirin use, N (%)</strong></td>
<td>1481 (16.6)</td>
<td>1477 (16.6)</td>
</tr>
</tbody>
</table>

All values are median (interquartile range) or N (%).
JUPITER
Primary Trial Endpoint: MI, Stroke, UA/Revascularization, CV Death

HR 0.56, 95% CI 0.46 - 0.69
P < 0.00001

Number Needed to Treat (NNT₅) = 25

Placebo 251 / 8901
Rosuvastatin 142 / 8901

- 44 %
Other outcomes

- No increase in liver toxicity, myalgias over placebo
- Increased physician reporting of DM and HbA1C in rosuvastatin treated groups
What to do with results?

- Statins safe in women for primary prevention
- hsCRP may help to determine which women (>60yo) would be more likely to benefit from statin
- Stay tuned for new guidelines. ? will include hsCRP
Coronary artery disease in women
Which patient has CAD?

- A) 42 yo female with chest pain occasionally after eating, not ass’d with exercise. Only cardiac risk factor is father MI in 40’s? ECG normal. Positive EST.
- B) 35 yo female 9 mo post-partum with residual HTN and new onset chest pain after eating dinner lasting 20 min. T-wave inversion inferiorly.
- C) 62 yo female presents feeling SOB and pleuritic chest pain. Smoker, strong family Hx. CXR ? Pneumonia, troponin 0.8, ECG T-wave inversion V1-V3
- D) all the above
Answer

D) all of the above
- A) LAD lesion requiring CABG
- B) coronary artery dissection
- C) LAD lesion requiring stenting
Gender differences in prevention and treatment of CVD

- Women more likely to have delays in angiogram than men
- Women with DM increased risk of dying of CAD and developing CHF than men
- Women more likely to have depression increasing risk of second MI
- Women less likely to be referred to cardiac rehab and more likely to drop out
True or false

- In hospital mortality is greater in females than males post MI.
• in hospital mortality post MI ♂ > ♀ (16.7% vs 11.5%) below age of 74 (p<0.0001)
Sexed based differences in early mortality after myocardial infarction

NEJM 1999

- Younger women
  - waited longer than men before going to hospital
  - Had more severe symptoms
  - Less likely to present initially with chest pain and ST elevation
  - less likely to be given Dx of MI at admission
  - less likely to receive thrombolytics or undergo angiogram (and more likely to receive benzo’s)
  - More likely to have diabetes, CHF, stroke
  - Had lower rate of use of established treatments
Sex differences in Medical Care and early death after MI

- 78254 pts with AMI in 420 hospitals between 2001-2006
- Women older, more comorbidities, less STEMIIs, higher mortality from STEMI
- Women less likely to receive ASA, B-blocker, revascularization
Differences in **men** and **women**

- Women less likely to present with chest pain or ST elevation

**Frequency of presenting symptoms other than chest pain in acute MI**

Source: Milner et. al *AM J Cardiol.* 1999; 84:396-399
Where to improve

- Educate women on their risk and on symptoms to watch for
- Decrease higher early mortality from AMI by increasing early recognition
  - Ensure timely reperfusion among hospitalized women
- Increase use of guideline-based medical treatment
Established risk factor

- Increases risk of coronary artery disease as much 35-70%

Woman > 60 y two times more likely to be depressed than men
• Association between current major depression and medication adherence.
• Of 904 participants, 22% had major depression
• Depressed patients were 2.5X more likely to stop, forget or skip their medications than non-depressed
• Independent of age, ethnicity, severity of disease, social supports
Heart and soul study results

- Patients more likely to be female, single and earn <$20000/yr
  - 27% women depressed vs 13% men
- Emphasizes need to screen for depression as may increase medication adherence (and hopefully decrease second event)
Treatment of depression in CAD

- SSRI’s appear most effective
  - Sertraline and citalopram have been shown to have decreased drug-drug interaction
  - Treatment with SSRI’s have shown decrease of 40% of second event
- TCA’s may precipitate MI and ventricular arrhythmias
- Cardiac rehabilitation decreased rates of depression
Cardiac Rehabilitation
Heart 2005

- Programs reduce mortality by 20-25%
- Rate of participation of women half that of men
- Women less likely to be referred
- Old age, obesity, disease severity, presence of disease comorbidity, family obligations and role resumptions reduced adherence.
How to improve female involvement

- Increase referral rate
- Tailor to individual preferences and needs
- Pay attention to emotional needs of women
  - More often widows, primary caregivers
  - Less often drive
  - More depression
  - Need more positive feedback than men
Female specific cardiac syndromes

- **Takotsubo**
  - Stress induced cardiomyopathy
  - ECG suggestive of ant MI and pt presents with sudden CHF
  - Apical ballooning seen on angiogram with normal coronaries and preservation of function of LV base
  - Acetylcholine provocation test may induce vasospasm during angiogram
  - Thought to involve high circulating levels of cathecholamines
  - More common in post-menopausal women
Female Specific cardiac syndromes

- Syndrome X
  - Angina and positive stress test with no evidence of significant coronary artery disease on angiogram
  - Coronary spasm ? related to microvascular disease
  - More common in post-menopausal women
  - Nitrates, CCB may be effective
Female specific cardiac syndromes

- Spontaneous Coronary Artery Dissection
  - 73% women
  - Increased risk in peripartum period
  - Likely related to hormonal changes
Take home points

- Women need to be better educated about their risk for cardiovascular disease
- Currently Framingham is standard for risk stratification model but Reynold’s risk score may be useful in certain patients
- Watch for new guidelines for hsCRP
Take home points

• Statins are safe and effective in women >60 in primary prevention at reducing CVD events
• Improvement is needed in treatment of AMI in women
  – Screen for depression
  – Consider referral to Cardiac Rehab
Questions?