CORONARY ARTERY CALCIFICATION

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Coronary Heart Disease in the U.S.

- 1 out of 6 deaths in 2006
- 2006 mortality: 425,425
- 2010 estimates: 785,000 new coronary attacks and 470,000 recurrent coronary attacks
- New coronary event: every 25 sec
- Someone dies from a coronary event: every minute
- 138,000 coronary deaths within 1 hr of symptom onset
- Estimated 195,000 silent first MI/year


Coronary Heart Disease

Percentage breakdown of deaths due to CVD (United States: 2006).

- Between 1996-2006, 35.9% decrease in coronary heart disease mortality
- Based on 1980-2000 data, decrease attributable to:
  - evidence based medical therapies: 47%
  - modification of risk factors (lifestyle and environmental): 44%


Significance of CAC: 1994

- The fact that a direct relationship exists between presence and extent of coronary arterial mural calcification and severity of coronary atherosclerosis has been repeatedly confirmed in autopsy studies, but not previously exploited for patient evaluation for potential coronary artery disease.
- As early as 1980, JR Margolis and colleagues described 5-year survival rate for patients with fluoroscopically detected coronary calcification, independent of other risk factors. But... the ability to demonstrate small calcified plaques was poor; highly operator-dependent; limited by body habitus; overlap with other structures, e.g. vertebrae, and other calcifications, e.g. valve annuli.
- CT is being increasingly used to evaluate coronary artery disease in the hope of detecting early atherosclerotic disease before cardiac events occur.
- Consequently, it is imperative for physicians involved in imaging coronary arteries to understand the importance of coronary calcification as a marker of atherosclerosis.

Earlier CAC studies

- NPV value of CAC = 0: 98% for obstructive coronary artery disease.1
- Absence of calcific deposits negates the presence of significant (>50%) luminal stenosis.2
- CAC scores do not predict site-specific significant stenosis.3
- "Cut points" in CAC scores to provide 90-95% sensitivity and specificity for predicting angiographically-significant stenosis.4
- Prevalence of coronary calcification in women is half that of men until age 60 years, then the difference diminishes.5
- CAC score ≥100 is highly predictive in separating patients with cardiac events (during 31 month follow-up) from those without events.6


1994 CT is being increasingly used to evaluate coronary artery disease in the hope of detecting early atherosclerotic disease before cardiac events occur.

- Risk factors for coronary disease cannot be equated with actual disease, whereas coronary calcification is a marker of coronary atherosclerosis, regardless of the number of risk factors

Guerci et al. JACC 1998
Focus of More Recent CAC Research

1. Risk assessment for coronary heart disease in asymptomatic populations
2. Role of CAC scoring in assessment of symptomatic patients
3. Use of Coronary CT for assessment of progression or regression of coronary atherosclerosis
4. Cost-effectiveness of coronary calcium scoring for assessment of cardiac death or MI

Pathophysiology of Coronary Atherosclerosis

• Extracellular fatty deposits, inflammation, lipid-laden smooth muscle cells, scar tissue build up in arterial walls
• Active calcium hydroxyapatite deposition
• Disruption of fibrous cap and exposure of plaque components – thrombus, inflammatory reaction of circulating blood
• Hematoma can organize & calcify
• Repeated episodes can produce fixed stenosis
• Highly variable plaque deposition and progression of occlusive disease.

Total Coronary Artery Burden: “CAC is the tip of the atherosclerotic iceberg”

• Calcified plaque volume is approximately one-fifth that of associated non-calcified plaque.
• CAC versus atherosclerotic burden: a linear, but not 1-to-1 relationship.

Vulnerable plaque versus vulnerable patient

• Vulnerable Plaque = plaques prone to thrombosis or high probability of rapid progression, i.e. becoming culprit plaques (responsible for occlusion and death)
• Vulnerable Blood = prone to thrombosis
• Vulnerable Myocardium = ischemic with chronic damage, or non-ischemic causes; prone to life-threatening arrhythmia

Agatston score

- Pixel attenuation of > 130 HU by coronary arteries = calcium
- 2-4 contiguous pixels
- 3 contiguous pixels: 1.03mm² with 30 cm FOV and 512 x 512 matrix
- Area of calcified plaque x non-linear weighting factor based on peak density of the plaque: Agatston calcium score = Σ (Area · cofactor)

- Limitations:
  - Partial volume effects
  - Limited interscan reproducibility
  - Motion-related artifacts
Interpretation of Agatston CAC Scores:

<table>
<thead>
<tr>
<th>Score</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No identifiable atherosclerotic plaque</td>
</tr>
<tr>
<td>1-10</td>
<td>Minimal atherosclerotic plaque burden</td>
</tr>
<tr>
<td>11-100</td>
<td>Mild atherosclerotic plaque burden</td>
</tr>
<tr>
<td>101-400</td>
<td>Moderate atherosclerotic plaque burden</td>
</tr>
<tr>
<td>&gt;400</td>
<td>Severe atherosclerotic plaque burden</td>
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</table>

Interpretation of Agatston CAC Scores:

Age and Gender Percentiles*

<table>
<thead>
<tr>
<th>PERCENTILE</th>
<th>AGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PERCENTILE</td>
<td>MEN</td>
</tr>
<tr>
<td>19-40</td>
<td>0</td>
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<tr>
<td>41-50</td>
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<td>96-100</td>
<td>0</td>
</tr>
</tbody>
</table>

* Percentile rankings in 19,200 asymptomatic patients from University of Illinois self-referral database.

