Recent Advances in Nuclear Cardiology, Cardiac CT, and Cardiac MRI: Applications for CAD in the Era of Value-based Imaging

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Cedars-Sinai Heart Institute
Professor of Medicine
UCLA School of Medicine

SWC-SNMMI
2015
Value-based Cardiac Imaging in CAD: Nuclear Cardiology, Cardiac CT and CMR

• The exciting:
  – Technology: always improving

• The realistic:
  – Proven value will be required for its use
Value-based Cardiac Imaging in CAD
Nuclear Cardiology, Cardiac CT and CMR

• Technologic improvements
• Value-based imaging
  – Prevention
  – Acute coronary syndromes
  – Stable ischemic heart disease
  – Heart failure
• Challenges
Value-based Cardiac Imaging in CAD
Nuclear Cardiology

• Instrumentation/software
  – Automatic quantitation
  – Increased resolution
    • SPECT: CZT
    • PET: Flurpiridaz

• Assessments: Adding to Perfusion and Viability
  – Anatomy and function: CAC scanning
  – Coronary flow reserve
  – Molecular imaging
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Automated assessment with machine learning will become routine

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Machine learning
Arsanjani...Slomka
JNC 2013
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Nakazato, et al JNC 2014
Einstein, et al JNC 2014
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CZT: Accurate in morbidly obese; 1 mSv imaging

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Nakazato, et al JNC 2014
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Berman, Maddahi
JACC 2013
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Improved defect detection through new tracer in trials

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Adding CAC to PET/SPECT increases diagnostic certainty
Detects subclinical atherosclerosis

- Anatomy and function: CAC scanning
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M. Di Carli
Value-based Cardiac Imaging in CAD
Nuclear Cardiology

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PET/CT: Quantitative absolute flow measurements: routine

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Murthy: Circ, 2011
Value-based Cardiac Imaging in CAD

Nuclear Cardiology

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  - Increased resolution
    - SPECT: CZT
    - PET: Flurpiridaz

CFR: Adds prognostic information to perfusion defect
Increases certainty; identifies diffuse disease

- Anatomy and function: CAC scanning
- Coronary flow reserve
- Molecular imaging

Murthy: Circ, 2011
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Distinguishing Stable from Active Atherosclerosis
Identifying the Vulnerable Patient

Fibroatheroma: Stable Plaque
TCFA with Cap Rupture

Narula & Willerson, JACC (ed)  Narula & Virmani, 1999
Atherosclerosis and PET imaging

Figure 2: Atherosclerosis and molecular imaging: The vulnerable atherosclerotic plaque protrudes into the vessel lumen as a result of progressive inflammation of the vessel wall intima. Monocytes are continuously recruited from the blood and into the intima where they differentiate to macrophages and become foam cells due to lipid ingestion. Eventually, foam cells are overcome and become apoptotic amassing to form a necrotic core which is covered by a thin fibrous cap. Expansion of the intima leads to hypoxia which drives angiogenesis whereby an angiogenic sprout from the vasa vasorum in the vessel wall media. PET-tracers are depicted in blue and arrows point to their respective receptors: integrin αvβ3, integrin receptor dimer alphaβ2; 18F-FDG, 2-[18F]-fluoro-2-deoxy-D-glucose; 18F-FMISO, 18F-fluoromisonidazole; sodium fluoride; 64Cu-DOTATATE, 68Ga-[1,4,7,10-tetraazacyclododecane-N,N,N,N'-tetraaceticacid]-Phe1,Tyr3-octreotate; GLP-1 receptor; PET, positron emission tomography; SSTR2, somatostatin receptor subtype 2.

