Asymptomatic 55 Year Old White Male

- CC: Should I be on a statin?
- Cardiac Risk Factors
  - Smoking
  + Lipids: TC 222; TG 122; HDL 42; LDL 156
  - HTN
  - DM
  + FHx: Father is alive at 78; had MI at 50 and 55; had CABG; athletic, butcher
What would you recommend?

A. Prescribe a statin and aspirin.
B. Do not prescribe a statin or aspirin.
C. Intensify lifestyle management.
D. Calculate ASCVD risk.
What is the ASCVD 10-Year Risk?

A. 3.3%
B. 6.6%
C. 9.9%
D. 13.2%
10-year ASCVD risk is 6.6%

A. What would you do now?
B. Prescribe a statin and aspirin.
C. Do not prescribe a statin or aspirin.
D. Intensify lifestyle management.
E. Order a coronary calcium scan.
Coronary Artery Scanning

- SEVERE CALCIFICATION

CALCIUM SCORE 1153
What would you do next?

A. Prescribe a statin and aspirin.
B. Would not prescribe a statin or aspirin.
C. Order a stress test.
D. Refer for cardiac catheterization.
HEART ATTACKS: THE FACTS

https://vimeo.com/123658890
Coronary Artery Calcium

Matthew Budoff, MD, FACC
Endowed Chair of Preventive Medicine
Professor of Medicine, UCLA Medical Center
Harbor-UCLA Medical Center
Torrance, CA
Coronary Heart Disease (CHD): Diagnosis Often Comes Too Late

Myocardial infarction (MI) or death as initial presentation of CHD

Men: 62%
Women: 46%

Patients diagnosed with CHD (%)

Cardiovascular Disease Deaths: United States 1979–1999

Leading Causes of Death for All Males and Females in US (2011)

A Total CVD  C Accidents  E Diabetes
B Cancer  D COPD  F Alzheimer’s disease

AHA Heart Disease and Stroke Statistics—2015 Update
CHD - Breast Mortality

<table>
<thead>
<tr>
<th>Age, Years</th>
<th>30-34</th>
<th>40-44</th>
<th>50-54</th>
<th>60-64</th>
<th>70-74</th>
<th>80-84</th>
<th>90-94</th>
<th>100+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of Deaths</td>
<td>0%</td>
<td>5%</td>
<td>10%</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
<td>30%</td>
<td>35%</td>
</tr>
</tbody>
</table>

- **CAD Mortality**
- **Breast Cancer Mortality**
CONVENTIONAL (Population based) RISK FACTORS

- Family History
- Diabetes Mellitus
- Elevated LDL Cholesterol
- Low HDL Cholesterol
- Tobacco Use
- Hypertension
- Obesity/Physical Inactivity
CT Coronary Artery Calcium (CAC)

- CAC: a marker of CAD in an individual patient
  - Burden of coronary atherosclerosis
- Integrated lifetime effect of all risk factors
  - Overcomes the limitations of population-based risk assessment
  - Consistent evidence: incremental prognostic value

<1 mSv
(~ mammogram)
Single breath
No contrast
Coronary Artery Scanning

- NORMAL CONDITION
Coronary Artery Scanning

- SEVERE CALCIFICATION
**DIAGNOSTIC SENSITIVITY**

**NON-INVASIVE MODALITIES**
- Stress ECG: $300
- Stress Echo: $900
- Stress Thallium: $1600
- PET Scanning: $2200
- Coronary Calcium with CT: $150

**INVASIVE MODALITIES**
- Intravascular Ultrasound: $3,000
- Coronary Angiography: $5,000

DATA TAKEN FROM “THE DAWN OF A NEW ERA - NON-INVASIVE CORONARY IMAGING” R. ERBEL HERZ 1996; 21, 75-77
The challenge in diagnosis of coronary heart disease

“The majority of people destined to die suddenly will not have a positive exercise test. The likely reason that they will die suddenly is that only a mild, non-flow-limiting coronary plaque will have been present before the sudden development of an occlusive thrombus.”

- Stephen Epstein
New England Medical Journal 1989
All Cause Mortality and CAC Scores:

Long Term Prognosis in 25,253 patients

$\chi^2=1363, p<0.0001$ for variable overall and for each category subset.

Budoff, et al. JACC 2007; 49: 1860-70
MESA Study – 6,814 Patients: 3.5 year follow-up

Nonfatal MI & CHD Death

Hazard Ratio

Ref
None 1-100 100-300 >300

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
“measurement of coronary calcium is an option for advanced risk assessment. High coronary calcium scores (e.g., >75th percentile for age and sex) denotes advanced atherosclerosis and provides rationale for intensified LDL-lowering therapy.”
This recommendation - to measure atherosclerosis burden, in clinically selected intermediate CAD risk patients (eg, those with a 10% to 20% Framingham 10-year risk estimate) to refine clinical risk prediction and to select patients for altered targets for lipid-lowering therapies.
11. Quantitative evaluation of coronary calcium to be used as a triage tool for lipid-lowering therapy in patients with an intermediate to high Framingham risk score.

