Combining Coronary Artery Calcium Scanning with SPECT/PET Myocardial Perfusion Imaging

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Cedars-Sinai Heart Institute
Professor of Medicine and Imaging
Cedars-Sinai

Controversies 2018
Beverly Hills
DISCLOSURES

Daniel S. Berman, M.D.
declares the following relationships:

Software royalties from CSMC
• 70 y/o male physician tennis player
• Asymptomatic
• Total cholesterol: 220 mg/dL; LDL 152
• Recent exercise thallium scan was normal
• After normal thallium:
  – No changes
• After normal thallium:
  – No changes
• Offered a coronary calcium scan
<table>
<thead>
<tr>
<th>Location</th>
<th># Calcified Lesions</th>
<th>Calcified Plaque Volume (mm$^3$)</th>
<th>Calcium Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>2</td>
<td>806</td>
<td>1063</td>
</tr>
<tr>
<td>LCX</td>
<td>4</td>
<td>645</td>
<td>782</td>
</tr>
<tr>
<td>RCA</td>
<td>2</td>
<td>830</td>
<td>1101</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>2282</td>
<td>2946*</td>
</tr>
</tbody>
</table>

* 97th percentile
• After CAC scan:
  – Started statin and aspirin
  – Changed eating habits
  – Lost 10-15 lbs within one month
  – Increased exercise
  – Alive and well 17 years later
Value of an Imaging Test

- Does the test result in improved outcomes or reduce costs?
- Does the test PREDICT risk?
Value of an Imaging Test

- Does the test result in improved outcomes or reduce costs?
- Does the test predict risk?
- Must affect patient management

Does the test PREDICT risk?
Coronary Artery Calcium (CAC)

- CAC: a marker of CAD
  - Burden of coronary atherosclerosis
- Integrated lifetime effect of all risk factors
  - Overcomes the limitations of global risk scores
  - Improves risk stratification

<1 mSv
(~ mammogram)
Single breath
No contrast
All Cause Mortality and CAC Scores:
Long Term Prognosis in 25,253 patients

\[ \chi^2 = 1363, \ p < 0.0001 \]

Budoff, et al. JACC 2007; 49: 1860-70
All Cause Mortality and CAC Scores:
Long Term Prognosis in 25,253 patients

Consistent findings in multiple large registries and population-based studies

Budoff, et al. JACC 2007; 49: 1860-70
CAC leads to better treatment / lifestyle

- More targeted preventive treatment
- Upscale or downscale
- Improvement in risk factor profile\(^1\)
- Intensification of Rx\(^2\)
- Better adherence to Rx\(^3,5\)
- Dietary modifications\(^4\)
- Increased exercise\(^4\)

\(^1\) Rozanski et al, JACC 2011 (EISNER Study)
\(^2\) Nasir K et al, Circ Cardiovasc Qual Outcomes 2010 (MESA)
\(^3\) Kalia NK et al, Atherosclerosis. 2006
\(^4\) Orakzai RH et al, Am J Cardiol 2008
\(^5\) Taylor A t al, JACC 2008
CAC in Guiding Treatment in Patients with 5-20% ASCVD Risk

Modified from Hecht, et al JCCT 2017
Primary Prevention:
Emphasize Adherence to Healthy Lifestyle

Age 40-75y and LDL-C ≥70 - <190 mg/dL without diabetes mellitus
10-year ASCVD risk percent begins risk discussion

7.5% - <20%
“Intermediate risk”

Risk discussion:
If risk estimate + risk enhancers favor statin,
initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

If risk decision is uncertain:
Consider measuring CAC in selected adults:

<table>
<thead>
<tr>
<th>CAC</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Consider no statin</td>
</tr>
<tr>
<td>1-99</td>
<td>Favors statin (especially &gt;age 55)</td>
</tr>
<tr>
<td>100+ or ≥75th percentile</td>
<td>Initiate statin therapy</td>
</tr>
</tbody>
</table>

Grundy SM, et al. Circulation 2018
Noninvasive Imaging for CAD

Suspected CAD

Pre-test likelihood of CAD

Intermediate to High (50-100%)

Ischemia Testing
Post-SPECT Cardiac Mortality and Rx Given Early Revascularization vs Medical Therapy

N=10,627
F/U: 1.9 ± 0.6 yrs
Risk adjusted

* \( p < 0.001 \)

