Insights on Preventive Cardiology
Treatment Advances:
Coronary Calcium scoring in 2018 AHA/ACC Lipid Guidelines
Implications looking forward to HF

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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

Central Illustration: Cardiovascular Risk Prediction in Clinical Care: Comparison of Observed Versus Expected ASCVD Risks

Overall Non-diabetic 40-75 Years Old, n = 307,591

Cumulative 5-Year Risk (%)

5-Year Predicted Risk Group

- <2.5%
- 2.5% to <3.75%
- 3.75% to <5.0%
- ≥5.0%

RANA et al. REGARDS STUDY JACC 2016
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.

Primary Prevention: Assess ASCVD Risk in Each Age Group Emphasize Adherence to Healthy Lifestyle

- Age 0-19 y: Lifestyle to prevent or reduce ASCVD risk Diagnosis of Familial Hypercholesterolemia— statin
- Age 20-39 y: Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Age 40-75 y and LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus 10-year ASCVD risk percent begins risk discussion
- Age >75 y: Clinical assessment, Risk discussion

ASCVD Risk Enhancers:
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:
- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/l
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

Risk discussion: Emphasize lifestyle to reduce risk factors (Class I)
Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)
Risk discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)
Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy
### CAC IN 2018 GUIDELINES

<table>
<thead>
<tr>
<th>IIa</th>
<th>B-NR</th>
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<tbody>
<tr>
<td><strong>6.</strong> 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><strong>7.</strong> 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>
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<tr>
<td>• If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ( \geq 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>
<td></td>
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</tbody>
</table>
Coronary calcium test could help clarify heart disease risk – and control cholesterol

By American Heart Association News
Total Coronary Artery Plaque and Coronary Calcium

- Calcified: 20%
- Fibrotic: 80%
- Lipid Rich: 80%
Net Reclassification Improvement (NRI)

MESA: Intermediate Risk (n=1,330)  
NRI: Improved Detection of Low & High Risk Individuals

<table>
<thead>
<tr>
<th></th>
<th>NRI</th>
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<tbody>
<tr>
<td>FRS + Brachial FMD</td>
<td>0.024</td>
</tr>
<tr>
<td>FRS + ABI</td>
<td>0.036</td>
</tr>
<tr>
<td>FRS + Hs-CRP</td>
<td>0.079</td>
</tr>
<tr>
<td>FRS + Family History</td>
<td>0.160</td>
</tr>
<tr>
<td>FRS + C-IMT</td>
<td>0.102</td>
</tr>
<tr>
<td><strong>FRS + CAC</strong></td>
<td><strong>0.659</strong></td>
</tr>
</tbody>
</table>

FRS: Framingham Risk Score

NRI: FRS Model vs. FRS + Screening Test

Models estimating 7-y MI, CHD death, resuscitated cardiac arrest, or angina followed by PCI/CABS

Quantification of CAC score improves stratification between subjects at high versus low risk for coronary events, indicating that CAC scoring helps match intensified risk factor modification to atherosclerotic plaque burden as well as actual risk while avoiding therapy in subjects with low coronary atherosclerosis that have low 10-year event rate.
Reclassification of ATP III Risk Categories Using CAC

CAC Score
- high
- Intermediate
- Zero

ATP III Score Risk Assessment

Scheme according to Wilson PWF et al
JACC 41:1889 – 1906, 2003 with HNR data
MESA Study – 6,814 Patients: 3.5 year follow-up

Nonfatal MI & CHD Death

Hazard Ratio

- None
- 1-100
- 100-300
- >300

Ref

4.47 (2.45, 8.13)

10.26 (5.62, 18.71)

14.13 (7.91, 25.22)

Fully adjusted – Detrano et al – NEJM - 2008
MESA STUDY 10 year outcomes Budoff EHJ 2018
NNT for CAC >100 12

Kaplan-Meier survival estimates

- 6,944 (42%) CAC=0
- 48 deaths
- 99.3%
- 99.6%

Followup (years)

FH CHD (-)  FH CHD (+)

Ketlogetswe AHA 2010
CAC & Risk Factor Burden

FIGURE 1 Mortality Rate Per 1,000 Person-Years for CVD, CHD, Cancer, and All-Cause Mortality by CAC Score Group

Incidence rates increased for all-cause and cause-specific mortality with increasing CAC scores. Particularly those with CAC score $\geq 1,000$ had
CAC Zero as Negative Risk Marker

CENTRAL ILLUSTRATION: Shift in Pre- to Post-Test Risk for Coronary Heart Disease and Cardiovascular Disease in the Presence of Each Negative Risk Marker

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
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
Does CAC scanning improve outcomes?

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No SCAN</th>
<th>CACS</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>
</tbody>
</table>

EISNER Study – Costs Compared to No Scan Group

P<0.005 for both measures

Rozanski JACC 2011
CAC scoring and Heart Failure (1)

- “... recent data suggest CAC scoring may be useful for identifying congestive heart failure in early stages, especially in asymptomatic populations”
- “Given the high sensitivity of coronary artery calcium (97–99%), this may prove to be an effective screen prior to angiography in patients with congestive heart failure of unclear etiology”
- “the presence of CAC is superior to that of segmental wall motion abnormalities by echocardiography to distinguish ischemic from nonischemic CM”

Muhammad A Latif1 & Matthew J Budoff*1
1Los Angeles Biomedical Research Institute, UCLA Harbor Medical Center, 1124 W Carson Street, Torrance, CA 90502, USA
CAC and CHF – Rotterdam JACC 2012

- 1897 Patients
- 6.8 year follow up
- CAC scores were associated with heart failure (p 0.001), with a hazard ratio of 4.1
- Net reclassification index 34.0%.
ST FRANCIS RANDOMIZED TRIAL
Randomized Double Blind Placebo Controlled Trial of Atorvastatin in the Prevention of Cardiovascular Events Among Individuals With Elevated CAC Score

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

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.
Very High NNT in Almost 50% of Individuals Meeting JUPITER Criteria in MESA

<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>
</thead>
<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>
</tbody>
</table>
MESA – Aspirin Use
Miedema Circ CQO 2014
CAC IMPROVES STATIN DELIVERY

- Better Risk Stratification
  - matching risk with intensity of therapy
- 50% (or MORE) will have zero scores
  - Statins in this population will cause more rhabdomyolysis than prevent events

- IMPROVE COMPLIANCE
  - We all recognize the new guidelines (treat most) will lead to low compliance in asymptomatics
Top 7 Indications for CAC Testing (primary prevention)

1. “Intermediate” Risk Patient
   - ASCVD 5-20%, Risk Uncertain
   - Family History, lower risk diabetes
2. Statin Reluctant
3. Statin Intolerant
4. Decisions for Non-Statin Rx
5. Decisions For Aspirin Rx
6. Low Risk Chest Pain Syndrome
7. MOTIVATION!
CAC CAUTIONS

- Younger Age
  - Generally < 40 years old
  - Exceptions: ESRD, Early onset Diabetes, Familial hyperlipidemia, Extreme Fam Hx

- DO NOT DO INVASIVE ANGIOGRAMS after CAC in Asymptomatics – yield is very low and intervention may not improve outcomes

- Do NOT Fear prior use of Statins – statins cause mild calcification only, doesn’t change risk stratification
Coronary Calcium

Superior doctors prevent the disease. Mediocre doctors treat the disease before evident. Inferior doctors treat the full-blown disease.

--Huang Dee: Nai-Ching (2600 BC First Chinese Medical Text)
The Widowmaker - watch the trailer

Widowmakerthemovie.com

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Questions?

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