Coronary Calcium: Population Risk and Assessment

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PROBLEM WITH CONVENTIONAL RISK FACTOR ASSESSMENT:
Moderate accuracy

Examples:
1. High sensitivity, low specificity
   ≈ 90% of patients with CAD have ≥ 1 risk factor
   ≈ 75% of persons without CAD have ≥ 1 risk factor
   i.e., sensitivity ≈ 90%, specificity ≈ 25%
2. Odds ratio of 2
   Sensitivity 58.6%
   Specificity 58.6%
Total Coronary Artery Plaque and EBCT Coronary Calcium

- Lipid Rich: 80%
- Fibrotic: 20%
- Calcified: 80%

Plaque Detectable by IVUS, Pathology
CIRCUMSTANTIAL EVIDENCE IN SUPPORT OF FAST CT SCREENING FOR CAD

• Pathology: 3 to 9X as much calcium in coronary vs. other deaths
• Angiography: calcium score predicts obstructive CAD better than risk factors
• X-sectional: mean/median calcium score 4/30 X higher in MI survivors

_____

8 studies, > 1200 hearts, >3800 patients, NO EXCEPTIONS!
## CORONARY CALCIUM AND CAD/ASCVD EVENTS:
### RETROSPECTIVE STUDIES

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age ± SD</th>
<th>f/u yrs/%</th>
<th>Independent?</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Francis</td>
<td>1,172</td>
<td>53 ± 11</td>
<td>3.6/99</td>
<td>Yes</td>
</tr>
<tr>
<td>Nashville</td>
<td>632</td>
<td>52 ± 9</td>
<td>2.7/ ?</td>
<td>Yes</td>
</tr>
<tr>
<td>So Cal</td>
<td>926</td>
<td>54 ± 10</td>
<td>3.3/61</td>
<td>Yes</td>
</tr>
<tr>
<td>U of Ill</td>
<td>5,635</td>
<td>51 ± 10</td>
<td>3.1/64</td>
<td>Yes</td>
</tr>
<tr>
<td>Cooper</td>
<td>16,097</td>
<td>54 ± 10</td>
<td>3.5/69</td>
<td>Yes</td>
</tr>
<tr>
<td>Shaw</td>
<td>10,377</td>
<td>53 ± 0.1</td>
<td>5.0/99</td>
<td>Yes</td>
</tr>
</tbody>
</table>

> 50,000 patient years
## CORONARY CALCIUM AND CAD/ASCVD EVENTS: PROSPECTIVE STUDIES

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age ±</th>
<th>f/u yrs/%</th>
<th>Independent?</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBHW</td>
<td>967</td>
<td>66 ± 8</td>
<td>6.4/?</td>
<td>Yes</td>
</tr>
<tr>
<td>St. Francis</td>
<td>4,613</td>
<td>59 ± 6</td>
<td>4.3/94</td>
<td>Yes</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>1,795</td>
<td>71 ± 6</td>
<td>3.3/100</td>
<td>Yes</td>
</tr>
<tr>
<td>PACC</td>
<td>2,000</td>
<td>43 ± 3</td>
<td>3.0/99</td>
<td>Yes</td>
</tr>
<tr>
<td>Munich</td>
<td>1,490</td>
<td>58 ± 14</td>
<td>5.5/?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

> 45,000 patient years
# CORONARY CALCIUM AND CORONARY DISEASE EVENTS

<table>
<thead>
<tr>
<th>Calcium Score Threshold</th>
<th>≥ 100</th>
<th>≥ 200</th>
<th>≥ 600</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects above threshold (%)</td>
<td>25</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>79</td>
<td>63</td>
<td>33</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>77</td>
<td>85</td>
<td>95</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>8.9</td>
<td>10.5</td>
<td>15.0</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>99.2</td>
<td>98.7</td>
<td>98.0</td>
</tr>
<tr>
<td>Relative risk</td>
<td>11.3</td>
<td>8.3</td>
<td>7.4</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(7.4-17.1)</td>
<td>(5.8-11.8)</td>
<td>(5.2-10.5)</td>
</tr>
</tbody>
</table>
Prediction of Cardiac Events in Asymptomatic Patients by EBT

The St. Francis Heart Study, ACC 2003

Prediction of CORONARY DISEASE EVENTS

![Graph showing relative risk versus calcium score](image)
Prediction of Cardiac Events in Asymptomatic Patients by EBT

*The St. Francis Heart Study, ACC 2003*

Calcium Score >100 vs <100

- Any Event: 9.5
- Cor. Event: 10.7
- MI/SCD: 9.9
### DETERMINANTS OF CORONARY DISEASE EVENTS

