The Emerging Role of Cardiac CT for Risk Stratification and Prevention

BACPR Cardiff 2016

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“Prevention is Better than Cure”
Prevention is Difficult

Pre-mordial Prevention

Primary Prevention

Secondary Prevention

Prevention Paradox
### Women’s Health Study: age 45+ (IQR: 49-59y)

<table>
<thead>
<tr>
<th>10-year predicted risk:</th>
<th>&lt;5%</th>
<th>5-10%</th>
<th>10-20%</th>
<th>≥20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ♀, n=7911:</td>
<td>6944</td>
<td>653</td>
<td>255</td>
<td>59</td>
</tr>
<tr>
<td>All events, n=199:</td>
<td>99</td>
<td>48</td>
<td>34</td>
<td>18</td>
</tr>
</tbody>
</table>

Primary prevention, nondiabetic women (Table 5, Ridker et al. JAMA 2007;297:611-9)
Prevention is difficult

- 65% do not have risk factors under control
- 30% of high risk patients achieve LDL targets
- 66% of high risk patients do not take their medications
Prediction is Difficult

An episode of *The Simpsons* titled “Bart to the Future” first aired back in March of 2000. In it, Bart is given a look into the future, where a country is brought down to its knees by the financial mismanagement and a crime wave ushered in by Donald Trump after being elected President.
Prediction is Difficult
<table>
<thead>
<tr>
<th>Predictor</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.586</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.562</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.573</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.577</td>
</tr>
<tr>
<td>Ethnic origin</td>
<td>0.518</td>
</tr>
<tr>
<td>Increased lipids</td>
<td>0.484</td>
</tr>
<tr>
<td>Family history</td>
<td>0.440</td>
</tr>
</tbody>
</table>
Prediction is Difficult
Risk Prediction & Lipids

- **CAD with normal LDL**: 77%
- **CAD with normal HDL**: 45.4%
Prediction is Difficult
RF & Lifetime Risk CV Events

Circulation. 2010;121:1768-1777
Prediction is Difficult
Risk Scores
### Risk Scores

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Framingham</th>
<th>PROCAM</th>
<th>Heart-Score</th>
<th>QRSK2</th>
<th>Reynolds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>≤74</td>
<td>≤65</td>
<td>≤65</td>
<td>&lt;74</td>
<td>&lt;60</td>
</tr>
<tr>
<td>Sex difference</td>
<td>Yes</td>
<td>Yes (no analyses)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>&lt;140</td>
<td>&lt;120</td>
<td>&lt;130</td>
<td>RRs continuous</td>
<td>RR nil</td>
</tr>
<tr>
<td>Cholesterolaemia</td>
<td>Total cholesterol</td>
<td>LDL-cholesterol</td>
<td>Total cholesterol</td>
<td>Total cholesterol/ HDL-cholesterol</td>
<td>Total cholesterol</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>HDL-cholesterol</td>
<td>HDL-cholesterol</td>
<td>HDL-cholesterol</td>
<td>HDL-cholesterol</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Triglyceride</td>
</tr>
<tr>
<td>hs-C-reactive protein</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Family heart disease</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Smoking</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Physical activities</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Endpoint definition</td>
<td>AP, cardiovascular death</td>
<td>Myocardial infarction</td>
<td>Cardiovascular death</td>
<td>MI AP, CAD, stroke, and TIA</td>
<td>MI, stroke, coronary revascularization, cardiovascular death</td>
</tr>
<tr>
<td>High-risk definition 10 years</td>
<td>20%</td>
<td>20%</td>
<td>5%</td>
<td>20%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Prediction is Difficult
Risk Scores

AHA/ACC

SCORE

Santos JACC 2015
Prevention @ Patient Level
Imaging-CAD - Latency

High Prevalence of Coronary Atherosclerosis in Asymptomatic Teenagers and Young Adults: Evidence From Intravascular Ultrasound

E. Murali Tuzcu, Samir R. Kapadia, Erich Tutar, Khaheld M. Zada, Robert E. Hobbs, Patrick M. McCarthy, James B. Young and Steven E. Nissen

