Cardiovascular Risk Assessment

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Disclosures

Received honorariums for participating as a consultant or as a member of advisory boards for AstraZeneca, CSL-Behring, Lilly, Merck and Roche and for giving lectures for AstraZeneca and Merck.
Unmodifiable Risk Factors

- Age
- Gender
- Family history of premature cardiovascular disease
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
Modifiable Risk Factors

- **Smoking**
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
PROCAM (Münster Heart Study): Age Standardized Death Rates in Men According to Cigarette Smoking

- **nonsmoker (n=7,378)**
- **smoker (n=3,478)**

Deaths per 1,000

- **total**
  - nonsmoker: 21
  - smoker: 48

- **coronary death**
  - nonsmoker: 6
  - smoker: 16

- **cancer**
  - nonsmoker: 9
  - smoker: 18

10,856 men aged 35-65 years;
Number of deaths: total: 313; coronary deaths: 94; cancer: 129

Cullen et al. Circulation 1997; 96:2128
EUROASPIRE

Risk factor management in coronary patients – results from a European wide survey

EUROASPIRE I: 1995-1996
EUROASPIRE II: 1999-2000
EUROASPIRE III: 2006-2007
EUROASPIRE III
Prevalence of Smoking*

* Self-reported smoking or CO in breath > 10 ppm

Survey 1
- Czech Rep.: 22.0%
- Finland: 12.8%
- France: 25.0%
- Germany: 16.8%
- Hungary: 23.3%
- Italy: 18.6%
- Netherlands: 31.8%
- Slovenia: 13.3%
- ALL: 20.3%

Survey 2
- Czech Rep.: 19.3%
- Finland: 21.6%
- France: 24.2%
- Germany: 16.8%
- Hungary: 30.1%
- Italy: 15.1%
- Netherlands: 28.3%
- Slovenia: 14.6%
- ALL: 21.2%

Survey 3
- Czech Rep.: 22.2%
- Finland: 16.8%
- France: 24.8%
- Germany: 18.4%
- Hungary: 18.3%
- Italy: 14.0%
- Netherlands: 15.1%
- Slovenia: 12.0%
- ALL: 18.2%

S2 vs. S1: P=0.83
S3 vs. S2: P=0.37
S3 vs. S1: P=0.48

www.esccardio.org
Modifiable Risk Factors

- Smoking
- **Elevated LDL-C**
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
Serum Cholesterol and CHD in 361,662 US Men: MRFIT

6-Year CHD Death Rate per 1000 Men

Serum Cholesterol (mg/dl)
Lipoprotein classes and atherosclerosis

Chylomicrons, VLDL, and their catabolic remnants

Pro-atherogenic

LDL

Anti-atherogenic

HDL
## All statin clinical outcome trials

Relative risk reduction in MCVEs per 1.0 mmol/L (40 mg/dL) reduction in LDL-cholesterol

(26 Trials; 169,138 subjects; 24,323 events)

### Number of Events

<table>
<thead>
<tr>
<th>End point</th>
<th>Treatment-arm (n=84573)</th>
<th>Control-arm (n=84565)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any major vascular event</td>
<td>10973</td>
<td>13350</td>
<td>0.78 (0.76-0.80)</td>
</tr>
<tr>
<td>Any major coronary event</td>
<td>5105</td>
<td>6512</td>
<td>0.75 (0.70-0.82)</td>
</tr>
<tr>
<td>Any coronary revascularisation</td>
<td>5353</td>
<td>6807</td>
<td>0.71 (0.65-0.78)</td>
</tr>
<tr>
<td>Any stroke</td>
<td>2302</td>
<td>2680</td>
<td>0.82 (0.74-0.92)</td>
</tr>
</tbody>
</table>

EUROASPIRE III
Use of Statins

S2 vs. S1 : P<0.0001
S3 vs. S2 : P<0.0001
S3 vs. S1 : P<0.0001

Czech Rep. 6.3% 34.9%
Finland 20.2% 61.0%
France 31.1% 89.1%
Germany 6.7% 85.4%
Hungary 6.8% 76.7%
Italy 14.0% 90.0%
Netherlands 23.2% 91.4%
Slovenia

ALL
18.1% 57.3% 87.0%

P<0.0001
EUROASPIRE III
Prevalence of raised LDL-C*

S2 vs. S1 : P=0.001
S3 vs. S2 : P<0.0001
S3 vs. S1 : P<0.0001

• LDL C ≥ 2.5 mmol/L for patients fasting for at least 6 hours

www.esccardio.org
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
Triglyceride and CHD Risk
PROCAM Study

