Gender-Related Risk for the Development of Cardiovascular Events in Health Middle-Aged Adults

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Disclosure

• None
Background

- Women are under-represented in cardiovascular clinical trials.

- Data regarding gender differences in primary prevention of CVD are limited.

- Whether gender is risk factor by itself or mediated by traditional CVD risk factors is a controversial issue.
Study Aims

- To evaluate gender differences in cardiovascular risk in a large cohort of asymptomatic men and women.

- To assess whether gender–related risk is related to the presence of traditional CVD risk factors and comorbidities.
METHODS
Study Population

- 14,966 men and women.
- 10,524 men and 4,442 women.
- Free of diabetes, hypertension, ischemic heart disease and cerebrovascular disease.
- Were annually screened.
- They filled health questionnaire and underwent physical examination, routine blood tests and treadmill exercise stress test.
End Points

• Primary end point - **Composite Cardiovascular disease** (CVD) defined as ACS or symptom driven PCI or ischemic CVA.

• Secondary end points – all cause mortality, CVA and ischemic heart disease.

• New diagnosis was based on medical chart and follow-up clinic.
Statistical analysis

• Kaplan Meier survival analysis.

• Multivariate cox regression models.
RESULTS
## Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Men (N=10,524)</th>
<th>Women (N=4,442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.2 ± 9.9</td>
<td>46.5 ± 10.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>123.6 ± 14.5</td>
<td>114.4 ± 16.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI &gt; 30 (%)</td>
<td>1291 (12.3%)</td>
<td>367 (8.5%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Current Smoker (%)</td>
<td>1936 (18.9%)</td>
<td>778 (17.8%)</td>
<td>0.119</td>
</tr>
<tr>
<td>Physical Active (%)</td>
<td>6564 (64.1%)</td>
<td>2813 (64.4%)</td>
<td>0.736</td>
</tr>
<tr>
<td>Exercise duration (min)</td>
<td>10.8 ± 2.9</td>
<td>9.09 ± 2.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
## Laboratory Characteristics

<table>
<thead>
<tr>
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<th>Men (N=10,524)</th>
<th>Women (N=4,442)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mg/dl)</td>
<td>124.9 ± 28.3</td>
<td>116.8 ± 28.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>43.7 ± 9.3</td>
<td>57.4 ± 12.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>134.7 ± 134.7</td>
<td>99.9 ± 49.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>90.4 ± 13.3</td>
<td>85.4 ± 10.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Impaired fasting glucose (%)</td>
<td>1576 (15.0%)</td>
<td>301 (6.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GFR&lt;60 (mL/min/1.73 m²)*</td>
<td>984 (9.4%)</td>
<td>705 (16.0%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*GFR is calculated by MDRD formula  \( GFR = 175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \)
Composite Cardiovascular Disease Survival Curve

Composite Cardiovascular Free Disease Survival

Gender
- Women
- Men

Cum Survival (%)
- 1.00
- 0.95
- 0.90
- 0.85
- 0.80

Time (years)
- 0
- 1
- 2
- 3
- 4
- 5
- 6

p (log rank) < 0.001
Table: Male vs. Female Risk for Study Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Men (N=10,524)</th>
<th>Women (N=4,442)</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite CVD (%)*</td>
<td>640 (6.1%)</td>
<td>79 (1.8%)</td>
<td>3.4 (2.7-4.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IHD (%)</td>
<td>562 (5.3%)</td>
<td>40 (0.9%)</td>
<td>5.9 (4.3-8.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CVA (%)</td>
<td>103 (1.0%)</td>
<td>40 (0.9%)</td>
<td>1.0 (0.7-1.5)</td>
<td>0.847</td>
</tr>
<tr>
<td>All Cause Mortality (%)</td>
<td>226 (2.1%)</td>
<td>59 (1.3%)</td>
<td>1.5 (1.1-1.9)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*Composite – Ischemic Heart Disease or Cerebrovascular Disease
## Multivariate Model for CVD Risk

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male vs. Female</strong></td>
<td>3.19</td>
<td>2.40-4.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Age ≥ 50 years</strong></td>
<td>4.70</td>
<td>3.82-5.78</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Adjusted for: Age, Systolic Blood Pressure ≥ 120 mmHg, Obesity (BMI >30), High LDL ≥ 130 mg/dl, Low HDL < 45 mg/dl, High Triglycerides ≥ 150 mg/dl, Impaired Fasting Glucose, Current Smoking, Physically Active, Exercise Duration - 25% quartile.
Interaction between Cardiovascular Risk Factors and Gender

Male vs. Female

- Age < 50
- Age ≥ 50
- Non-obese BMI ≤ 30
- Obesity BMI > 30
- Low HDL
- High HDL
- High LDL
- Low LDL
- Triglycerides < 150
- Triglycerides ≥ 150
- Systolic BP < 120
- Systolic BP ≥ 120
- Normal Glucose
- IFG
- Normal Renal Failure
- Chronic Renal Function
- Non-smokers
- Smokers
- Non-physically Active
- Physically Active
- Exercise Duration 75 tile
- Exercise Duration 25 tile
- Overall risk

p=0.267
p=0.366
p=0.739
p=0.250
p=0.405
p=0.286
p=0.975
p=0.702
p=0.642
p=0.677
p=0.725
Conclusions

• Men have 3-fold higher risk for developing cardiovascular disease than women.

• The risk for developing CVD in men is higher regardless of traditional CVD risk factors.
Limitations

- Selection bias - study population is part of executive screening program.
- Low event rate in women.