12. Quantitative evaluation of coronary calcium in patients with an equivocal stress imaging test or in cases in which discordance exists between stress imaging testing and clinical findings.
UTILITY OF CORONARY ARTERY CALCIUM MEASUREMENT IN CARDIOVASCULAR DISEASE

INTRODUCTION

The California Technology Assessment Forum is requested to review the scientific evidence for the use of coronary
That the use of EBCT to measure Coronary Artery Calcium:

(1) As a screening test for asymptomatic patients who are at intermediate risk for coronary heart disease, EBCT calcium scoring meets CTAF Technology Assessment Criteria 1 through 5.

(2) As a diagnostic test in patients with symptoms suggestive of CAD (patients with chest pain), EBCT calcium scoring is a useful technology to predict those patients who will have underlying coronary heart disease, and meets CTAF Technology Assessment Criteria 1 through 5.

(3) To assess response to therapy for coronary heart disease does not meet CTAF Technology Assessment Criteria.
• After quantitative risk assessment: assessment of 1 or more of the following—family history, hs-CRP, CAC score, or ABI—may be considered to inform treatment decision making.
“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.”

2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk
FIGURE 1  Statin Eligibility Among the Baseline Study Population

Overall, 50% of the study population was recommended for moderate- to high-intensity statin, 12% was considered for statin, and 38% was not eligible for statin therapy. ASCVD = atherosclerotic cardiovascular disease; LDL = low-density lipoprotein.
MESA - CAC Distribution Across Statin Eligibility Groups*

*According to 2013 ACC/AHA Cholesterol Management Guidelines

10 year event rates in CAC 0:

- 0.5%/year in recommend statins (high intensity)
- 0.1%/year in consider statins (moderate intensity)

Nasir et al JACC 2015
CAC Distribution Across Statin Eligibility Groups*

*According to 2013 ACC/AHA Cholesterol Management Guidelines

10 year event rates in CAC 0:
- 0.5%/year in recommend statins (high intensity)
- 0.1%/year in consider statins (moderate intensity)

Nasir et al JACC 2015
CAC Distribution Across Statin Eligibility Groups*

*According to 2013 ACC/AHA Cholesterol and Management Guidelines

CAC 0 reclassifies ~ 1/2 of candidates as not eligible for statins
10 year event rates in CAC 0:

- 0.5%/year in recommend statins (high intensity)
- 0.1%/year in consider statins (moderate intensity)

Nasir et al JACC 2015
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

### 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>

Rozinski, Berman, EISNER. JACC 2011;57:1622. CACS 0 = 631. CACS>400 = 109.
EISNER Study – Costs Compared to No Scan Group

-37%  -26%

Procedure Costs  Medication Costs

P<0.005 for both measures

Rozanski JACC 2011
What do Others Think?

Coronary Artery Calcium Scoring
Are We There Yet?*

Donald M. Lloyd-Jones, MD, ScM

• In the broad middle, perhaps from 5% to 20% 10-year ASCVD risk, there is room for the patient-clinician discussion espoused by recent guidelines which could well be informed by judicious use of CAC screening.

• Starting with a quantitative risk-based assessment, the patient and clinician first calculate the 10-year risk. If, after discussion, they are uncertain whether the individual patient is likely to benefit from initiating a statin, obtaining CAC score would be reasonable.

• Finding a CAC score of 0 in someone otherwise thought to be in a net benefit group is a powerful reason to consider withholding statin therapy.

• Likewise, the presence of a high CAC score in an individual at only moderate predicted risk should be a powerful motivator to initiate and adhere to statin therapy.
Figure. Multivariable-adjusted HR for incident coronary heart disease.

Marker | HR (95% CI)
---|---
NT-proBNP | 2.5 (1.7–3.6)
vWF antigen | 1.2 (0.9–1.6)
Fibrinogen | 1.4 (1.1–2.0)
CKD | 1.4 (1.1–1.8)
Leukocyte count | 1.8 (1.3–2.5)
CRP | 1.6 (1.0–2.5)
Homocysteine | 1.4 (1.0–2.0)
Uric acid | 0.9 (0.7–1.3)
CAC score | 6.2 (3.4–11.5)
cIMT | 1.6 (1.1–2.3)
PAD | 1.3 (1.0–1.7)
PWV | 1.2 (0.8–1.8)

CAC = coronary artery calcium; cIMT = carotid intima–media thickness; CKD = chronic kidney disease; CRP = C-reactive protein; HR = hazard ratio; NT-proBNP = N-terminal fragment of prohormone B-type natriuretic peptide; PAD = peripheral arterial disease; PWV = pulse wave velocity; vWF = von Willebrand factor.
WHAT CORONARY ARTERY CALCIFICATION MEANS

- Atherosclerosis present in this vessel
- Higher levels of coronary calcium correlate with higher risks
- Zero calcification (none seen) suggests a very low probability of obstructive disease and less than 1% chance of heart attack and stroke over the next 5 years
ST FRANCIS RANDOMIZED TRIAL

*Randomized Double Blind Placebo Controlled Trial of Atorvastatin in the Prevention of Cardiovascular Events Among Individuals With Elevated CAC Score*

- **No Prior CVD**
  - Men, Women 50-70 years
  - CAC >80% of age-gender

- **Atorvastatin 20 mg (N=490)**
  - MI
  - Stroke
  - CVD Death
  - CABG/PTCA

- **Placebo (N=515)**

- 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)

Measurement of CAC is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (10% to 20% 10-year risk).

