Cardiovascular Disease in Women -Vive La Difference?

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Mortality Rates in Women

At Every Age, More Women Die From Heart Disease Than From Cancer

- Coronary artery disease
- Stroke
- Lung cancer
- Breast cancer
- Colon cancer
- Endometrial cancer

50% of women (1 in 2) will die from CVD compared with 4% (1 in 25) who will die from breast cancer

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CVD is responsible for 36% of deaths in women (37% in men)

Higher than deaths from all cancers combined

Breast CA is responsible for 4% deaths in women

Deaths from CVS is almost 9 times higher than deaths from breast cancer.
CVD is responsible for 55% of deaths in women (43% in men)

18 x mortality compared to Breast cancer
CVD in Women – *under-diagnosed, under-treated under-researched*

**Gender Differences**

- Presentation
- Investigation
- Treatment
- Prognosis
Why isn’t CV mortality declining in women

- Framingham risk score may underestimate the CVD risk in women
- Awareness: In a recent survey, 75% of women identified cancer as their leading cause of death...
- Present later to hospital with AMI (? atypical symptoms, less awareness, man’s disease)
- 2/3 of women who die suddenly have no previously recognized symptom
- Atypical symptoms (chest pain is the presenting symptom in <50% of women)
- Women experience MI differently than men (50% of MIs in women present with SOB, nausea, indigestion, fatigue and shoulder pain)
- Women presenting with MI and CAD are more likely to be older, have a history of DM, HTN, Hyperlipids, CHF, and unstable angina than male counterparts. (J Am Coll Cardiol 1997;29)
- Higher proportion of ‘silent AMI’ (? older, diabetes, less awareness)
- Present more often with NSTEMI than with STEMI
- Increased incidence in young women (<45 yrs)
women are more likely than men to **die within a few weeks** of a heart attack - 1 in 4 women vs. 1 in 5 men,

(Scottish-MONICA, population of Glasgow 1985 to 1991)

- Only half of women know that heart disease is the leading cause of death among women
- Because they wait longer than men to call for help
- Because they have heart attacks generally at older ages than men do
- Atypical symptoms...underDG, underTX
- More women than men will suffer a **second** heart attack within five years after their first heart attack
Women have higher rate of complications:
- cardiogenic shock
- congestive cardiac failure
- reinfarction
- peripheral bleeding
- stroke

• Higher risk of cerebral bleeding with thrombolysis
• Higher early mortality than men
• Mortality rate in younger women (<45 years) is over twice that in men
  - Late presentation to hospital
  - Less aggressively treated
  - increased thrombosis risk, DM
CHD Mortality in Younger Women

Women under 65 suffer the highest relative sex-specific CHD mortality

Figure 1. Rates of death during hospitalization for Myocardial Infarction among women and men, according to age. The interaction between sex and age was significant (P<0.001).
Case Fatality within 28 Days after Hospitalization for Patients with Acute Myocardial Infarction in Sweden, 1987 to 1995

Not straightforward:

• Women are more prone to non-cardiac chest pain.....
• Women may experience more dizziness, nausea, indigestion, and *fatigue* than men.
• Women are more likely to have *neck, arms, back and shoulder pain*.
• Women are under-diagnosed and can therefore get a false sense of security.
• Because of these *atypical symptoms*, women seek medical care *later* than men and are more likely to be misdiagnosed.
• Because of these *comorbid conditions*, there tends to be diagnostic confusion.
CV RF

- Age
- *Smoking
- *Diabetes Mellitus: Women with diabetes have more than two and a half times the risk of dying from coronary heart disease than women without diabetes.
- *Hypertension (LVH)
- *Hyperlipidaemia (especially HDL,TG in women) Rajkhowa et al. (1997); Orio et al. (2004)
- Family History of CHD(>55 for men, >65 for women)
  - Microalbuminuria, (eGFR<60 ml/min)
  - Homocysteine (Carmina et al. 2005)
  - *CRP (Taponen et al. 2004; Boulman et al. 2004)
  - Menopause (Fioretti et al., 2000) - two to three times greater after menopause
  - Sedentary Lifestyle

*Biggest Risk factor is the misconception that CHD is a "Man’s Disease"
Non-modifiable Risk Factors

• Age > 55
  – CAD rates are 2-3x’s higher in postmenopausal women

• Family history
  – CHD in primary 1\textsuperscript{st} degree relative male<55 or female<65
Smoking

• A. 50% of heart attacks among women are due to smoking. Smokers tend to have their first heart attack 10 years earlier than nonsmokers.

• B. If you smoke, you are 4-6x’s more likely to suffer a heart attack and increase your risk of a stroke.

