Increased interest in cardiovascular screening

Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging

- Matthias Oudkerk
- Arthur E. Niforou
- Samira S. Saltzburg
- Will A. Kalender
- Stefan Mietzschkap
- Cynthia H. McCollough
- Rosemarie Vriendt
- Leslie J. Show
- William Stanford
- Allen J. Taylor
- Peter M. A. van Ooijen
- Lewis M. Fuster
- Paolo Raggi

This statement reiterates the current call for routine coronary calcium scanning as an effective strategy for the prevention of coronary artery disease (CAD) and its complications. The use of coronary calcium scoring is recommended for all individuals with intermediate or high cardiovascular risk, as defined by international guidelines. The statement also highlights the importance of patient education and counseling regarding the benefits and limitations of coronary calcium scoring.

The recommendations are based on the latest evidence, including the results of the Multi-Ethnic Study of Atherosclerosis (MESA) and the Framingham Heart Study, which have demonstrated the prognostic value of coronary calcium scoring. These findings have led to the development of new clinical guidelines that emphasize the role of coronary calcium scoring in risk assessment and management.

The statement calls for continued research and development in the field of coronary calcium imaging, with a focus on improving the accuracy and feasibility of the technique. It also highlights the need for further education and training for healthcare professionals in the interpretation and clinical application of coronary calcium scores.

The European Society of Cardiac Radiology and the North American Society for Cardiovascular Imaging (NASCI) are committed to promoting the use of coronary calcium scoring as a tool for the prevention and management of CAD. They encourage healthcare providers to consider the use of coronary calcium scoring in their clinical practice, and to collaborate with other stakeholders in the field to advance the science and practice of coronary calcium imaging.
What has motivated the surge in interest in cardiovascular screening?

- The belief that the Framingham Score is inadequate
- The emergence of new screening methods
- The availability of new effective preventive therapies, particularly statins
- The perception that early identification of high risk leads to improved outcome

National Heart Lung and Blood Institute
People Science Health

MESA
Atherosclerosis: A Progressive Process

Normal → Fatty Streak → Fibrous Plaque → Occlusive Atherosclerotic Plaque → Plaque Rupture/Fissure & Thrombosis

Age: 20s → 30s → 50s → 60s

Non-invasive tests abnormal

Effort Angina or Claudication

Unstable Angina
MI
Coronary Death
Stroke
Critical Leg Ischemia

Modified from P Greenland 2004
MESA Objectives (brief, 1999)

- Identify factors related to progression of subclinical CVD
- Determine ethnic, age, and sex differences
- Identify new risk factors
- Compare newer measures to traditional risk factors
MESA Objective Related to Screening (expanded)

- To develop methods, suitable for application in future screening and intervention studies, for characterizing the risk of asymptomatic persons
MESA Centers and PIs

Field Centers
- Wake Forest University – Gregory Burke
- University of Minnesota – Aaron Folsom
- Northwestern University – Kiang Liu
- UCLA – Karol Watson
- Columbia University – Steven Shea
- Johns Hopkins University – Moyses Szklo
MESA Centers and PIs

**Coordinating Center**
- University of Washington – Richard Kronmal

**Central Laboratory**
- University of Vermont – Russell Tracy

**CT Reading Center**
- LA BioMed – Matt Budoff

**Ultrasound Reading Center**
- New England Medical Center – Daniel O’Leary

**MRI Reading Center**
- Johns Hopkins University – David Bluemke
MESA Cohort

- N=6,814 recruited 2000-02
- Exams 2, 3, and 4, ending 2007
- 45-84 years (mean age 62)
- White, Black, Hispanic, and Chinese
- 53% women
- No clinical CVD or atrial fibrillation at baseline
Distribution of participants by MESA Field Centers and Ethnicity

- Winston-Salem
- Baltimore
- Los Angeles
- Chicago
- St. Paul
- New York
Distribution of participants by MESA Field Centers and Ethnicity

