Cardiac CT for Risk Assessment: Do we need to look beyond Coronary Artery Calcification

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MESA Study – 6,814 Patients: 3.5 year follow-up

Nonfatal MI & CHD Death

Fully adjusted – Detrano et al – NEJM - 2008

MESA – ROC for Different Risk Algorithms
Yeboah JAMA 2012
• If, after quantitative risk assessment, a risk-based treatment decision is uncertain, assessment of 1 or more of the following—family history, hs-CRP, CAC score, or ABI—may be considered to inform treatment decision making.

• The contribution to risk assessment for a first ASCVD event using ApoB, CKD, albuminuria, or cardiorespiratory fitness is uncertain at present.

• CIMT is not recommended for routine measurement in clinical practice for risk assessment for a first ASCVD event.

“The Work Group notes that assessing CAC is likely to be the most useful of the current approaches to improving risk assessment among individuals found to be at intermediate risk after formal risk assessment.”
Background

Aortic Valve Calcification
Mitral Annular Calcification
Thoracic Aortic Calcification


Background

EXTRACoronary CALCIFICATION (ECC)

MVC
AVC
Aortic Calcification

Coronary Heart Disease Events
All-cause mortality

Methods

- Gated cardiac CT scans were obtained in all subjects
- CT scans were interrogated at four sites for ECC:
  - aortic valve calcification (AVC)
  - mitral valve calcification (MVC)
  - thoracic aorta calcification (TAC)
  - aortic root calcification.
- CAC was also measured
Methods

- Follow-up: Median of 8.5 years
- Outcomes:
  - CHD-events
  - All-cause mortality

Table 2b: Multivariable Adjusted hazard ratios for all-cause mortality by ECC

<table>
<thead>
<tr>
<th>Extracoronary calcification</th>
<th>Model 1 (TRF)</th>
<th>Model 2 (TRF + ECC)</th>
<th>Model 3 (TRF + Lag(4)/ECC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC, AVC, TAC, AVR</td>
<td>99/1186</td>
<td>1.17 (0.99-1.50)</td>
<td>1.12 (0.92-1.55)</td>
</tr>
<tr>
<td>MVC</td>
<td>105/864</td>
<td>1.94 (1.12-2.11)</td>
<td>1.41 (1.01-1.95)</td>
</tr>
<tr>
<td>AVC</td>
<td>65/377</td>
<td>1.77 (1.22-2.55)</td>
<td>1.58 (1.08-2.31)</td>
</tr>
<tr>
<td>TAC</td>
<td>42/138</td>
<td>5.03 (1.98-4.63)</td>
<td>2.62 (1.68-4.05)</td>
</tr>
</tbody>
</table>

* TRF: age, gender, race, total cholesterol, high density lipoprotein, smoking status, cigarette pack-years, systolic blood pressure, hypertension medication and creatinine

Conclusions

- Extracoronary Calcification (MVC, AVC, TAC, AVR) + Coronary Heart Disease Events + All-cause mortality
NAFLD IN MESA

Hazard Ratio for Outcomes with Liver fat (n=4,119 after exclusion)
7.5 year median FU, 5.1% CHD Events
Model 1: age, gender, race, site adjusted
Model 2: Model 1 + RF (DM, LDL, TG, HDL, Cholesterol lowering meds, BMI, HTN, Cig smoking)
Model 3: Model 2 + CAC Scores+ CRP

<table>
<thead>
<tr>
<th>Model</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1.73</td>
<td>1.25-2.41</td>
<td>0.01</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.41</td>
<td>1.00-1.99</td>
<td>0.05</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.43</td>
<td>1.01-2.03</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Epicardial (Pericardial) Fat
Pericardial Fat Predicts MI/CVD Death in MESA

MESA – Pericardial Fat

- Pericardial fat predicts incident coronary heart disease independent of conventional risk factors, including body mass index.


Budoff JACC Imag 2010

4,609 consecutive asymptomatic individuals
Budoff Progression MESA
JACC 2013

Coronary CTA Under 1 mSv

Patient:
- Male
- BMI: 22
- Cardiac risk factors
- Heart rate: 54-56 bpm

Scan:
- Tube: 350 mA & 100 kVp
- X-ray Exposure: 0.93 sec
- Radiation Dose: 0.95 mSv

Findings:
- LAD: mild stenosis

CTA for Risk Assessment

- Since calcium scoring is already acknowledged in both appropriate use and ACC/AHA Guidelines
- AND...The radiation dose of CTA can be similar
- AND...We derive so much more information on a CTA...Why NOT?
Discriminatory Power of CCTA over CACS in Asymptomatic Individuals