F-18 Sodium Fluoride PET Identifies Ruptured and High-Risk Coronary Plaques

- **40 AMI**
  - 93% uptake in culprit plaque at ICA

- **40 Stable angina**
  - 45% uptake in plaques with high risk features (IVUS)

Joshi...Newby
Lancet 2013
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Fluride F-18: Potential to alter treatment paradigm in SIHD

Joshi...Newby
Lancet 2013
Coronary CTA
Value-based Cardiac Imaging in CAD
Cardiac CT

• Instrumentation/software
  – Full coverage single beat
  – Higher temporal resolution 66 msec
  – Lower radiation <1 mSv
  – Model based interactive reconstruction

• Assessments
  – Plaque
  – Perfusion
  – Flow
Value-based Cardiac Imaging in CAD
Cardiac CT

- Instrumentation/software
  - Full coverage, single beat
  - Higher temporal resolution, 66 msec
  - Lower radiation, <1 mSv
  - Model based interactive reconstruction

- Assessments
  - Plaque
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**Assessments**
- **Plaque**
- **Perfusion**
- **Flow**

Plaque characteristics
- Positive remodeling
- Lipid core
- Spotty calcification
- Volume
Value-based Cardiac Imaging in CAD
Cardiac CT

- Instrumentation/software
  - Full coverage single beat
  - Higher temporal resolution 66 ms
  - Lower radiation <1 mSv
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- Assessments
  - Plaque
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Plaque characteristics
- Predict
  - SPECT Ischemia
    Shmilovich, 2011
  - FFR ischemia
    Nakazato, 2013
  - Diaz-Zamudio, 2015
  - Events
    Motoyama, 2009
APFs on CCTA Predict Ischemia

Shmilovich, Cheng, et al., Atherosclerosis 2011
AutoPlaq: Automated method for quantitative plaque characterization

- % Diameter Stenosis
- % Area Stenosis
- NCP volume
- Low-attenuation plaque volume
- CP volume
- Total plaque volume
- Plaque composition
- % Aggregate plaque volume
- Remodeling index
- “Spotty” calcification

Source: Dey et al JCCT 2009
Value-based Cardiac Imaging in CAD
Cardiac CT

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  – Full coverage single beat
  – Higher temporal resolution 66 ms
  – Lower radiation <1 mSv
  – Spectral CT
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CORE320 Rochitte; EHJ 2013
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CT perfusion:
Predicts:
  Stenosis on ICA
  Rochitte, EHJ 2013
  Ischemia on SPECT
  Cury, JCCT 2015
Diagnostic Performance of Stress CT Perfusion (CTP)

CTP for SPECT ≥ 2 reversible defects

N = 124 with known or suspected CAD
11 centers; core lab analysis

AUC 0.93

CTP vs SPECT for ICA (≥50% stenosis)

N = 257 with known or suspected CAD
11 centers; core lab analysis

N = 257
p = 0.08

Cury et al JCCT 2015

George et al Radiology 2014
Value-based Cardiac Imaging in CAD
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  \[ FFR_{CT} \]
  - Uses rest CCTA
    - Computational fluid dynamics
    - No additional radiation
    - No adenosine
Value-based Cardiac Imaging in CAD
Cardiac CT

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- **Assessments**
  - Plaque
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$FFR_{CT}$ Validated vs invasive FFR
Koo: JACC 2011
Min: JAMA 2102
Norgaard: JACC 2014
Cardiac MR in CAD

- Anatomy & morphology
- Function & wall motion
- Perfusion
- Coronary plaque
- Coronary MRA
- Viability
Diagnostic accuracy of CMR perfusion for ischemic stenosis with FFR as reference: meta-analysis

Per patient (n=650): 90% sensitivity; 87% specificity
Per vessel (n=1073): 89% sensitivity; 86% specificity

Li M, et al JACCi 2014
Biograph mMR
Simultaneous, whole-body molecular MR (PET/MR)
Biograph mMR
Simultaneous, whole-body molecular MR (PET/MR)

Operational at CSMC 2015
Initial cardiac focus: plaque imaging, sarcoidosis
Value-based Cardiac Imaging in CAD

• Technologic improvements

• Applications
  – Prevention
  – Acute coronary syndromes
  – Stable ischemic heart disease
  – Heart failure

• Challenges
Value-based Cardiac Imaging in CAD

• Value = quality/cost
  – Quality ≈ outcomes (e.g., MACE, QOL)
  – Cost: total costs related to diagnosis

• Future:
  – Cost will be the driver;
    • Tests/procedures that add value will be “purchased” by third party carriers
Value-based Cardiac Imaging in CAD

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CT Coronary Artery Calcium (CAC)

