De-Risking Primary Prevention: Role of Imaging

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Disclosure

The following speakers have conflicts of interest:

Matthew Budoff
Grant Support from General Electric
We Can Improve Preventive Screening!

New Risk Calculator

- **External Validation**
- Discriminating of Low to High Risk Subsets Unimpressive
- **Risk Overestimation**

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

Nonfatal MI & CHD Death

Hazard Ratio

Fully adjusted – Detrano et al– NEJM - 2008
MESA STUDY 10 year outcomes
Budoff EHJ 2018

[Graphs showing cumulative incidence of hard ASCVD (%) over years from baseline exam for White, Chinese, Black, and Hispanic populations with CAC categories 300+, 101 to 300, 1 to 100, and 0.]
Figure. Receiver Operator Characteristic Curves Showing Area Under the Curve for Incident Coronary Heart Disease and Incident Cardiovascular Disease in Intermediate-Risk MESA Participants

A. Incident coronary heart disease

B. Incident cardiovascular disease

- Framingham Risk Score (FRS) alone (reference)
- FRS plus coronary artery calcium
- FRS plus carotid intima-media thickness
- FRS plus brachial flow-mediated dilation
- FRS plus C-reactive protein
- FRS plus family history
- FRS plus ankle-brachial index

A. Receiver operator characteristic curves showing area under the curve for FRS alone, 0.623; FRS plus coronary artery calcium, 0.784 (P<.001); FRS plus intima-media thickness, 0.652 (P=.01); FRS plus flow-mediated dilation, 0.639 (P=.06); FRS plus high-sensitivity C-reactive protein, 0.640 (P=.03); FRS plus family history, 0.675.
“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.”
ST FRANCIS RANDOMIZED TRIAL
Randomized Double Blind Placebo Controlled Trial of
Atorvastatin in the Prevention of Cardiovascular Events
Among Individuals With Elevated CAC Score

- Mean duration of treatment was 4.3 years.
- Treatment with atorvastatin reduced clinical endpoints by 30% (6.9% vs. 9.9%), and MI/Death by 44% (NNT 30)
- Event rates were more significantly reduced in participants with baseline calcium score >400 (8.7% vs. 15.0%, p=0.046 [42% reduction]). (NNT 16)

Using the Coronary Artery Calcium Score to Guide Statin Therapy: A Cost-Effectiveness Analysis

<table>
<thead>
<tr>
<th></th>
<th>FRS</th>
<th>TO</th>
<th>HDL</th>
</tr>
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<tbody>
<tr>
<td>55 yo woman</td>
<td>7.5%</td>
<td>221</td>
<td>40</td>
</tr>
<tr>
<td>55 yo man</td>
<td>7.5%</td>
<td>159</td>
<td>40</td>
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</tbody>
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<thead>
<tr>
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<tbody>
<tr>
<td><strong>Treat if CAC&gt;0</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QALY</td>
<td>+229</td>
<td>+172</td>
<td></td>
</tr>
<tr>
<td>$ per QALY</td>
<td>$18,000</td>
<td>$78,000</td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QALY</td>
<td>+248</td>
<td>+144</td>
<td></td>
</tr>
<tr>
<td>$ per QALY</td>
<td>$19,000</td>
<td>$80,000</td>
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</table>

Walter Reed Cohort
23,637 followed for 11.4 years
JACC Imaging 2018

**Figure 1** Cumulative Incidence of Myocardial Infarction, Stroke, MACE, and Death Stratified by CAC Severity

- **A** Myocardial Infarction
  - Cumulative incidence vs Years Since CAC Score
  - $p < 0.0001$

- **B** Stroke
  - Cumulative incidence vs Years Since CAC Score
  - $p < 0.0001$

- **C** MACE
  - Cumulative incidence vs Years Since CAC Score
  - $p < 0.0001$

- **D** Mortality
  - Cumulative incidence vs Years Since CAC Score
  - $p < 0.0001$

*CAC Group*
- 401+
- 101-400
- 1-100
- 0
Kaplan-Meier survival estimates

- 6,944 (42%) CAC=0
- 48 deaths

Followup (years)

FH CHD (-)  FH CHD (+)

Warranty of a CAC Score

Ketlogetswe AHA 2010
**EISNER Randomized Controlled Trial**

2137 middle-aged + risk factors without CVD
45-79y without CAD/CVD followed 4 years

- **No Scan**
  - Clinical evaluation
  - Questionnaire
  - Risk factor consultation

- **Scan**
  - Clinical evaluation
  - Questionnaire
  - Risk factor consultation
  - CAC scan
  - Scan consultation

Rozanski, Berman. Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research. JACC 2011;57:1622.
**EISNER Trial**

**Primary Endpoint:**

- Change in Framingham Risk Score

<table>
<thead>
<tr>
<th>CAC Scan (n=1,311)</th>
<th>No Scan (n=623)</th>
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<tbody>
<tr>
<td>0.002±5%</td>
<td>0.7±5%</td>
</tr>
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</table>

- Risk Factor Changes

  - Compared to No-Scan, Scan showed a net favorable Δ in:
    - SBP (p=0.02),
    - LDL-Cholesterol (p=0.04),
    - Waist Circumference for those w/ ↑ abdominal girth (p=0.01), and
    - Weight Loss (among overweight) (p=0.07)
# Does CAC scanning improve outcomes?