Hachamovitch, et al. (Cedars-Sinai) Circulation 2003
Post-SPECT Cardiac Mortality and Rx Given Early Revascularization vs Medical Therapy

N=10,627
F/U: 1.9 ± 0.6 yrs
Risk adjusted

*p<0.001

Fundamental limitation of SPECT/PET MPI
Does not detect subclinical atherosclerosis

Hachamovitch, et al. (Cedars-Sinai) Circulation 2003
Noninvasive Imaging for CAD
Suspected CAD

Pre-test likelihood of CAD

Intermediate to High (50-100%)

Ischemia Testing + CAC
Noninvasive Imaging for CAD
Suspected CAD

Pre-test likelihood of CAD

Intermediate to High (50-100%)

Ischemia Testing + CAC

Potential of SPECT/PET+CAC vs CCTA has not been tested in RCT
Hybrid SPECT/CT and PET/CT

- GE SPECT/CT
  - Attenuation correction
  - Coronary artery calcium scoring

- Siemens PET/CT
Hybrid SPECT/CT and PET/CT

GE SPECT/CT

Siemens PET/CT

CAC: Routine with hybrid or low-cost separate add-on procedure

- Attenuation correction
- Coronary artery calcium scoring
CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
- Improves risk assessment
- Increases diagnostic certainty
- Improves identification of patients at highest risk
- Leads to greater change in patient management
CAC Distribution in Normal SPECT-MPI Patients

Berman et al

- 16% 0
- 3% 1-9
- 17% 10-99
- 26% 100-399
- 37% ≥400

JACC 2004

CAC score

He et al

- 11% 0
- 6% 1-9
- 23% 10-99
- 39% 100-399
- 23% ≥400

Circulation 2000
CAC Distribution in Normal SPECT-MPI Patients

**Berman et al**
- CAC score 0: 16%
- CAC score 1-9: 3%
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- CAC score 0: 11%
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*JACC 2004, Circulation 2000*
CAC in Patients Undergoing SPECT/PET-MPI

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- Leads to greater change in patient management
Added Prognostic Value of CAC in Rb-PET MPI

PET/CT:
N=695
FU 6-28 months
Adjusted:
age, sex, symptoms and RF

Added Prognostic Value of CAC in SPECT MPI
Event Rates by CAC in Normal and Abnormal Scan

- N=4897 symptomatic patients
- F/u: median 940 days
- MACE (278): MI, ACD, late revascularization (>90 days)
- MACE rate: 2.3%/year

### CAC+MPS: Multivariable Predictors of MACE

- **Age +10 y**: 1.40 <0.001
- **Male**: 1.32 0.04
- **CAC score category**
  - 100-399: 3.31 <0.001
  - 400-999: 4.87 <0.001
  - ≥1000: 7.57 <0.001
- **SPECT findings**
  - Small: 1.64 0.001
  - Moderate: 2.21 <0.001
  - Large: 3.74 <0.001

- N=4897 symptomatic patients
- F/u: median 940 days

CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
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CAC: Aid in Pre-test Likelihood of Coronary Stenosis

CONFIRM Patients with no prior CAD
Prevalence of Obstructive CAD with any CP symptom

N=8,660

CONFIRM: Unpublished
### CAC: Aid in Pre-test Likelihood of Coronary Stenosis

**CONFIRM Patients with no prior CAD**

**Prevalence of Obstructive CAD with any CP symptom**

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<thead>
<tr>
<th>CAC Category</th>
<th>0-49%</th>
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<th>≥70%</th>
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</tr>
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<tbody>
<tr>
<td>CAC ≥1000</td>
<td>29</td>
<td>18</td>
<td>36</td>
<td>18</td>
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<tr>
<td>CAC 400-999</td>
<td>44</td>
<td>20</td>
<td>21</td>
<td>14</td>
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<td>63</td>
<td>16</td>
<td>13</td>
<td>8</td>
</tr>
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<td>CAC 1-99</td>
<td>85</td>
<td>9</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>CAC 0</td>
<td>97</td>
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<tr>
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<td>97</td>
<td>21</td>
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N=8,660  CAC ≥400: 35-54% have ≥70% stenosis
WIZMAL (2018) 65 F SOB; Abnl ECG Chol, DM, HTN; Regadenoson
WIZMAL (2018) 65 F SOB; Abnl ECG Chol, DM, HTN; Regadenoson