- CAC: a marker of CAD
  - Burden of coronary atherosclerosis
- Integrated lifetime effect of all risk factors
  - Overcomes the limitations of FRS
  - Consistent evidence: incremental prognostic value

<1 mSv
(~ mammogram)
Single breath
No contrast
Interplay of CAC and Traditional Risk Factors (RFs) in Prediction of All-Cause Mortality*

44,052 asymptomatic
F/U: 5.6±2.6y
Risk Factors:
  Smoking
  Diabetes
  Dyslipidemia
  Hypertension
  Family History

* Per 1000 person yrs

Nasir Circ Cardiovasc Imaging 2012
Interplay of CAC and Traditional Risk Factors (RFs) in Prediction of All-Cause Mortality*

44,052 asymptomatic

F/U: 5.6±2.6y

Risk Factors:
- Smoking
- Diabetes
- Dyslipidemia
- Hypertension
- Family History

* Per 1000 person yrs

- 43%: no risk factors
- 47% of these had CAC>0
- CAC stratified risk in all risk factor groups
CAC to Guide ASA Rx: MESA
Risk/benefit of ASA by CAC

Redline: ASA 5 year needed to harm (442)
Assumptions: 0.23% increase in major bleeding;
18% reduction in CHD events with ASA

Miedema et al
Circ CV Outcomes 2014
CAC may lead to better treatment / lifestyle

- More targeted preventive treatment
- 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
Detection of CAD/Risk Assessment: Asymptomatic

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<thead>
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<td>7. Low global CHD risk</td>
<td>R</td>
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<td>8. Intermediate global CHD risk</td>
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<td>9. Intermediate global CHD risk</td>
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<td>10. High global CAD Risk</td>
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<td>11. High global CAD Risk</td>
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Wolk et al JACC 2014
Value-based Cardiac Imaging in CAD

Prevention

- CT coronary calcium: potential for screening
- Coronary CTA: no role at present
- No primary role for stress imaging
- Stress imaging: “appropriate” for guiding management when CCS is high (~10%)
Imaging for Prevention
Coronary Calcium Screening

- **Outcomes**: ↑↑
- **Costs**: ↑
- **Value**: probably ↑
Value-based Cardiac Imaging in CAD

- Technologic improvements
- Applications
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  - Acute coronary syndromes
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- Challenges
Rest or rest/stress MPI for Chest Pain in ED

49 M in ED

- Can be performed in any patient
- Particularly useful in known CAD/ high CAC
Day 0 – Can be performed in any patient
Day 5 – Particularly useful in known CAD/ high CAC

49 M in ED

ERASE Trial (2002): 20% reduction in unnecessary admissions
Coronary CTA

- Sensitivity and specificity: ~ 95%/90%
- Higher than all other modalities
  - Per patient
  - Per vessel
  - Per segment
Coronary CTA

- Sensitivity and specificity: ~ 95%/90%
- Higher than all other modalities
  - Per patient
  - Per vessel
  - Per segment
- Very high negative predictive value for events
Primary Outcome - Length of Hospital Stay

Hoffman, et al ACC 2012
Coronary CTA in Suspected ACS

- Reduces length of stay and time to diagnosis
- Safely increases direct ED discharge rates
- No increase in costs of care
Coronary CTA in Suspected ACS

- Reduces length of stay and time to diagnosis
- Safely increases direct ED discharge rates
- No increase in costs of care

• Consistent results in three large RCTs:
  Goldstein, et al JACC 2011
  Litt, et. al. NEJM, 2012
  Hoffman, et al ACC 2012
Imaging for Acute Chest Pain
Coronary CTA

- Outcomes: no $\Delta$
- Costs: ↓
- Value: ↑
Investigational and Not Medically Necessary:

Coronary computed tomography angiography (CCTA) or coronary magnetic resonance angiography (MRA) is considered investigational and not medically necessary for all other indications, including, but not limited to, the following:

- Screening for coronary artery disease (CAD), either in asymptomatic individuals or as part of a preoperative evaluation; or
- Diagnosis of CAD, in individuals with acute or non-acute symptoms, or after a coronary intervention; or
- As a technique to evaluate cardiac function.
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Noninvasive Imaging for CAD
Suspected CAD: Stable