While the level of plasma triglyceride is predictive of CV risk, there is currently no evidence that reducing the level of triglyceride translates into a reduction in risk.
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- **Low HDL-C**
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
CHD and HDL-C

N = 302,430
Adjusted for multiple factors

HDL-C and CV risk

- Evidence that the level of HDL-C is an independent negative predictor of risk is compelling.
- There is also clear evidence that HDLs have several properties with the potential to reduce CV risk.
- Furthermore, increasing the concentration of HDL-C by a variety of mechanisms decreases susceptibility to the development of atherosclerosis in animal models.
- In addition, intravenous infusions of HDLs in humans promotes regression of coronary atherosclerosis as assessed by intravascular ultrasound.
BUT

- Studies with HDL raising agents in humans have, to date, been disappointing, and have failed to provide evidence that raising the concentration of HDL-C in humans will translate into a reduction in clinical CV events.

- So, whether or not HDL-C should be a therapeutic target to reduce CV risk remains an unanswered question.
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- **Elevated blood pressure**
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
BP and CHD death in 361,662 US Men: MRFIT

Relative risk of CHD mortality

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)

SBP (mmHg) < 112
DBP (mmHg) < 71
112-118
118-121
121-125
125-129
129-132
132-137
137-142
≥142
71-76
76-79
79-81
81-84
84-86
86-89
89-92
≥92
98-151

**EUROASPIRE III**

**Prevalence of raised BP**

* SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg

<table>
<thead>
<tr>
<th>Country</th>
<th>Survey 1</th>
<th>Survey 2</th>
<th>Survey 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Czech Rep.</td>
<td>60.1%</td>
<td>46.9%</td>
<td>62.5%</td>
</tr>
<tr>
<td>Finland</td>
<td>56.1%</td>
<td>52.0%</td>
<td>67.1%</td>
</tr>
<tr>
<td>France</td>
<td>48.4%</td>
<td>55.5%</td>
<td>48.1%</td>
</tr>
<tr>
<td>Germany-Hungary</td>
<td>58.4%</td>
<td>67.0%</td>
<td>50.9%</td>
</tr>
<tr>
<td>Italy</td>
<td>50.6%</td>
<td>40.4%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Netherlands</td>
<td>55.3%</td>
<td>50.8%</td>
<td>60.5%</td>
</tr>
<tr>
<td>Slovenia</td>
<td>54.0%</td>
<td>54.4%</td>
<td>59.6%</td>
</tr>
<tr>
<td><strong>ALL</strong></td>
<td>54.6%</td>
<td>54.0%</td>
<td>55.2%</td>
</tr>
</tbody>
</table>

P = 0.79

S2 vs. S1 : P = 0.83
S3 vs. S2 : P = 0.51
S3 vs. S1 : P = 0.65

*SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg

www.esccardio.org
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- **Diabetes**
- Abdominal obesity
- Lp(a)
- hsCRP
Effect of diabetes on CVD in MRFIT Screenees

*Serum cholesterol >200 mg/dl, smoking, SBP >120 mmHg

Diabetes and CHD


![Incidence of fatal/nonfatal MI during 7-year follow-up (%)]

- Patients without diabetes
  - No prior MI
  - Prior MI
- Patients with diabetes
  - No prior MI
  - Prior MI

*P* < 0.001 for diabetes vs no diabetes

*P* < 0.001
EUROASPIRE III
Prevalence of Diabetes*

* Self-reported history of diagnosed diabetes

Survey 1
- Czech Rep.: 21.8%
- Finland: 15.4%
- France: 16.7%
- Germany: 13.5%
- Hungary: 26.6%
- Italy: 17.2%
- Netherlands: 10.3%
- Slovenia: 17.4%

Survey 2
- Czech Rep.: 21.5%
- Finland: 18.7%
- France: 27.5%
- Germany: 13.5%
- Hungary: 21.1%
- Italy: 21.8%
- Netherlands: 13.2%
- Slovenia: 23.8%

Survey 3
- Czech Rep.: 30.8%
- Finland: 19.1%
- France: 34.2%
- Germany: 22.6%
- Hungary: 44.8%
- Italy: 21.7%
- Netherlands: 20.6%
- Slovenia: 18.8%

ALL
- Czech Rep.: 17.4%
- Finland: 20.1%
- France: 28.0%

S2 vs. S1: P = 0.21
S3 vs. S2: P = 0.02
S3 vs. S1: P = 0.001

P = 0.004

www.esccardio.org
All statin clinical outcome trials:

Effects in diabetes

Relative risk reduction in major vascular events per 40 mg/dL reduction in LDL-cholesterol

(26 Trials; 169,138 subjects; 24,323 events)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Treatment-arm (n=84573)</th>
<th>Control-arm (n=84565)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes</td>
<td>2494</td>
<td>2920</td>
<td>0.80 (0.74-0.86)</td>
</tr>
<tr>
<td>No diabetes</td>
<td>8272</td>
<td>10163</td>
<td>0.78 (0.75-0.81)</td>
</tr>
</tbody>
</table>

Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
Prevalence of CVD across quintiles of waist circumference

EUROASPIRE III
Prevalence of Central Obesity*

* Waist circumference ≥ 102 cm in men or ≥ 88 cm in women

Survey 1
- 49.7%
- 30.6%
- 54.6%
- 40.3%
- 44.8%
- 42.6%
- 42.9%
- 34.2%
- 42.2%

Survey 2
- 52.1%
- 48.3%
- 58.8%
- 46.8%
- 56.3%
- 55.4%
- 55.2%
- 52.6%

Survey 3
- 56.1%
- 41.3%
- 54.8%
- 51.3%
- 65.6%
- 52.0%
- 56.0%
- 54.9%

Czech Rep. Finland France Germany Hungary Italy Netherlands Slovenia ALL

S2 vs. S1: P=0.0001
S3 vs. S2: P=0.47
S3 vs. S1: P<0.0001

www.esccardio.org
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
Lipoprotein(a)

K4-2 copy number variant: 2 to >40 repeats

apo(a)

LDL-like particle

Lp (a) and Risk of CHD, Stroke, Non CV mortality

While the level of Lp(a) is predictive of CV risk, there is currently no evidence that reducing the level of Lp(a) will translate into a reduction in risk
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
hs-CRP and Risk of Future MI in Apparently Healthy Men

Cumulative Incidence of CHD by CRP: The Hisayama Study

Arima et al. ATVB. 2008; 28:1385-1391

Proportion with CHD

Follow-up (years)

hs-CRP levels (mg/L)

- > 1.02
- 0.44 - 1.02
- 0.21 - 0.43
- < 0.21
Recurrent MI or CHD Death by Achieved Levels of LDL-C and CRP

PROVE IT–TIMI 22

# CVD Events, LDL and hsCRP

The JUPITER Study

<table>
<thead>
<tr>
<th>LDL, hsCRP Conditions</th>
<th>N</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>7832</td>
<td>1.11</td>
</tr>
<tr>
<td>LDL≥70 mg/dL, hsCRP≥2 mg/L</td>
<td>1384</td>
<td>1.11</td>
</tr>
<tr>
<td>LDL&lt;70 mg/dL, hsCRP≥2 mg/L</td>
<td>2921</td>
<td>0.62</td>
</tr>
<tr>
<td>LDL≥70 mg/dL, hsCRP&lt;2 mg/L</td>
<td>726</td>
<td>0.54</td>
</tr>
<tr>
<td>LDL&lt;70 mg/dL, hsCRP&lt;2 mg/L</td>
<td>2685</td>
<td>0.38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LDL, hsCRP Conditions</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>7832</td>
<td>1.11</td>
</tr>
<tr>
<td>LDL≥70 mg/dL, hsCRP≥1 mg/L</td>
<td>1874</td>
<td>0.95</td>
</tr>
<tr>
<td>LDL&lt;70 mg/dL, hsCRP≥1 mg/L</td>
<td>4662</td>
<td>0.56</td>
</tr>
<tr>
<td>LDL≥70 mg/dL, hsCRP&lt;1 mg/L</td>
<td>236</td>
<td>0.64</td>
</tr>
<tr>
<td>LDL&lt;70 mg/dL, hsCRP&lt;1 mg/L</td>
<td>944</td>
<td>0.24</td>
</tr>
</tbody>
</table>

P < 0.001

There is good evidence that the level of CRP is predictive of CV risk but there is currently no evidence that CRP should be a therapeutic target.
Unmodifiable Risk Factors

- Age
- Gender
- Family history of premature cardiovascular disease
Modifiable Risk Factors

- Smoking
- Elevated LDL-C
- Elevated Plasma TG
- Low HDL-C
- Elevated blood pressure
- Diabetes
- Abdominal obesity
- Lp(a)
- hsCRP
ISA 2015

XVII International Symposium on Atherosclerosis
May 24–27, 2015

Amsterdam RAI, Amsterdam, The Netherlands

Visit: www.isa-2015.com for more information