CT angiography of plaque and plaque progression

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Global causes of disability and death: 2010

Ischemic heart disease #1, 29% increase since 1990
18% reduction in cardiac death rate
24% reduction in cardiovascular events compared to placebo.

Conversely, ~70-80% of CV events occur despite statin therapy.
Despite statin therapy, ASCVD risk remains high, as evidenced from the large Cholesterol Treatment Trialists Collaboration, where among 90,056 patients, one in five (21.7%) of those with prior cardiovascular disease and one in ten (9.5%) of those without prior cardiovascular disease developed a future major cardiovascular event within 5 years*


- Primary prevention trial, 45-64 yrs old, men
- Pravastatin 40 mg qd vs. placebo, 5 yrs monitoring
- 20 year follow up
- 18% reduction in cardiovascular disease in treated group; 24% lower MI rate. No decrease in stroke rate.
Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials


Lancet 2010; 375: 735–42

• 91149 participants in 13 statin trials
• 9% increased risk for developing incident diabetes
• Risk increased with older age.
Statin therapy for primary prevention

• Assuming attainment of 40 years of age, symptomatic coronary heart disease occurs in 49% of men and 32% of women over their lifetime (Stone, Robinson et al. 2014).

• New guidelines for statin therapy indicate nearly 50% of adults age 40-75 years may be eligible for lifelong statin therapy

• Can expect that 20% of patients will be ‘winners’ during lifelong therapy, with no CV event

• But 80% are “losers”, despite statin therapy.
Coronary atherosclerosis is a necessary “prerequisite” for CV events:

• Pooled analysis, six studies of 27,622 asymptomatic patients:

  ~43% of subjects had CAC Score of 0, have a low 3–5 year event rate of only 0.4%*

* J Am Coll Cardiol. 2007 Jan 23;49(3):378-402
Plaque reduction in high risk patients who had multiple IVUS studies (6 IVUS trials*):

- Median regression of total atheroma volume: -2.4 mm$^3$
- (Interquartile range of -12.7 to +7.9 mm$^3$)

→ ~40% of high risk patients have plaque progression despite statin treatment.

Intravascular ultrasound to track plaque regression. Requires repeat cardiac cath.

Nissen, AJC 2001
Symptomatic patients: optical coherence tomography

CT calcium score

• Improves risk stratification
• CAC score = 0 → high correlation with no CV events
• MESA: age 45-84, 50% of patients with zero CAC
• Low radiation dose (~1 mSv)
<table>
<thead>
<tr>
<th>Agatston score</th>
<th>Probability of significant CAD</th>
<th>CV risk</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very unlikely (&lt;5 %)</td>
<td>Very low</td>
<td>Primary prevention</td>
</tr>
<tr>
<td>1–10</td>
<td>Very unlikely (&lt;10 %)</td>
<td>Low</td>
<td>Primary prevention</td>
</tr>
<tr>
<td>11–100</td>
<td>Mild or minimal coronary stenosis likely</td>
<td>Moderate</td>
<td>strict adherence with primary prevention goals. Daily ASA</td>
</tr>
<tr>
<td>101–400</td>
<td>Non obstructive CAD, highly likely, obstructive CAD possible</td>
<td>Moderately high</td>
<td>risk factor modification. Consider exercise testing</td>
</tr>
<tr>
<td>&gt;400</td>
<td>High likelihood of significant coronary stenosis (&gt;90 %)</td>
<td>High</td>
<td>Very aggressive risk factor modification. Consider exercise or pharmacological nuclear stress testing</td>
</tr>
</tbody>
</table>

(Adapted from: Cademartiri F, Casolo G, Midiri M, eds: Calcium score and coronary plaque, In Clinical Applications of Cardiac CT. New York: Springer; 2012:121) [41]
Coronary Artery Calcium Score Combined With Framingham Score for Risk Prediction in Asymptomatic Individuals

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The Framingham Risk Score (FRS) is a multivariable statistical model that uses age, sex, smoking history, blood pressure, cholesterol, high-density lipoprotein cholesterol (HDL-C), and blood glucose levels or history of diabetes to estimate coronary event risk among individuals without previously diagnosed coronary heart disease (CHD).1

Context Guidelines advise that all adults undergo coronary heart disease (CHD) risk assessment to guide preventive treatment intensity. Although the Framingham Risk Score (FRS) is often recommended for this, it has been suggested that risk assessment may be improved by additional tests such as coronary artery calcium scoring (CACS).

Objectives To determine whether CACS assessment combined with FRS in asymptomatic adults provides prognostic information superior to either method alone and whether the combined approach can more accurately guide primary preventive strategies in patients with CHD risk factors.

Design, Setting, and Participants Prospective observational population-based study, of 1461 asymptomatic adults with coronary risk factors. Participants with at least 1 coronary risk factor (>45 years) underwent computed tomography (CT) examination, were screened between 1990–1992, were contacted yearly for up to 8.5 years after CT scan, and were assessed for CHD. This analysis included 1312 participants with CACS results; excluded were 269 participants with diabetes and 14 participants with either missing data or had a coronary event before CACS was performed.

Main Outcome Measure Nonfatal myocardial infarction (MI) or CHD death.
Areas under the curves are 0.63 for FRS alone, 0.68 for FRS plus CAC. (P < 0.001)
Reclassification of risk using CAC

Caveat: 60% of events occurred in participants *not* classified as high risk with or without CAC
What is the annual rate of increase of CAC score?

• In subjects at an average Framingham Risk Score, the annual CAC progression typically ranges from 20–25%*

• MESA: annual increase was 25 Agatston units**

• Repeat testing not recommended due to high correlation with age


Can CAC score be used to monitor statin therapy?