Pre-test likelihood of CAD

Low-to-Intermediate (15-85%)

Stress imaging

• Most common approach
• CAC scanning could strengthen
Noninvasive Imaging for CAD
Suspected CAD: Stable

Pre-test likelihood of CAD

Low-to-Intermediate (15-85%)

Coronary CTA

• Growing as initial test
Detection of CAD/Risk Assessment: Symptomatic

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Prognostic value of CCTA is widely generalizable

CONFIRM Registry: Coronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry (James K. Min, PI)

- Dynamic registry of >32,000 consecutive patients undergoing CCTA
- V.1. 12-centers in 6 countries (US, Canada, Germany, Switzerland, Italy, and S. Korea), Database lock 09/10 – Derivation Cohort
- V.2. 6 add’l sites (Miami, California, Vancouver, New York, Innsbruck, Seoul) – Validation Cohort
Prognostic Value of CCTA CAD Extent / Severity

23,854 patients w/o known CAD (57±13 years), 2.3 year f/u

Source: CONFIRM Min et al. J Am Coll Cardiol 2011
Consistent findings in all populations studied to date

Source: CONFIRM Min et al. J Am Coll Cardiol 2011
### Long-term Prognosis For Normal CCTA

#### “Warranty Period” of a Normal CT: at least 7 years

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<th>Study</th>
<th>Patients</th>
<th>Follow-up</th>
<th>CT Description</th>
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<td>Ostrom (ACM)</td>
<td>2538</td>
<td>6.5 yr</td>
<td>EBCT</td>
</tr>
<tr>
<td>CONFIRM (ACM)</td>
<td>1000</td>
<td>&gt;4 yr</td>
<td>&gt;64-row CT</td>
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<tr>
<td>Andreini (MACE)</td>
<td>1304</td>
<td>4.3 yr</td>
<td>64-row CT</td>
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<tr>
<td>Hadamitzky (MACE)</td>
<td>1584</td>
<td>5.6 yr</td>
<td>16- / 64-row CT</td>
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<td><strong>Total</strong></td>
<td><strong>6426</strong></td>
<td>~5.5 yr</td>
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</table>

- CONFIRM >5 year f/u anticipated for ~10,000 patients 4/13

Source: Ostrom et al. JACC 2008; Min et al. J Am Coll Cardiol 2011; Andreini et al. JACC CVImaging 2012; Hadamitzky et al. (In press)
**Long-term Prognosis For Normal CCTA**

"Warranty Period" of a Normal CT: at least 7 years

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Follow-up</th>
<th>Imaging Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostrom (ACM)</td>
<td>2538</td>
<td>6.5 yr</td>
<td>EBCT</td>
</tr>
<tr>
<td>CONFIRM (ACM)</td>
<td>1000</td>
<td>&gt;4 yr</td>
<td>&gt;64-row CT</td>
</tr>
<tr>
<td>Andreini (MACE)</td>
<td>1304</td>
<td>4.3 yr</td>
<td>64-row CT</td>
</tr>
<tr>
<td>Hadamitzky (MACE)</td>
<td>1584</td>
<td>5.6 yr</td>
<td>16- / 64-row CT</td>
</tr>
</tbody>
</table>

6426 patients, ~5.5 yr f/u

- CONFIRM >5 year f/u anticipated for ~10,000 patients 4/13

**Source:** Ostrom et al. JACC 2008; Min et al. J Am Coll Cardiol 2011; Andreini et al. JACC CVImaging 2012; Hadamitzky et al. (In press)
Scottish COnputed Tomography of the HEART (SCOT-HEART) Trial

- 9849 patients referred for assessment of suspected angina (12 clinics)
- 4146 randomized to CCTA vs standard of care (47% of eligible)
- 9% previous CAD; 85% stress ECG
- Clinical diagnosis of CAD: 47%
- Follow-up: median 1.7 years
- Site interpretation: evaluation at 6 weeks
- Primary endpoint: certainty of diagnosis of angina due to CAD at 6 weeks
- Secondary endpoints:
  - Changes in therapies (preventive and anti-anginal)
  - Further tests
  - Clinical outcomes (68 CD/MI; 1.6%)