Circulation. 2001;103:2705-2710
“....the most important problem we face is to find a way of recognizing these people before they drop dead.... ”

Mason Sones 1978
Why do we not look for it?
CV Imaging
CV-Imaging Opportunity
Subclinical Atherosclerosis Imaging

A. Traditional 10-Year Risk Model
   - Unaccounted for Risk Factor Exposure

B. “Lifetime” Risk Model
   - Unaccounted for Risk Factor Exposure

C. Subclinical Disease Detection Model
   - Integrated Risk Exposure
CV Imaging
Cardiac CT
CV Imaging - Opportunity
CV Imaging
Cardiac CT
Coronary Artery Calcium Scan

- Non-enhanced scan
- 2sec scan
- Short breath-hold
- Prospective Triggering
- Low radiation dose
- Semi-automated analysis
- 5mins Post-Processing

Diagnostic & Prognostic
CV Imaging
Cardiac CT

FBP 1mSv
iDose\(^4\) 0.15mSv
FBP 0.15mSv

<table>
<thead>
<tr>
<th></th>
<th>L.MAIN</th>
<th>LAD</th>
<th>LCX</th>
<th>RCA</th>
<th>Total Coronaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series 10363</td>
<td>1017.09</td>
<td>69.78</td>
<td>61.83</td>
<td>96.48</td>
<td>1245.18</td>
</tr>
<tr>
<td>31 Mar 2011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 10249</td>
<td>1031.88</td>
<td>66.12</td>
<td>75.18</td>
<td>73.91</td>
<td>1247.09</td>
</tr>
<tr>
<td>31 Mar 2011</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
CV Imaging
Cardiac CT- Association
CV Imaging
Cardiac CT-Association

Distribution of CAC Scores
- CAC = 0: 35%
- CAC 1-100: 33%
- CAC > 100: 32%

Intermediate Risk Group (10-20% 10-yr risk)

% All Events by CAC Score
- CAC = 0: 9%
- CAC 1-100: 35%
- CAC > 100: 56%

Distribution of hsCRP
- hsCRP < 2: 41%
- hsCRP > 2: 59%

Intermediate Risk Group (10-20% 10-yr risk)

% All Events by hsCRP
- hsCRP < 2: 46%
- hsCRP > 2: 54%

CAC Score Group | 5-year NNT for Generic Statin
--- | ---
CAC=0 | ~450
CAC 1-100 | ~125
CAC >100 | ~50

hsCRP Group | 5-year NNT for Generic Statin
--- | ---
hsCRP <2 | ~150
hsCRP ≥2 | ~125
Diabetes – A CHD Risk Equivalent or Risk Non-Equivalent?

Distribution of CAC Scores
- CAC = 0: 35%
- CAC 1-100: 38%
- CAC > 100: 27%

% All Events by CAC Score Group
- CAC = 0: 9%
- CAC 1-100: 25%
- CAC > 100: 66%

<table>
<thead>
<tr>
<th>CAC Score Group</th>
<th>Annual CHD event rate</th>
<th>Estimated 10-year Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAC = 0</td>
<td>0.4</td>
<td>Low (4%)</td>
</tr>
<tr>
<td>CAC 1-100</td>
<td>1.5</td>
<td>Intermediate (15%)</td>
</tr>
<tr>
<td>CAC &gt; 100</td>
<td>2.9</td>
<td>High (29%)</td>
</tr>
</tbody>
</table>

Data from the Multi-Ethnic Study of Atherosclerosis
### CV Imaging
Cardiac CT- Reclassification