<table>
<thead>
<tr>
<th></th>
<th>SHORT AXIS</th>
<th></th>
<th>HORIZONTAL LONG AXIS</th>
<th>VERTICAL LONG AXIS</th>
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<tbody>
<tr>
<td></td>
<td>APICAL</td>
<td>MID</td>
<td>BASAL</td>
<td>MID</td>
</tr>
<tr>
<td>STRESS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REST</td>
<td></td>
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</table>

CAC 0

<table>
<thead>
<tr>
<th></th>
<th>Str</th>
<th>Est</th>
<th>Rev</th>
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<tbody>
<tr>
<td>SSS</td>
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<tr>
<td>SS%</td>
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<td>SRS</td>
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<tr>
<td>SR%</td>
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</tr>
<tr>
<td>SDS</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>SD%</td>
<td></td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

Stress Extent (%)
Rest Extent (%)
Reversibility Extent (%)
STARIC (2018) 73 M Chol, HTN, FH
No walk regadenoson
STRESS

REST

STRESS

REST

CAC 3056
STARIC (2018) 73 M Chol, HTN, FH
No walk regadenoson

CAC 3056
Staged PCI of LAD and LCX
PET-MPI + CAC: Improved Prediction of Obstructive CAD*

Per-vessel CAD by Ischemic TPD (ITPD) and CAC category

* ≥70% stenosis

Per-vessel analysis 456 (152 patients)

Brodov….Slomka, JNM, 2015
PET-MPI + CAC: Improved Prediction of Obstructive CAD*

Per-vessel CAD by Ischemic TPD (ITPD) and CAC category

Per-vessel Analysis (n = 456)

Obstructive CAD (%)

* ≥70% stenosis

Per-vessel analysis 456 (152 patients)  
Brodov….Slomka, JNM, 2015
CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
- Improves risk assessment
- Increases diagnostic certainty
- Improves identification of patients at highest risk
- Leads to greater change in patient management
101 consecutive SPECT-MPI pts with LM CAD (≥50% stenosis)
101 consecutive SPECT-MPI pts with LM CAD (≥50% stenosis)

Berman et al, JNC 2007
Underestimation of the Extent of CAD by SPECT MPI

Berman et al, JNC 2007

101 consecutive SPECT-MPI pts with LM CAD (≥50% stenosis)
RJ 75 F ATA/SOB, DM, no walk regadenoson
RJ 75 F ATA/SOB, DM, no walk regadenoson

<table>
<thead>
<tr>
<th>Short Axis</th>
<th>Horizontal Long Axis</th>
<th>Vertical Long Axis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apical</td>
<td>Mid</td>
<td>Basal</td>
</tr>
</tbody>
</table>

CAC 1463
RJ 75 F ATA/SOB, DM, no walk regadenoson

CAC 1463
LM: CABG
CABG : Aids in identification of patients at high risk
CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
- Improves risk assessment
- Increases diagnostic certainty
- Improves identification of patients at highest risk
- Leads to greater change in patient management
Impact of CAC Score on Preventive Medication Use
Patients with Normal SPECT-MPI

1033 stable symptomatic patients
*Adjusted for risk factors and baseline medication use

Engbers, et al: Am Heart J 2017
Yearly Prevalence of Abnormal and Ischemic SPECT Myocardial Perfusion Imaging Studies between 1991 and 2009

N=39, 515
Rozanski, et al JACC 2012 (Cedars-Sinai)
CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
- Improves risk assessment
- Increases diagnostic certainty
- Improves identification of patients at highest risk
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CAC in Patients Undergoing SPECT/PET-MPI

- Detects subclinical atherosclerosis
- Improves risk assessment
- Increases diagnostic certainty
- Improves identification of patients at highest risk
- Leads to greater change in patient management

Should be considered in all patients without known CAD referred for SPECT/PET MPI
Thank you very much
During follow-up, patients assigned to CTA were more likely than patients assigned to standard care alone to have commenced preventive therapies.