Total 6,814

- White 599
- Hispanic 456
- Black 302
- Chinese 301

- White 557
- Black 155
- Hispanic 536
- Chinese 497

- White 223
- Hispanic 494
- Black 562
- Chinese 301

- White 574
- Black 503
Measurements – Exam 1

Demographic characteristics
● Race and ethnicity
● Parents’, grandparents’ immigration
● Education
● Income, occupation, employment
● Insurance status, health care access
● Neighborhood characteristics
Measurements – Exam 1

Basic physical clinical assessments

- Blood pressure
- Anthropometry
- Electrocardiography
Measurements – Exam 1

Clinical questionnaires
- Smoking
- Medical history
- Medications
- Diet history, Physical activity
- Psychosocial data
Measurements – Exam 1

Laboratory measures
- LDL-, HDL-cholesterol, triglycerides
- Inflammation
- Hemostasis and fibrinolysis
- Insulin resistance
- Oxidative damage and stress
- Plaque destabilization
- Endothelial cell function
- Microalbuminuria
Measurements – Exam 1

Genetics
• DNA
• Cell cryopreservation
Measurements

67 ancillary studies

- MESA Family
- MESA Air Pollution
- MESA Lung
- MESA Toe (pending)
- SNPs and Atherosclerosis (SEA)
Measurements – Exam 1

Subclinical CVD measures

- Cardiac computed tomography
- Carotid ultrasound
- Cardiac MRI
- Brachial artery reactivity
- Ankle-brachial blood pressure
- Arterial compliance

PROPOSED SCREENING TOOLS
Cardiac computed tomography
Coronary Calcium Study

No Coronary Artery Calcium

Extensive Coronary Artery Calcium
Carotid ultrasound
Carotid IMT

Intimal-medial thickness of common carotid artery is the distance between the green lines.

Blood Flow
Surveillance (~370 as of 2/09)

- Acute MI
- Angina
- Atrial fibrillation – being added
- Stroke
- Peripheral vascular disease
- Congestive heart failure
- Surgical interventions
- Mortality
Level of Evidence
(Evaluative hierarchy for clinical guidelines)

A: Recommendation based on evidence from multiple randomized trials or meta-analyses

B: Recommendation based on evidence from a single randomized trial or nonrandomized studies

C: Recommendation based on expert opinion, case studies, or standards of care

MESA and CVD Screening

ACC/AHA Expert Consensus Document

American College of Cardiology/American Heart Association
Expert Consensus Document on Electron-Beam Computed Tomography for the Diagnosis and Prognosis of Coronary Artery Disease

MESA and CVD Screening

ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring By Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain


tile ranking. In addition, in our review of the current published evidence, the relative risk ratio for a high risk CAC measurement is higher for clinical registries as compared with population studies (relative risk = 19.3 vs. 5.0); suggesting an overestimation in risk due to selection bias (18–20,22). Data from the ongoing Multi-Ethnic Study of Atherosclerosis (MESA) should allow for more accurate risk estimation of CAC scores as based on a prospectively-derived large population sample (33).

MESA and CVD Screening

The Deadly Double Standard (The Saga of Screening for Subclinical Atherosclerosis)

Harvey S. Hecht, MD*

Subsequently, critically important data have emerged from the National Institutes of Health–sponsored Multi-Ethnic Study of Atherosclerosis (MESA) that have confirmed, in a prospective, population-based study, the remarkable prognostic power of CAC and its superiority to the Framingham risk score.5,6

Coronary calcium predicts CVD

Figure 1. Unadjusted Kaplan-Meier Cumulative-Event Curves for Coronary Events among Participants with Coronary-Artery Calcium Scores of 0, 1 to 100, 101 to 300, and More Than 300.

Panel A shows the rates for major coronary events (myocardial infarction and death from coronary heart disease), and Panel B shows the rates for any coronary event. The differences among all curves are statistically significant (P<0.001).