<table>
<thead>
<tr>
<th>Study</th>
<th>% Reclassified</th>
<th>N</th>
<th>Age, yrs</th>
<th>Follow-up, yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>MESA (31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS 0%-6%</td>
<td>11.6</td>
<td>5,878</td>
<td>62.2</td>
<td>5.8</td>
</tr>
<tr>
<td>FRS 6%-20%</td>
<td>54.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS &gt;20%</td>
<td>35.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRI</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heinz Nixdorf (21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS &lt;10%</td>
<td>15.0</td>
<td>4,487</td>
<td>45-75</td>
<td>5.0</td>
</tr>
<tr>
<td>FRS 10%-20%</td>
<td>65.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS &gt;20%</td>
<td>34.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRI</td>
<td>22.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotterdam (30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS &lt;10%</td>
<td>12</td>
<td>2,028</td>
<td>69.6</td>
<td>9.2</td>
</tr>
<tr>
<td>FRS 10%-20%</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRS &gt;20%</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRI</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reprinted with permission from Hecht and Narula (12).
• Consistently improve model discrimination

• Net Reclassification Index- 25-70%

• High Variability-(More Study Required)

• Particularly relevant to intermediate risk
CV Imaging
Cardiac CT - Outcomes

South Bay Heart Watch:

<table>
<thead>
<tr>
<th>CACS</th>
<th>0</th>
<th>1-100</th>
<th>101-300</th>
<th>≥301</th>
</tr>
</thead>
<tbody>
<tr>
<td>% death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Framingham Risk Score, %

St. Francis: Middle aged

Rotterdam

MESA

Coronary artery calcium score

Cumulative incidence of major coronary events (%)

Years to Event
CV Imaging
Cardiac CT - Low Scores
CV Imaging
Cardiac CT - 0 Score

- 72,000
- 4.5Yrs
- 0.5% CV Mortality

- Reassurance?
- Target Resource?
- Defer Medicalisation?
- Improve Compliance?
CV Imaging
Cardiac CT-Incremental Value

Receiver-Operating Characteristic Curves Noting the Incremental Value of the Total Agatston Scores Over and Above the Total Number of Clinical Risk Factors as Well as Age
CV Imaging
Cardiac CT - Incremental Value-Aggressive Disease

- CAC
- Progressors
- Non-Progressors

Cumulative MI-Free Survival

Years of Follow-up

<15% Change

≥15% Change

Raggi, Callister, Shaw, A
How do I use CT in clinical practice?
<table>
<thead>
<tr>
<th>CV Imaging</th>
<th>Cardiac CT-Case History</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 64Yr Male</td>
<td>• Normotensive</td>
</tr>
<tr>
<td>• Non-Smoker</td>
<td>• Non-Diabetic</td>
</tr>
<tr>
<td>• T Chol 5.2, LDL 2.3</td>
<td>• BMI 29</td>
</tr>
<tr>
<td>• Positive FH</td>
<td>• SCORE - 3%</td>
</tr>
<tr>
<td></td>
<td>• FRS - 18%</td>
</tr>
<tr>
<td></td>
<td>• QRISK 2 - 18%</td>
</tr>
</tbody>
</table>
CV Imaging
Cardiac CT-Case History

• In a crowd of 100 people with the same risk factors as you, 18 are likely to have a heart attack or stroke within the next 10 years

• Relative Risk 1.4
• Heart Age 69
• Lifetime Risk 56%
CV Imaging
Cardiac CT-Case History

- Agatston Score: 1623
- >20% All Cause Mortality
- High CV Risk
- High probability of Ischaemia
Universal Screening?
Statins for >50% of our population?
First do no harm..
CV Imaging
Targeting Medical Intervention

"If everything has to be double-blinded, randomised, and evidence-based, where does that leave new ideas?"

See Correspondence page 122

Why we need a new deal on disease definition
CV Imaging
Targeting Medical Intervention - Fringe Benefits?

• Better understanding of risk?

• Reinforce Healthy Behaviour?

• Better Clinical Decisions?
Lower NNT than any other method
CV Imaging
Cardiac CT - Limitations

- Radiation..
- Incidental Findings..
- Increased Cost..
- RCT rather than registry data
Prevention Through Behavioural Change → Early Diagnosis → Effective Intervention
“Nobody can go back and start a new beginning, but anyone can start today and make a new ending.”  M Robinson

Why not take a peek?