Newby et al Lancet 2015
CT Coronary Angiography: Diagnosis Baseline Compared to 6 Weeks

Overall Changes in Diagnosis of CHD: 27% versus 1%, P<0.001

Certainty | Frequency | Relative Risk [95% Confidence Intervals]
---|---|---
2.56 [2.33-2.79] | 1.09 [1.02-1.17] |

Overall Changes in Diagnosis of Angina due to CHD (1° End-point): 23% versus 1%

Certainty | Frequency | Relative Risk [95% Confidence Intervals]
---|---|---
1.79 [1.62-1.96] | 0.93 [0.85-1.02] |

Newby et al Lancet 2015
**CTCA and Medical Therapy**

*Baseline Compared to 6 Weeks*

Overall Changes in Treatments: 23% versus 5%, P<0.001

### Cancellations

- **Preventative Therapy**
- **Anti-Anginal Therapy**
- **All Therapies**

### New Treatments

- **Preventative Therapy**
- **Anti-Anginal Therapy**
- **All Therapies**

**CTCA + Standard Care**

**Standard Care**

Newby et al Lancet 2015
CTCA and Clinical Outcome

1.7 Years of Follow-up

CHD Death and Non-Fatal MI

HR 0.62 [0.38-1.01], P=0.053

CHD Death, Non-Fatal MI and Non-fatal Stroke

HR 0.64 [0.41-1.01], P=0.056

Newby et al Lancet 2015
CTCA and Clinical Outcome

Coronary Angiography & Revascularisation

Coronary Angiography

HR 1.06 [0.92-1.21], P=0.451

Coronary Revascularisation

HR 1.20 [0.99-1.45], P=0.061

Newby et al Lancet 2015
Scot-Heart: Conclusions

In patients presenting with suspected angina due to coronary heart disease, the addition of CCTA:

- Changes and clarifies the diagnosis: 1 in 4
- Alters subsequent investigations: 1 in 6
- Changes treatments: 1 in 4
- May increase coronary revascularization and reduce fatal and non-fatal myocardial infarction

Newby et al Lancet 2015
PROMISE Trial

- 10,003 symptomatic patients with no prior CAD
- referred for noninvasive testing for CAD; 193 North American sites
- Pre-test probability of CAD: 53%
- Follow-up: median 25 months
- Randomized to CCTA or functional testing
  - nuclear stress MPI (67%); stress echo (9%) stress ECG (10%)
- Site interpretation: immediate evaluation
- Primary endpoint: death, MI, hospitalization for UA, procedural complications (n=315, 3.1%; death or MI: 216, 2.1%)
- Secondary endpoints:
  - Invasive coronary angiography without obstructive CAD
  - Death or non-fatal MI
  - Radiation exposure

Primary Endpoint:
Death, MI, Unstable Angina, Major Complications

CTA: Functional
Hazard Ratio: 1.04
(95% CI: 0.83, 1.29)
P = 0.750

Secondary Endpoint:
Death or Non-fatal MI

CTA: Functional
Hazard Ratio: 0.88
(95% CI: 0.67, 1.15)
P-value: 0.348

## Secondary Endpoint: Catheterization Without Obstructive CAD ≤90 days

<table>
<thead>
<tr>
<th>Invasive catheterization without obstructive CAD — N (%)</th>
<th>CTA (n=4996)</th>
<th>Functional (n=5007)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive catheterization</td>
<td>170 (3.4%)</td>
<td>213 (4.3%)</td>
<td>0.022</td>
</tr>
<tr>
<td>With obstructive CAD (% of caths)</td>
<td>609 (12.2%)</td>
<td>406 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>439 (72.1%)</td>
<td>193 (47.5%)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>311 (6.2%)</td>
<td>158 (3.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Douglas et al NEJM 2015
Conclusions

- Compared to usual care using a functional testing strategy, use of an initial anatomic testing strategy employing CTA did not improve clinical outcomes in patients with suspected CAD.

- Our results suggest that CTA is a viable alternative to functional testing.

- These real-world results should inform noninvasive testing choices in clinical care as well as provide guidance to future studies of diagnostic strategies in suspected heart disease.