Volume score

- Improved inter-scan reproducibility
- Compared to Agatston score:
  - Less susceptible to partial volume effects
  - Allows quantification independent from section thickness or image overlap
- Volume = \( \Sigma \) (Area \cdot increment)
- Lack of reference data for large populations

Absolute CAC mass*

- Improved reliability of Ca measurement, regardless of differences in CT systems and scanning protocols if appropriate calibration (external standard or phantom in scan field) is used
- Calcium mass proportional to mean CT number of a calcified plaque multiplied by lesion volume
- Mass = calibration factor \( \times \) CT Ca \( \times \) volume
- Lack of reference data for large populations

* mg of calcium hydroxyapatite

Coronary Calcium Coverage Score (CCCS):

- From MESA


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- From MESA


All Cause Mortality and CAC Scores:

Long Term Prognosis in 25,253 patients

Budoff, et al. JACC 2007;49: 1860-70
Multiethnic Study of Atherosclerosis (MESA)

Prospective randomized cohort; 10-year NHLBI study begun in 2000


10-fold risk for calcium score > 300
Doubling of calcium score: 15 – 40% increase of coronary event risk.

CACS Utility Above & Beyond Various Risk Factor Based Risk Algorithms


Adjusted odds ratios for CHD events

Prognostic Value of CAC in Diabetes

- N = 10,377 (903 diabetic)
- Average follow-up = 5.0 ± 3.5 years
- Statistically significant higher CCS in diabetics
- All-cause mortality increased in asymptomatics with diabetes in proportion to screening CCS
- CCS = 0: Low risk of short-term death even in the presence of diabetes mellitus


Early Identification of Subclinical Atherosclerosis by Non-invasive Imaging Research (EISNER)

- Randomized; 4 year follow-up for CVD death or MI
- Compared downstream cost differential of CAC vs FRS
- CAC scanning is associated with a marked differential in downstream frequency of medical tests and costs, ranging from a very low frequency of testing and invasive procedures among a predominantly large percentage of subjects with low CAC scores, to selectively concentrated testing and procedures among a small number of subjects with CAC scores of more than 400.

The presence of CAC indicates that at least some atherosclerotic plaque is present.

- CAC is defined by an Agatston score >0.
- Clinically significant, often an indication for more aggressive risk factor management, is often defined by a score >= 100 or a score >=75th %ile for one's age and sex/gender.
- A score >=400 can be an indication for further diagnostic evaluation for coronary artery disease (e.g. exercise testing or myocardial perfusion imaging).


CAC for Risk Assessment in General Population (Asymptomatic)

<table>
<thead>
<tr>
<th>Score</th>
<th>CHD risk</th>
<th>Appropriateness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td></td>
<td>inappropriate 1</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>uncertain 6</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>uncertain 5</td>
</tr>
</tbody>
</table>

* by Framingham risk criteria

- Cardiac CT improves risk prediction, especially in individuals determined to be at intermediate risk according to the NCEP ATP III criteria and for whom decisions concerning prevention strategies may be altered based on the test results.

Budoff et al, Circulation 2006;114:1761-1791.

CAC: implications for preventive measures

- Using traditional, non-imaging based risk stratification:
  - less aggressive primary prevention model for asymptomatic patients
  - post-event secondary prevention model, i.e. based on clinical presentation, not plaque burden
- Asymptomatic patient post-CAC screening: preventive treatment depends on score [marker of plaque burden]
  - score = 0: no demonstrable atherosclerosis → follow primary prevention guidelines
  - score > 0: atherosclerosis present → follow secondary prevention standards


Increase utilization of CAC by the general medical community

- Publish practice guidelines in major medical journals, such as JAMA
- Easy access to free on-line evidence-based tools that calculate adjustments to conventional pre-CAC 10-year risk estimates and generate post-test estimate for individual patients

In Search of Vulnerable Patients

1,469,009 Annual Heart Attacks (ACS + SDB)

40,000,000 Americans over the age of 35

MESA public website

http://www.mesa-nhlbi.org

Framingham algorithm for "hard CHD*" events

* Myocardial infarction and cardiac death

from the National Cholesterol Education Program website:

Downloadable spreadsheet

http://www.biomedcentral.com/content/supplementary/1741-7015-2-31-S1.xls

Another example

http://www.biomedcentral.com/content/supplementary/1741-7015-2-31-S1.xls

Patient Motivation: effect of visualization of CAC on lifestyle behavioral changes

Conclusions

- CAC is a marker of subclinical coronary atherosclerotic plaque burden in asymptomatic patients
- CAC is NOT a surrogate for clinical risk stratification schemes
- CAC for incremental risk prediction for intermediate (10-20% 10-year) risk of coronary events
  - Reclassifying to higher risk status: alters therapeutic goal (LDL, BP, etc.)
  - NOT for reclassifying to lower risk status, even with calcium score = 0
  - Score = 0: do not need further evaluation
- Screening for CAC is NOT recommended for lower-risk general population screening or for persons with pre-existing heart disease, diabetes mellitus, or other high-risk conditions

Coding Changes

- Effective January 1, 2010, CMS Category III CPT code 0144T eliminated
- New CMS Category I CPT code 75571: CT heart without contrast material, with quantitative evaluation of coronary calcium
- Physician Payment Rule:
  - Interim payment rate = $94.59
  - TC = $72.72
  - 26 = $21.87
  - Physician work RVU = 0.58
- HOPPS APC 0340: Minor Ancillary Procedure
  - Technical = $45.11