- **St Francis heart study:** change of CAC after 2 and 4 yrs was not affected by treatment with atorvastatin

- **BELLES study:** atorvastatin 80 vs. pravastatin 40 mg: no difference in CAC volume after 1 year (15% and 14% increase, respectively)

- **Arad et al:** 1005 asymptomatic adults with CAC scores above the 80th percentile for age and sex were randomized to 20 mg atorvastatin versus placebo.

  After 4 years, there was no difference in CAC scores between the two arms, despite a 43% reduction in LDL among those taking atorvastatin*

*J Am Coll Cardiol. 2005 Jul 5; 46(1):166-72*
Is your statin working?

- CAC cannot track successful statin therapy
- 70-80% of patients taking statins are ‘losers’ and do not have CV event reduction
- IVUS is not an alternative for primary prevention to track statin success or failure
- Other noninvasive imaging methods?
  - MRI of the coronary arteries
  - MRI of the carotid arteries
  - Coronary CT angiography
Limitations of 1.5 T coronary MRA

- Study success rate is low (80-95%)
  - Coronary MRA fails in patients with irregular breathing pattern or drift of diaphragm position.
- Accuracy only 80-90%; many coronary segments are not visualized
- Prolonged scan time; 10-15 minutes with failure due to irregular breathing patterns
- Large body habitus results in low image quality
Direct assessment of wall by MRI

Stuber, Hazirolan, Bluemke et al, JCMR 2005
Normal lumen, but coronary plaque was associated with CVD risk factors

Miao, Bluemke et al.
Carotid MR Angiography

X-ray angiogram

3d Gad MRA
Carotid MRI defines extent of plaque

Carotid Artery Plaque Morphology and Composition in Relationship to Incident Cardiovascular Events: The MESA study

- FRS
- FRS + Carotid US, IMT: 0.15 \( (p = 0.16) \)
- FRS + MRI area + lipid core: 0.28 \( (p = 0.02) \)
Assessment of plaque in the carotid artery by MRI

- Corti et al: 18% wall volume regression during statin therapy  *JACC 2005;46:106-112*
- Sibley et al: 10% wall volume regression during statin therapy  *Heart 2013;99:1675-1680*
Coronary CT Angiography (CTA)

Allows measurement of **all** subclinical coronary plaque (not just *stenotic plaque*)
Coronary CTA
Coronary plaque quantification ≤1 mSv
## Coronary CT Angiography: change in plaque, 12-18 mths

<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Main imaging finding</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffman et al.</td>
<td>Retrospective observational</td>
<td>Noncalcified plaque increased by 38%</td>
<td>63</td>
</tr>
<tr>
<td>Tardif et al.</td>
<td>Prospective, randomized</td>
<td>Volume of noncalcified plaque Placebo: 6% increase</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VIA-2291: -4.9% decrease</td>
<td></td>
</tr>
<tr>
<td>Burgstahler et al.</td>
<td>Prospective, Atorvastatin</td>
<td>Noncalcified plaque decreased by 24%</td>
<td>20</td>
</tr>
<tr>
<td>Zeb et al.</td>
<td>Retrospective</td>
<td>28% decrease in noncalcified plaque volume</td>
<td>60</td>
</tr>
<tr>
<td>Lo et al.</td>
<td>Prospective, randomized, Atorvastatin</td>
<td>Plaque volume Placebo: +18.2%, Atorvastatin: -4.7%</td>
<td>37</td>
</tr>
</tbody>
</table>
Coronary CT Angiography:
Variability of CT Scanners and Readers in Measurement of Plaque Volume

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Purpose:
To determine reader and computed tomography (CT) scan variability for measurement of coronary plaque volume.

Materials and Methods:
This HIPAA-compliant study followed Standards for Reporting of Diagnostic Accuracy guidelines. Baseline coronary CT angiography was performed in 40 prospectively enrolled subjects (mean age, 67 years ± 6 [standard deviation]) with asymptomatic hyperlipidemia by using a 320-detector row scanner (Aquilion One Vision; Toshiba, Otawara, Japan). Twenty of these subjects underwent coronary CT angiography repeated on a separate day with

Radiology. 2016 Sep 16:161670.
Figure 6

Table 6

Estimated Sample Sizes Required in Each Group to Detect a Change in Noncalcified Plaque with Coronary CT Angiography Follow-up in a Clinical Trial and an \( \alpha \) Error of .05

<table>
<thead>
<tr>
<th>Power (%)</th>
<th>Same Vendor</th>
<th>Different Vendor</th>
<th>Same Vendor</th>
<th>Different Vendor</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>162</td>
<td>439</td>
<td>214</td>
<td>563</td>
</tr>
<tr>
<td>85</td>
<td>185</td>
<td>502</td>
<td>245</td>
<td>644</td>
</tr>
<tr>
<td>90</td>
<td>217</td>
<td>587</td>
<td>286</td>
<td>753</td>
</tr>
</tbody>
</table>

Note.—Sample size is derived from the interstudy standard deviation of noncalcified plaque volume, as described by Machin et al (17) and Altman (18).

Radiology. 2016 Sep 16:161670.
Summary: assessment of plaque change

1. 50% of U.S. population is eligible for statin therapy, that may be lifelong

2. Most people treated with statins will not have successful treatment, as measured by CV event reduction.

3. By IVUS: reduction in plaque can be detected and is associated with lower CV events in high risk patients.
Summary: assessment of plaque change

4. **CAC score** assesses risk, but cannot be used to assess successful statin treatment

5. **Carotid MRI** can show change in plaque during treatment, but is awkward, expensive and not widely available

6. **Coronary CT angiography** shows:
   - detection of plaque components
   - noncalcified plaque
   - new methods can be used to detect both progression and regression of plaque over time
Acknowledgements

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