• C. Women who smoke and take OCP’s increase their risk of heart disease 30x’s.
SMOKING:

- **Stop!!!! (avg. attempt = 8 times)**
- Women who have other smokers in their household have a 2.5 X's greater likelihood of relapse. *Circulation 2002:106*
- Smoking cessation was associated with a 36% reduction in mortality among patients with CHD. *JAMA 2003:290*
Diabetes

- Diabetes increases the risk of CHD 3-7 X’s in women versus 2-3 X’s in men.

- Diabetic women who smoke have a 84% higher risk of developing stroke than nonsmokers.

- 2 of 3 people with diabetes die from CHD or stroke

- Treatment of hyperglycemia has been shown to reduce or delay complications of diabetes such as retinopathy, neuropathy, and nephropathy

- keep HBA1C ≤6.5%
Relative Risk vs. Triglyceride Level (mg/dL)

- Men
- Women

n=5127

Source: J Am Board Fam Pract © 2004 American Board of Family Practice
Cholesterol

• Women at high risk should be considered for statin therapy regardless of cholesterol-LDL levels.

• Statin drugs have already surpassed all other classes of medicines in reducing the incidence of the major adverse outcomes of death, MI, and stroke.

NEJM 350:15 April 8, 2004
Obesity

A. 1/3 of adult women are obese and its increasing

B. Active women have a 50% risk reduction in developing heart disease.
Obesity and Coronary Heart Disease Mortality

Nurses’ Health Study: Women who never smoked

Relative Risk of Coronary Heart Disease mortality

Body Mass Index (kg/m²)

Relative Risk:
- Less than 19
- 19.0 - 21.9
- 22.0 - 24.9
- 25.0 - 26.9
- 27.0 - 28.9
- 29.0 - 31.9
- Greater than 32.0

Hypertension

- 65% of all hypertension remains either undetected or inadequately treated.
- People who are normotensive at 55 have a 90% lifetime risk of developing HTN.
- Prevalence increases with age and women live longer—hypertension is more common in females.
- HTN is more common with OCP and obesity.
## Lifestyle Modification for HTN

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Expected systolic reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Goal of BMI 18-25</td>
<td>5-20 mm Hg per 10kg wt loss</td>
</tr>
<tr>
<td></td>
<td>Waist &lt;35inches</td>
<td></td>
</tr>
<tr>
<td>DASH</td>
<td>Fruits, veges, low-fat dairy products, less fat</td>
<td>8-14 mm Hg</td>
</tr>
<tr>
<td>Sodium restriction</td>
<td>&lt;2.4 g every day</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>30 mins of aerobic 4x’s a week</td>
<td>4-9 mm Hg</td>
</tr>
<tr>
<td>Reduced EtOH (1/2 for women)</td>
<td>2-12 oz beer, 1 10oz wine, 3 oz 80proof whiskey in men</td>
<td>2-4 mm Hg</td>
</tr>
</tbody>
</table>
Exercise

• 30-45 mins of walking 5x’s/week reduces risk of MI in females 50%.
• Helps control BP, increases HDL, decreases body fat, DM risk, possibly prostate, breast and uterine cancers.
Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women

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CVD Prevention Strategies for Clinical Practice

- Stratify women into risk categories
  - High
    - CHD or CHD risk equivalents (10-y risk > 20%)
  - Intermediate
    - ≥2 risk factors (10-y risk 10–20%)
  - Lower
    - ≥2 risk factors (10-y risk < 10%)
  - Optimal
    - 0–1 risk factor
- Personalize management based on:
  - Individual risk status
  - Basic tests and clinical evaluation
<table>
<thead>
<tr>
<th>Class</th>
<th>High Risk (&gt;20%)</th>
<th>Intermediate risk (10–20%)</th>
<th>Lower Risk (&lt;10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Stop smoking</td>
<td>Stop smoking</td>
<td>Stop smoking</td>
</tr>
<tr>
<td></td>
<td>Physical activity/rehab</td>
<td>Physical activity</td>
<td>Physical activity</td>
</tr>
<tr>
<td></td>
<td>Diet therapy</td>
<td>Heart-healthy diet</td>
<td>Heart-healthy diet</td>
</tr>
<tr>
<td></td>
<td>Healthy weight</td>
<td>Healthy weight</td>
<td>Healthy weight</td>
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<tr>
<td></td>
<td>BP control</td>
<td>BP control</td>
<td>BP control</td>
</tr>
<tr>
<td></td>
<td>Cholesterol control/therapy</td>
<td>Cholesterol control</td>
<td>Cholesterol control</td>
</tr>
<tr>
<td></td>
<td>Aspirin</td>
<td></td>
<td>Treat individual</td>
</tr>
<tr>
<td></td>
<td>Beta-blocker</td>
<td></td>
<td>CV risk factors as indicated</td>
</tr>
<tr>
<td></td>
<td>ACE inhibitor (ARB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Manage diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>Rx for depression</td>
<td>Aspirin therapy</td>
<td></td>
</tr>
<tr>
<td>IIb</td>
<td>Omega 3 fatty-acid</td>
<td>Folic acid</td>
<td></td>
</tr>
</tbody>
</table>