CAC is a better predictor of CHD than carotid IMT

<table>
<thead>
<tr>
<th>Measure</th>
<th>HR Per 1-SD Increment (95% CI)</th>
<th>z Statistic</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CVD (n = 222)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-, race-, and sex-adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.3 (1.1-1.4)</td>
<td>4.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>2.1 (1.8-2.5)</td>
<td>8.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivariable-adjusted³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.2 (1.0-1.3)</td>
<td>2.7</td>
<td>.007</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>1.9 (1.6-2.2)</td>
<td>7.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>CHD (n = 159)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-, race-, and sex-adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.2 (1.0-1.4)</td>
<td>2.5</td>
<td>.01</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>2.5 (2.1-3.1)</td>
<td>8.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multivariable-adjusted³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.1 (1.0-1.3)</td>
<td>1.5</td>
<td>.12</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>2.3 (1.9-2.8)</td>
<td>7.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Stroke (n = 59)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-, race-, and sex-adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.4 (1.2-1.8)</td>
<td>3.5</td>
<td>.001</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>1.1 (0.8-1.5)</td>
<td>0.8</td>
<td>.41</td>
</tr>
<tr>
<td>Multivariable-adjusted³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>z Score max IMT</td>
<td>1.3 (1.1-1.7)</td>
<td>2.5</td>
<td>.01</td>
</tr>
<tr>
<td>ln(CAC score + 1)</td>
<td>1.1 (0.8-1.4)</td>
<td>0.4</td>
<td>.71</td>
</tr>
</tbody>
</table>

Abbreviations: CAC, coronary artery calcium; CHD, coronary heart disease; CVD, cardiovascular disease; IMT, intima-media thickness; ln, natural logarithm; max, maximum; MESA, Multi-Ethnic Study of Atherosclerosis; SD, standard deviation.

³ Coronary artery calcium and IMT were included as continuous variables in the same model. A 1-SD increment was 1.0 for z score max IMT and 2.5 for ln(CAC score + 1).

⁻ Adjusted as described in the "Methods" section.

Observational studies can inform the development of screening guidelines by providing data on:

- Disease prevalence and natural history
- Test characteristics of screening test
- Relevant information on important subgroups
Coronary calcium prevalence and amount differs by ethnicity

Figure 3. Relative risk for presence of coronary calcification by ethnicity, compared with whites: MESA. 95% CIs shown. Adjusted for age, gender, education, BMI, LDL cholesterol, HDL cholesterol, smoking, hypertension, diabetes, reported treatment for high cholesterol, and center.
Heart failure incidence is highest in African Americans

Figure 1. Nelson-Aalen plots of cumulative hazards for congestive heart failure (CHF) by racial/ethnic group in the Multi-Ethnic Study of Atherosclerosis.

LV mass predicts CHD and heart failure

Bluemke, et al. JACC 2008;52;2148-55.
Biventricular volume by CT correlates with LV mass by MRI

FIGURE 2. Correlation between NCE-CCT biventricular volume (MS2) and LV mass from cardiac MRI. The NCE-CCT and MRI values have been converted to normalized z scores to permit comparison of these measures on the same scale.

Renal dysfunction is associated with small artery stiffness

Relative difference (%) in small artery elasticity compared to 1st quintile of cystatin C

Adjusted for age, gender, race, body mass index, systolic blood pressure, high density lipoprotein cholesterol, interleukin-6, C-reactive protein, diuretics, and angiotensin-converting enzyme I. * p<0.05 compared to quintile 1.

Observational data can only take you so far . . .
Further steps in data analysis

- Determining and refining information on predictive value of screening tests
- Modeling effects of screening or treatment

www.mesa-nhlbi.org

- Paper proposal form
- Directory of investigators
- Working Groups based on scientific interests
Observational studies can provide essential basic information to lay the groundwork to determine the value of CVD screening.

Observational data cannot provide the highest level of evidence for making screening recommendations.
Summary (2)

- MESA includes a multi-ethnic population with a broad age range from six U.S. communities.
- MESA has a rich data set on risk factors, subclinical CVD, and outcomes.
- MESA has investigators who are eager to collaborate!

Further information: www.mesa-nhlbi.org