Coronary calcium score in the era of low radiation dose coronary CT angiography

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Disclosures

No conflicts of interest
CAC scoring revisited

Source: PubMed
Primary prevention based on risk factors

Framingham risk scoring

- **Low risk (<10% 10 yr risk)**
  - 35%
  - Reassurance
  - Advice healthy lifestyle

- **Intermediate risk (10-20% 10 yr risk)**
  - 40%
  - ? Consider non-invasive imaging

- **High risk (>20% 10 yr risk)**
  - 25%
  - Intensive therapy / risk factor modification

Risk factors:
- Smoking
- Diabetes
- Hypertension
- High cholesterol
- Etc

Greenland, NEJM 2003
Risk factor limitations

- 50-75% of acute coronary events in patients classified as low or intermediate risk
- Many individuals with 1 or more risk factors never develop coronary heart disease
- Most women classified as low risk (<60 y: 99% vs 40% for men)

Lifetime risk after age 40: 49% men, 32% women

Primary prevention: role for CAC scoring

- Low risk (<10% 10 yr risk) 35%
  - Reassurance
  - Advice healthy lifestyle

- Intermediate risk (10-20% 10 yr risk) 40%
  - CALCIUM SCORING

- High risk (>20% 10 yr risk) 25%
  - Intensive therapy / risk factor modification

Framingham risk scoring

Greenland, NEJM 2003
Scientific expert documents

Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging

ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain

ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography

2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults

Coronary calcium scoring by CT

- Since late eighties (first EBT, now ≥16-MDCT)
- Direct, non-invasive evaluation of coronary atherosclerosis; ~ 100% sensitivity
- Close correlation to total plaque burden
- Standardized scanning, reconstruction and scoring protocol
- Low inter-/intra-observer variability (1-3%)
- Radiation dose typically <1 mSv (annual: 3 mSv)

Sangiorgi, JACC 1998; Agatston, JACC 1990; Voros, JCCT 2011
Distribution CAC scores

<table>
<thead>
<tr>
<th>CAC Score</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>44%</td>
</tr>
<tr>
<td>1-10</td>
<td>14%</td>
</tr>
<tr>
<td>11-100</td>
<td>20%</td>
</tr>
<tr>
<td>101-400</td>
<td>13%</td>
</tr>
<tr>
<td>401-1000</td>
<td>6%</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>4%</td>
</tr>
</tbody>
</table>
# CAC score and risk of coronary events

<table>
<thead>
<tr>
<th>CAC</th>
<th>RR (vs. negative scan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>average 1-100</td>
<td>1.9 (1.3-2.5)</td>
</tr>
<tr>
<td>moderate 100-400</td>
<td>4.3 (3.1-6.1)</td>
</tr>
<tr>
<td>high 400-1000</td>
<td>7.2 (5.2-9.9)</td>
</tr>
<tr>
<td>very high &gt;1000</td>
<td>10.8 (4.2-27.7)</td>
</tr>
</tbody>
</table>

Greenland, Circulation/JACC 2007
Predictive power of CAC score beyond RFs

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>N</th>
<th>AUC risk factors</th>
<th>AUC + CAC score</th>
<th>NRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raggi</td>
<td>2001</td>
<td>676</td>
<td>0.71</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Greenland</td>
<td>2004</td>
<td>1,029</td>
<td>0.63</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Arad</td>
<td>2005</td>
<td>4,613</td>
<td>0.69</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Wong</td>
<td>2009</td>
<td>2,303</td>
<td>0.75</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>Erbel</td>
<td>2010</td>
<td>4,129</td>
<td>0.68</td>
<td>0.75</td>
<td>22 (66)%</td>
</tr>
<tr>
<td>Polonsky</td>
<td>2010</td>
<td>5,878</td>
<td>0.76</td>
<td>0.81</td>
<td>25 (54)%</td>
</tr>
<tr>
<td>Elias-Smale</td>
<td>2010</td>
<td>2,028</td>
<td>0.72</td>
<td>0.76</td>
<td>14 (63)%</td>
</tr>
</tbody>
</table>

AUC = Area under the receiver operating characteristic curve
NRI = netto reclassification improvement (intermediate risk category)
Power of zero CAC score

44052 asymptomatic individuals, mean f-up 5.6 y

0.5% risk of events in case of 0 CAC score

Tota-Maharaj, Eur Heart J 2012; Sarwar, JACC Img 2009
CAC score vs risk factors for risk prediction

44052 asymptomatic individuals, mean f-up 5.6 y

Risk in high CAC score/no RFs > no CAC/multiple RFs!
Primary prevention: increasing role CAC score?