<table>
<thead>
<tr>
<th></th>
<th>CCTA</th>
<th>Standard care</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventive therapies</td>
<td>19.4% (402/2037)</td>
<td>14.7% (305/2037)</td>
<td>1.40 [1.19, 1.65]</td>
</tr>
<tr>
<td>Antianginal therapies</td>
<td>13.2% (273/2037)</td>
<td>10.7% (221/2037)</td>
<td>1.27 [1.05, 1.54]</td>
</tr>
</tbody>
</table>

Adapted from Newby et al, Engl J Med 2018
CAC Distribution in Normal SPECT-MPI Patients

Berman et al

CAC score

He et al

Engberg et al (AHJ 2017)

JACC 2004

Circulation 2000
CAC Distribution in Normal SPECT-MPI Patients

- Berman et al. JACC 2000
- He et al. Circ 2004
- Engberg et al. AHJ 2017
Prevalence of Abnormal SPECT by CAC Score

4897 symptomatic patients

Impact of CAC on Prevention

- Increased exercise
- Dietary change
- Aspirin initiation
- Lipid lowering medications
- Blood pressure lowering medication

Meta-analysis

Gupta et al. JACC 2017
Impact of CAC on Lifestyle Changes

### Increased Exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Follow-up Years</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orakzai et al., 2008</td>
<td>2.22 [1.65, 2.99]</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Rozanski et al., 2011</td>
<td>1.45 [1.03, 2.03]</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Schwartz et al., 2011</td>
<td>1.92 [1.26, 2.93]</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1.84 [1.41, 2.41]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Dietary Change

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Follow-up Years</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Orakzai et al., 2008</td>
<td>2.00 [1.47, 2.72]</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Schwartz et al., 2011</td>
<td>1.85 [1.22, 2.79]</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1.94 [1.52, 2.49]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gupta et al; JACCi 2017
Impact of CAC on Preventive Medications

### Aspirin Initiation

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (M-H, Random, 95% CI)</th>
<th>Follow-up Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasir et al., 2010</td>
<td>1.82 [1.56, 2.11]</td>
<td>1.6</td>
</tr>
<tr>
<td>Orakzai et al., 2008</td>
<td>3.50 [2.55, 4.81]</td>
<td>3</td>
</tr>
<tr>
<td>Rozanski et al., 2011</td>
<td>2.40 [1.52, 3.81]</td>
<td>4</td>
</tr>
<tr>
<td>Taylor et al., 2008</td>
<td>3.17 [2.40, 4.20]</td>
<td>6</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2.61 [1.81, 3.78]</td>
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### Lipid Lowering Medication Initiation

<table>
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<tr>
<th>Study</th>
<th>Odds Ratio (M-H, Random, 95% CI)</th>
<th>Follow-up Years</th>
</tr>
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<tbody>
<tr>
<td>Nasir et al., 2010</td>
<td>1.98 [1.64, 2.38]</td>
<td>1.6</td>
</tr>
<tr>
<td>Rozanski et al., 2011</td>
<td>3.10 [2.32, 4.15]</td>
<td>4</td>
</tr>
<tr>
<td>Taylor et al., 2008</td>
<td>3.93 [2.97, 5.20]</td>
<td>6</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>2.86 [1.85, 4.41]</td>
<td></td>
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</tbody>
</table>

### Blood Pressure Lowering Medication Initiation

<table>
<thead>
<tr>
<th>Study</th>
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<th>Follow-up Years</th>
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<tbody>
<tr>
<td>Nasir et al., 2010</td>
<td>2.07 [1.69, 2.52]</td>
<td>1.6</td>
</tr>
<tr>
<td>Rozanski et al., 2011</td>
<td>1.69 [1.24, 2.30]</td>
<td>4</td>
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<tr>
<td>Total (95% CI)</td>
<td>1.94 [1.61, 2.33]</td>
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Gupta et al; JACCI 2017
Prevalence of Abnormal SPECT by CAC Score


4897 symptomatic patients referred for SPECT-MPI
CAC Distribution in Normal SPECT-MPI Patients

Berman et al

Engberg et al (AHJ 2017)

He et al

CAC score

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<td>0-9</td>
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<td>≥400</td>
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Engberg et al (AHJ 2017)

JACC 2004

Circulation 2000

CAC distribution in normal SPECT-MPI patients
CAC Score Increases Certainty of Interpretation of MPI

- N=151 SPECT/CT
- No prior MI
- Major interpretation change
  - N=39
  - ICA ≥70% standard
    - 24 correct change
    - 15 incorrect change

CAC Score Increases Certainty of Interpretation of MPI

- N=151 SPECT/CT
- No prior MI
- Major interpretation change
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