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No SCAN</th>
<th>CACS&gt;400</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in LDL-C</td>
<td>-11 mg/dL</td>
<td>-29 mg/dL</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change in SBP</td>
<td>-5 mm Hg</td>
<td>-9 mm Hg</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exercise</td>
<td>36%</td>
<td>47%</td>
<td>0.03</td>
</tr>
<tr>
<td>New Lipid Rx</td>
<td>19%</td>
<td>65%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New BP Rx</td>
<td>18%</td>
<td>46%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New ASA Rx</td>
<td>7%</td>
<td>21%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lipid Adherence</td>
<td>80%</td>
<td>88%</td>
<td>0.04</td>
</tr>
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Rozanski, Berman, ElSNER. JACC 2011;57:1622. CACS 0 = 631. CACS>400 = 109.
EISNER Study – Costs Compared to No Scan Group

P < 0.005 for both measures

Rozanski JACC 2011
EISNER Study

- CACS may effectively triage care – evaluation, intensification of therapy – without increasing cost
- Compared with the no-scan group, the scan group showed a net favorable change in systolic blood pressure ($p < 0.02$), low-density lipoprotein cholesterol ($p < 0.04$), and waist circumference ($p < 0.01$), and tendency to weight loss among overweight subjects ($p < 0.07$), and improvement of FRS compared to no scan group
GUIDELINES LEAD TO VAST OVERTREATMENT

<table>
<thead>
<tr>
<th>JUPITER population</th>
<th>Percent of Patients in MESA</th>
<th>CHD event rate at 5.8 years</th>
<th>Hazard Ratio (95% CI)</th>
<th>5-year NNT for CHD</th>
</tr>
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<tbody>
<tr>
<td>CAC=0</td>
<td>47%</td>
<td>0.48%</td>
<td>1 (ref)</td>
<td>549</td>
</tr>
<tr>
<td>CAC 1-100</td>
<td>28%</td>
<td>2.79%</td>
<td>4.91</td>
<td>94</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td>25%</td>
<td>10.76%</td>
<td>27.8</td>
<td>24</td>
</tr>
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</table>
MESA – Aspirin Use 2018

The graph illustrates the number needed to treat based on the coronary artery calcium score (CAC) and the risk of coronary heart disease (CHD). The Y-axis represents the number needed to treat, and the X-axis shows different CAC categories: CAC=0, CAC1-99, and CAC>100. The bars indicate the number of patients needed to treat to prevent one CHD event for two risk categories: CHD <10% and CHD >10%.
2018

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHa/ASPC/NLA/PCNA
Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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Conclusions

New cholesterol guidelines advocating for more therapy with CAC > 100 and less therapy with CAC = 0 should be applied to the type I DM population as well.
CAC IN 2018 GUIDELINES

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<tr>
<td>IIa</td>
<td>B-NR</td>
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<tr>
<td>6. In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy (S4.4.2-15, S4.4.2-17, S4.4.2-23).</td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
</tr>
<tr>
<td>7. In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND</td>
<td></td>
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<tr>
<td>• If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking);</td>
<td></td>
</tr>
<tr>
<td>• If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age;</td>
<td></td>
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<tr>
<td>• If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy (S4.4.2-17, S4.4.2-23).</td>
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Coronary calcium test could help clarify heart disease risk – and control cholesterol

By American Heart Association News
A picture is worth 1000 words

Motivational effects of coronary artery calcium scores on statin adherence and weight loss
Nove K. Kalia, Lucas Cespedes, George Youssef, Dong Li and Matthew J. Budoff

♦ SEVERE CALCIFICATION
CAC IMPROVES STATIN DELIVERY

- Better Risk Stratification
  - matching risk with intensity of therapy
- 50% (or MORE) will have zero scores
  - Can defer statin and aspirin for 5 years
- IMPROVE COMPLIANCE
  - New guidelines (treat most) will lead to lower compliance in asymptomatic patients and increase health care costs
Since the purpose of using CAC testing is to accurately reclassify patients with moderate risk into low or higher risk levels to direct therapy at those patients who will most benefit from aggressive preventive strategy, the cost-effectiveness of CAC testing is robust due to better and more accurate targeting, in particular, to statin and aspirin therapy, as well as promoting more adherence to those therapies.
“Imaging has at least 3 virtues”

- It individualizes risk assessment beyond use of age, which is a less reliable surrogate for atherosclerosis burden.
- It provides an integrated assessment of the lifetime exposure to risk factors.
- It identifies individuals who are susceptible to developing atherosclerosis beyond established risk factors.

“Imaging has at least 3 virtues”

Once subclinical atherosclerosis is detected, intensity of drug therapy could be adjusted for plaque burden

“And then wham! This thing just came right out of left field.”
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)
Widowmakerthemovie.com

WATCH THIS FILM – IT COULD SAVE YOUR LIFE

The Widowmaker - watch the trailer
Questions?

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