Measurement of CAC may be reasonable for cardiovascular risk assessment persons at low to intermediate risk (6% to 10% 10-year risk).

In asymptomatic adults with diabetes, 40 years of age and older, measurement of CAC is reasonable for cardiovascular risk assessment.
IMPROVED ADHERENCE

- SEVERE CALCIFICATION
The best predictor of a life threatening illness is the early manifestation of a life threatening illness

Sir Geoffrey Rose
Cardiac Epidemiologist
Known for “The Rose Principle”
Contact Us

- Phone: (310) 222-4107
- Email: Budoff@ucla.edu
CAC Expert Panel Algorithm

For Individuals Age 40-75, LDL 70-189, and Without Clinical ASCVD

Step 1
Calculate 10 yr Risk Using ACC/AHA ASCVD Risk Calculator

- 10 yr Risk <5%
- 10 yr Risk 5% to <7.5%
- 10 yr Risk ≥7.5%

Step 2
Family history of ASCVD

Coronary Artery Calcium (CAC) Score

- CAC = 0
- CAC = 1-299 & <75th %
- CAC ≥300 or ≥75th %

Step 3
Updated Risk Classification

- Lifestyle Management
  - Reassess risk at 4-6 years
  - Consider pharmacologic lipid Rx
  - Add pharmacologic lipid Rx

Lifestyle Management

1 ASCVD = atherosclerotic cardiovascular disease
2 http://tools.cardiosource.org/ASCVD-Risk-Estimator/
3 ACC/AHA 2013 Cholesterol Guidelines state "for those with a 5% to <7.5% estimated 10-year ASCVD risk, the potential for adverse effects may outweigh the potential for ASCVD risk reduction benefit when high-intensity statin therapy is used in this risk group. However, for moderate-intensity statin therapy the ASCVD risk reduction clearly exceeds the potential for adverse effects."
4 ACC/AHA 2013 Cholesterol Guidelines state "Before initiating statin therapy, the clinician and patient discussion should include consideration of the potential for ASCVD risk reduction benefits, adverse effects, and drug-drug interactions. Additional factors may also be considered to inform treatment decision making in selected individuals. Factors that may contribute to assessment of ASCVD risk include...coronary artery calcium score ≥300 Agatston units or ≥75 percentile for age, sex, and ethnicity." For additional information, see http://www.mesa-nhlbi.org/CACReference.aspx.
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults
Advise adults who would benefit from LDL-C or BP lowering* to:

1. Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages, and red meats.

   - Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes).

   - Achieve this pattern by following plans such as the DASH dietary pattern, the U.S. Department of Agriculture (USDA) Food Pattern, or the AHA Diet.

*Refer to 2013 Blood Cholesterol Guideline for guidance on who would benefit from LDL-C lowering.
Lipids:
In general, advise adults to engage in aerobic physical activity to reduce LDL-C and non–HDL-C: 3 to 4 sessions a week, lasting on average 40 minutes per session, and involving moderate- to vigorous-intensity physical activity.

BP:
In general, advise adults to engage in aerobic physical activity to lower BP: 3 to 4 sessions a week, lasting on average 40 minutes per session, and involving moderate- to vigorous-intensity physical activity.
4 Statin Benefit Groups

- Clinical ASCVD*
  - LDL–C ≥190 mg/dL, Age ≥21 years
- Primary prevention – Diabetes: Age 40-75 years, LDL–C 70-189 mg/dL
- Primary prevention - No Diabetes†: ≥7.5%‡ 10-year ASCVD risk, Age 40-75 years, LDL–C 70-189 mg/dL

*Atherosclerotic cardiovascular disease
†Requires risk discussion between clinician and patient before statin initiation.
‡Statin therapy may be considered if risk decision is uncertain after use of ASCVD risk calculator.
Intensity of Statin Therapy

High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL-C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL-C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL-C on average, by &lt;30%</td>
</tr>
<tr>
<td><strong>Atorvastatin (40†)-80 mg Rosuvastatin 20 (40) mg</strong></td>
<td><strong>Atorvastatin 10 (20) mg Rosuvastatin (5) 10 mg Simvastatin 20-40 mg‡ Pravastatin 40 (80) mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg</strong></td>
<td><strong>Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg</strong></td>
</tr>
</tbody>
</table>

*Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response.

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (Pedersen et al).

‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

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

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women with Heart Disease

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