Framingham risk scoring

Low risk
(<10% 10 yr risk)

Intermediate risk
(10-20% 10 yr risk)

High risk
(>20% 10 yr risk)

Reassurance
Advice healthy lifestyle

CALCIUM SCORING

Intensive therapy / risk factor modification

Also if CAC score is 0?
Primary prevention: CAC score as first step?

CALCIUM SCORING

CAC score 0
- 44%
- Reassurance
  - Advice healthy lifestyle
  - No need for testing < 5 years

CAC score positive
- 56%
- Risk factor assessment
  - Risk management based on combination of CAC score and RF levels
CAC score and downstream testing

- EISNER prospective randomized trial
- Risk factor counseling + or – CAC scoring
- 2137 volunteers, 4 year follow-up
- CAC scoring group:
  - superior risk factor control
  - no increase in downstream testing
  - in low CAC score: reduction of 37% in downstream procedures, reduction of 25% in medication
  - opposite in high CAC score

Rozanski, JACC 2011
CTA in asymptomatic persons?

- CONFIRM registry
- 7590 individuals without chest pain, 2 year follow-up for mortality / nonfatal MI
- CAC score and CTA-detected stenoses both predictive of events
- Increase in C statistic / NRI:
  - 0.12 / 0.62 for CAC score vs RFs
  - 0.03 / 0.09 for additional CTA
- CAC score seems sufficient for risk prediction

Cho, Circulation 2012
CAC scoring in symptomatic patients?

- Focus on 0 CAC score: filter before further testing?
- Calibration of CT technique to optimize sensitivity for calcium detection
- Prevalence 0 CAC score in non-acute patients undergoing CTA: 20-51%
- Negative predictive value for >50% stenosis on CTA: 92% (36-100% for individual studies)

Sarwar, JACC Cardiovasc Imaging 2009; Villines, JACC 2011
Power 0 CAC score in symptomatic patients

Villines, JACC 2011

- 10037 patients
- 51% CAC score 0
- 3.5% CAC +
- 1.4% ≥ 50% stenosis
- 0.3% ≥ 70% stenosis

<table>
<thead>
<tr>
<th>CAC 0 CTA nl</th>
<th>CAC + CTA nl</th>
<th>CAC 0 CTA &lt;50%</th>
<th>CAC + CTA &lt;50%</th>
<th>CAC 0 CTA &gt;50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow</td>
<td>Red</td>
<td>Yellow</td>
<td>Red</td>
<td>Yellow</td>
</tr>
<tr>
<td>Late Revasc</td>
<td>MI</td>
<td>Death</td>
<td>Death</td>
<td>Death</td>
</tr>
</tbody>
</table>

P < 0.001
### Zero CAC score in the emergency room

<table>
<thead>
<tr>
<th>CAC score and coronary CTA:</th>
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<tr>
<td>225 patients, 9% stenosis</td>
</tr>
<tr>
<td>59% CAC score 0 → NPV 99%</td>
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<table>
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<tr>
<th>CAC score and SPECT / short-term follow-up (7 months):</th>
</tr>
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<tr>
<td>1031 patients, 4% ischemia</td>
</tr>
<tr>
<td>61% CAC score 0 → NPV 99.7%</td>
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</table>

<table>
<thead>
<tr>
<th>CAC score and long-term follow-up (5 years):</th>
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</thead>
<tbody>
<tr>
<td>263 patients, 4% ischemia</td>
</tr>
<tr>
<td>51% CAC score 0 → NPV 99%</td>
</tr>
</tbody>
</table>

CAC scoring in atypical chest pain

- Patients with Chest Pain
- Estimate Likelihood of CAD
- Low (intermediate) risk of CAD
- CAC Testing
  - CAC=0
    - No further cardiac testing
    - Assess other causes of chest pain
  - CAC 1-400
    - Coronary CT Angiography
    - Or Myocardial Perfusion Imaging
  - CAC>400
    - Invasive Coronary Angiography

Nasir, Radiology 2012; Skinner, Heart 2010; Greenland, JACC 2007
Cost-effectiveness of CAC score in ER

- Compared to exercise treadmill testing, CAC scoring reduced cost from $1701 to $599 (reduction 65%)
- In patients with pre-test probability < 30%, CAC scoring more cost-effective than exercise treadmill testing
- Compared to standard of care, CAC scoring (including downstream costs) reduced cost from $2384-3134 to $750 (reduction 76%) in low to intermediate risk patients

Raggi, Am J Cardiol 2000; Raman, Eur Radiol 2012; Branch, Acad Radiol 2012
CAC scoring vs (additional) CTA

CAC score:
- Higher level of standardization
- Extensive evidence base for population cardiovascular risk stratification
- Accepted role in primary prevention
- Limited to very low radiation dose
- High through-put, technician-only examination
- Only virtual contra-indications

Role for CAC scoring? Undoubtedly!