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>$X^2$</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>4.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Gender</td>
<td>4.9</td>
<td>0.03</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>6.0</td>
<td>0.01</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>5.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Family history</td>
<td>1.4</td>
<td>0.24</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3.3</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.1</td>
<td>0.30</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.4</td>
<td>0.51</td>
</tr>
<tr>
<td>Calcium score</td>
<td>6.6</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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**C-statistic**: 0.85
## CALCIUM SCORE VS. FRAMINGHAM RISK INDEX PREDICTION OF CORONARY EVENTS

<table>
<thead>
<tr>
<th></th>
<th>Area under ROC Curve</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium score</td>
<td>0.81 ± 0.03</td>
<td>0.0002</td>
</tr>
<tr>
<td>Framingham</td>
<td>0.69 ± 0.03</td>
<td></td>
</tr>
</tbody>
</table>
All CAD Event Rates By Calcium Score Tertiles
(Within Framingham Risk Categories)

Percent per Year (Observed)

Percent per 10 Years (Predicted)

p < 0.0001

1st Tertile
2nd Tertile
3rd Tertile

n=654 n=506 n=86

SCCT Lecture Series
Budoff: Coronary Calcium
### All Cause Mortality in Patients Without Known CAD

**EBT Coronary Calcium Score**

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>DM</th>
<th>Smoke</th>
<th>HTN</th>
<th>&lt;10</th>
<th>10-100</th>
<th>101-400</th>
<th>&gt;1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured Data</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2.47</td>
<td>6.15</td>
<td>12.29</td>
</tr>
</tbody>
</table>

*EBT found to be independent and incremental to risk factors*

**Shaw, Raggi et al**
*Radiology 2003*

**All Cause Mortality [NDR]**
*n = 10,377 asymptomatic men and women f/u = 5.0+3.5 yrs**
EBT 5 year All-Cause Mortality – Shaw et al
Taylor et al – PACC Study – JACC 2005

- 2000 patients, mean age 43
- Coronary calcium was associated with an 11.8-fold increased risk for incident coronary heart disease (CHD) (p < 0.002) in a Cox model controlling for the Framingham risk score.
- In young, asymptomatic men, the presence of coronary artery calcification provides substantial, cost-effective, independent prognostic value in predicting incident CHD that is incremental to measured coronary risk factors.
Calcium Versus Framingham
5 USES OF CAC

• Use a calcium score to screen patients with moderate (intermediate) Framingham risk
  – Positive EBT scans indicate incremental risk
  – Alters therapeutic goal (LDL, BP, etc)

• **Identify patients who do not need further cardiac evaluation (scores of zero)**

• Consider serial imaging as ongoing management tool (progression)

• Improve compliance

• Non-invasive Angiography
Negative Predictive Power of EBT

- 1764 persons underwent Calcium scoring before invasive angiography
- 1242 with >50% stenosis
- 1237/1242 with CAC (>99% sensitivity)
- Sensitivity for Obstruction
  - 99.4% in men
  - 100% in women
- Negative predictive power > 99%
  - 525 angiograms (30%) could be appropriately avoided
- Can be used as a ‘filter’ prior to angiography to help avoid negative angiograms

Haberl et al. JACC Feb 2001
Figure 1. The frequency of an ischemic myocardial perfusion single-photon emission computed tomography (≥5% ischemic) (stippled bars) and of a moderate to severe ischemia (>10% ischemic) (black bars) for patients divided into six coronary artery calcium (CAC) score groupings.
Figure 2. Cox proportional hazards survival curves demonstrating time to acute MI for patients with a yearly calcium volume score change ≥15% or <15%.
Arad et al. JACC 2005

- In the largest study reported to date, multiple logistic regression, demonstrated only age (p 0.03), male gender (p 0.04), LDL cholesterol (p 0.01), HDL cholesterol (p 0.04), and two-year change in calcium score (p 0.0001) were significantly associated with subsequent CAD events.
- Thus, increasing calcium scores were most strongly related to coronary events.
Coronary Artery Scanning

- SEVERE CALCIFICATION
Odds ratio of maintaining statin therapy with various levels of baseline CAC
5 USES OF CAC

• Use a calcium score to screen patients with moderate (intermediate) Framingham risk
  – Positive EBT scans indicate incremental risk
  – Alters therapeutic goal (LDL, BP, etc)
• Identify patients who do not need further cardiac evaluation (scores of zero)
• Consider serial imaging as ongoing management tool (progression)
• Improve compliance
• **Adjunct to Non-invasive Angiography**
PROGNOSTIC DATA WITH CTA
Superior doctors prevent the disease. Mediocre doctors treat the disease before evident. **Coronary Calcium**
Inferior doctors treat the full-blown disease.

--Huang Dee: Nai-Ching
(2600 BC First Chinese Medical Text)