Content Provided by Cardiosource

Additional Aspirin Evidence

Women's Health Study (WHS)

39,876 women randomized to aspirin (100 mg every other day) or placebo for an average of 10 years

Aspirin doesn't reduce the risk of MI in women

Antiplatelets: Aspirin in Primary Prevention

RR of MI Among Men
- BDT, 1988
- PHS, 1989
- TPT, 1998
- HOT, 1998
- PPP, 2001

Combined: RR = 0.68 (0.54–0.86)  
\( P = .001 \)

RR of Stroke Among Men
- BDT, 1988
- PHS, 1989
- TPT, 1998
- HOT, 1998
- PPP, 2001

Combined: RR = 1.13 (0.96–1.33)  
\( P = .15 \)

RR of MI Among Women
- HOT, 1998
- PPP, 2001
- WHS, 2005

Combined: RR = 0.99 (0.83–1.19)  
\( P = .95 \)

RR of Stroke Among Women
- HOT, 1998
- PPP, 2001
- WHS, 2005

Combined: RR = 0.81 (0.69–0.96)  
\( P = .01 \)

Content Provided by Cardiosource

• Women were less likely to have an ECG or be admitted to the telemetry floors.
• Less aspirin, beta-blockers, statins, antiarrhythmic treatment, cardiac cath, PTCA, CABG
• Women were less likely to enroll in cardiac rehabilitation after an MI or bypass surgery.
Effect of sex on use of investigations: Initial 4wks

- Angiography: 0.60
- Exercise ECG: 0.81
- Stress imaging: 1.08

Adjusted odds ratio for women
Meds at 1 year in those with confirmed CAD

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>p value</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet</td>
<td>95%</td>
<td>93%</td>
<td>0.23</td>
<td>94%</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>81%</td>
<td>76%</td>
<td>0.05</td>
<td>80%</td>
</tr>
<tr>
<td>Antiplatelet &amp; lipid low.</td>
<td>79%</td>
<td>71%</td>
<td>0.01</td>
<td>76%</td>
</tr>
<tr>
<td>B Blocker</td>
<td>77%</td>
<td>82%</td>
<td>0.14</td>
<td>78%</td>
</tr>
<tr>
<td>MANAGEMENT METHOD</td>
<td>MEN (N=103)</td>
<td>WOMEN (N=98)</td>
<td>P VALUE</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-------------</td>
<td>--------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>79</td>
<td>49</td>
<td>&lt;0.005</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>61</td>
<td>57</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Angiotensin-converting-enzyme inhibitors</td>
<td>43</td>
<td>29</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Lipid-lowering drugs</td>
<td>15</td>
<td>11</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Long-acting nitrates</td>
<td>72</td>
<td>78</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>19</td>
<td>25</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Transfer to cardiac center</td>
<td>46</td>
<td>30</td>
<td>&lt;0.025</td>
<td></td>
</tr>
</tbody>
</table>

*The in-hospital mortality among men was 7 percent, and among women it was 10 percent, a difference that was not significant (P≥0.05). NS denotes not significant.

## Effect of sex on revascularisation

<table>
<thead>
<tr>
<th></th>
<th>*Adj. OR F vs M</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revascularisation planned/ performed within 4 wks</td>
<td>0.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Revascularisation at 1 year</td>
<td>0.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Revascularisation at 1 year in women with CAD</td>
<td>0.68</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Adjusted for age, symptom severity and other factors predictive at univariate level*
Coronary Revascularisation PCI/CAB

Increased co-morbid factors
- Older
- Smaller vessel size  Coronary lesion distribution and morphology is similar
- Hypertension
- Diabetes mellitus
- Hypercholesterolaemia
- Peripheral vascular disease
- Congestive cardiac failure (diastolic dysfunction)
  • Women tend to have more ostial vessel disease
  • Women receive less IMA conduits than men
  • Use of GPIIb/IIIa is less in women
  • Higher incidence of urgent procedures
Coronary Revascularisation- PCI/CABG

- Higher mortality rate
- In-hospital mortality –x 2 times higher for CABG
- Higher vascular (stroke, groin) complications
- Higher bleeding and renal complications in women
- At 5 years after CABG and PCI- survival similar for men & women
SERM/ERT/HRT

- Heart and Estrogen/progestin Replacement Study (HERS I-II)
- Estrogen Replacement and Atherosclerosis (ERA) Trial
- Observational epidemiological studies (35% reduction:  
  - Selection bias (healthier women on HRT)  
  - Prevention bias (more monitoring on HRT)

----------HRT is not recommended for the prevention of CVD in life
Summary

• Women are different than men
• Aggressive medical therapy appears particularly effective in women
• Women face more adverse outcomes with revascularization
• Long term revascularization outcomes for women are similarly beneficial to men