<table>
<thead>
<tr>
<th>Model</th>
<th>FRS C-statistic</th>
<th>Individual Risk Factors C-statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I: RFS only</td>
<td>0.54 (0.52 - 0.56)</td>
<td>0.76 (0.74 - 0.79)</td>
</tr>
<tr>
<td>Model II: RFS + CACS</td>
<td>0.71 (0.68 - 0.75)</td>
<td>0.79 (0.77 - 0.82)</td>
</tr>
<tr>
<td>Model III: RFS + CACS + SSS</td>
<td>0.73 (0.70 - 0.76)</td>
<td>0.79 (0.77 - 0.82)</td>
</tr>
<tr>
<td>Model IV: RFS + CACS + SSS</td>
<td>0.72 (0.69 - 0.75)</td>
<td>0.79 (0.76 - 0.81)</td>
</tr>
<tr>
<td>Model V: RFS + CACS + SSS</td>
<td>0.72 (0.69 - 0.75)</td>
<td>0.79 (0.76 - 0.81)</td>
</tr>
</tbody>
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Composite Outcome of All-Cause Mortality and Non-Fatal MI

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</tr>
</thead>
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<tr>
<td>Model I: RFS only</td>
<td>0.59 (0.57 - 0.61)</td>
<td>0.71 (0.69 - 0.73)</td>
</tr>
<tr>
<td>Model II: RFS + CACS</td>
<td>0.70 (0.68 - 0.74)</td>
<td>0.79 (0.76 - 0.81)</td>
</tr>
<tr>
<td>Model III: RFS + CACS + SSS</td>
<td>0.74 (0.71 - 0.77)</td>
<td>0.79 (0.76 - 0.80)</td>
</tr>
<tr>
<td>Model IV: RFS + CACS + SSS</td>
<td>0.74 (0.71 - 0.77)</td>
<td>0.79 (0.76 - 0.80)</td>
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<td>0.74 (0.71 - 0.77)</td>
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Source: Cho et al, Circulation 2012
Net Reclassification based upon CCTA in Asymptomatic Individuals

7,590 individuals without known CAD or chest pain syndrome (61% male; 58-72 years) undergoing both CACS and CCTA, followed for 24 months (IQR 18-35); all-cause mortality occurred in 136 individuals

<table>
<thead>
<tr>
<th>Model</th>
<th>Proportion of Events Reclassified</th>
<th>Proportion of Non-Events Reclassified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I: CACS</td>
<td>8.7% (5.1%)</td>
<td>8.3% (5.0%)</td>
</tr>
<tr>
<td>Model II: CACS + CCTA</td>
<td>12.0% (6.9%)</td>
<td>11.4% (6.3%)</td>
</tr>
<tr>
<td>Model III: CACS + SSB</td>
<td>12.7% (6.9%)</td>
<td>12.2% (6.4%)</td>
</tr>
<tr>
<td>Model IV: CACS + CCTA + SSB</td>
<td>13.7% (7.1%)</td>
<td>13.2% (6.7%)</td>
</tr>
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Future Directions with CTA

- 35% of young DM (age < 40) had only non-calcified plaques
  
  Madaj, Karlsberg, Karpman, Budoff
  * Acad Rad 2012

Plaque in Young – Jin – ICJI 2012

- Enrolled 914 asymptomatic subjects under the age of 45
- Subclinical coronary atherosclerosis was found in 86 subjects (9.4%).
- The most common type of plaque was non-calcified plaque (NCP) (58%), which was found in 63 subjects (6.9%).
Jin IJCI 2012

- Multivariate analysis revealed hazard ratios of 2.2 for subclinical coronary atherosclerosis, 49.17 for NCP, and 105.58 for significant stenosis.
- The prevalence of subclinical coronary atherosclerosis in asymptomatic young adults is not negligible.
- CCTA has the potential to enhance risk stratification and prediction for coronary artery disease in asymptomatic young adults.

SCOUT Trial – JACC 2008

- Consecutively enrolled 1,000 middle-aged asymptomatic subjects
- Atherosclerotic plaques were identified in 215 (22%, 2 1 segments/subject) individuals; 40 individuals (4%) had only noncalcified plaques.
- Midterm follow-up (17 months) revealed 15 cardiac events only in those with CAD on CTA.

SCOUT Study – STATIN USE
215 patients in the CCTA group had atherosclerosis. Medication use was increased in the CCTA-positive group compared with both the CCTA-negative (no atherosclerosis) and control groups at 90 days (statin use, 34% vs 5% vs 8%, respectively; aspirin use, 40% vs 5% vs 8%, respectively), and 18 months (MV analysis 3.3 fold use). An abnormal screening CCTA result was predictive of increased aspirin and statin use at 90 days and 18 months.

**APC’s (Atherosclerotic Plaque Characteristics)**

- Low Attenuation Plaque
- Positive Remodeling
- Spotty Calcification
- (20-fold higher event rates)
- Motoyama 2007,9

**Napkin Ring Sign**

[Images of napkin ring sign]
Superior doctors prevent the disease. Mediocre doctors treat the disease before evident. Subclinical Atherosclerosis. Inferior doctors treat the full-blown disease.

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