Douglas et al NEJM 2015
Noninvasive Imaging for CAD
Suspected-known CAD

Risk-assessment

• All modalities validated for prognosis across multiple clinical presentations
• Evidence base for coronary CTA now extensive
Risk-assessment

- All modalities validated for prognosis across multiple clinical presentations
- Evidence base for coronary CTA now extensive
- How to manage patients based on test results not yet established
“What should I do about it?”

Level of risk

<table>
<thead>
<tr>
<th>Very Low</th>
<th>Low</th>
<th>Borderline</th>
<th>Can’t tell</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assure</td>
<td>Prevent</td>
<td>+ Stress</td>
<td>+ Stress or cath</td>
<td>+ Cath</td>
<td></td>
</tr>
</tbody>
</table>
Suspected CAD
Hypothesis: Value of Coronary CTA Depends on Pre-test Likelihood of CAD
Low-to Intermediate

- Outcomes: no Δ
- Costs: ↓
- Value: ↑
Suspected CAD
Hypothesis: Value of Coronary CTA Depends on Pre-test Likelihood of CAD

Low-to Intermediate
- Outcomes: no Δ
- Costs: ↓
- Value: ↑

High
- Outcomes: no Δ
- Costs: ↑*
- Value: ↓
Suspected CAD
Hypothesis: Value of Coronary CTA
Depends on Pre-test Likelihood of CAD

Low-to Intermediate
- Outcomes: no $\Delta$
- Costs: ↓
- Value: ↑

High
- Outcomes: no $\Delta$
- Costs: ↑*
- Value: ↓

* Possible increase in ICA/PCI or additional testing
Coronary CTA is less useful in several settings

<table>
<thead>
<tr>
<th></th>
<th>CCTA</th>
<th>MPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>High CAC</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Renal failure</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Morbidly obese</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
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)

*Possibly without imaging if patient can exercise
SPECT: Risk Increases as a Function of Stress Perfusion Abnormality

- Men and women
- Sx and Asx
- Diabetics
- Obese
- Renal Failure
- Arrhythmia
- High CAC Score
- Known CAD
  - MI
  - PCI
  - CABG

Data from over 50,000 patients

Risk* as a Function of Extent/Severity of Perfusion Defects

*Adjusted or unadjusted
Post-SPECT Cardiac Mortality and Rx Given Early Revascularization vs Medical Therapy

Hachamovitch et al, Circulation 1998

*\( p < 0.05 \)
Post-SPECT Cardiac Mortality and Rx Given Early Revascularization vs Medical Therapy

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

Ischemia on MPI Predicts Benefit from Revascularization

- No Known CAD Circulation 2003
- No Known CAD + EF JNC 2006
- Elderly Circulation 2010
- Prior revascularization EHJ 2010
- Prior MI EHJ 2011

Hachamovitch, et al
CFR is Associated with Cardiac Events Independently of Stenosis and Modifies the Effect of Early Revascularization

329 patients referred for ICA after PET; median f/u 3.1 year for CV death or HF
CFR and CAD prognostic index (ICA): independent predictors
Significant interaction (p=0.039) between CRF and early CABG but not PCI

Taqueti, Hachamovitch…Di Carli Circulation 2015
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Taqueti, Hachamovitch…Di Carli Circulation 2015
CFR is Associated with Cardiac Events Independently of Stenosis and Modifies the Effect of Early Revascularization

CFR + or - vs Revasc + or -

CFR low, revasc +

CFR low, revasc -

CFR + or - vs Type of Revasc

CFR low, CABG

CFR low, PCI

329 patients referred for ICA after PET; median f/u 3.1 year for CV death or HF
CFR and CAD prognostic index (ICA): independent predictors
Significant interaction (p=0.039) between CRF and early CABG but not PCI

Taqueti, Hachamovitch…Di Carli Circulation 2015
**Primary Outcome**

All-cause death, MI, or urgent revascularization

---

FAME 2 Trial: FFR-Guided PCI versus Medical Therapy in Stable CAD

De Bruyne B et al. *NEJM* 2012
FAME 2: FFR-Guided PCI versus Medical Therapy in Stable CAD

Death from any Cause

<table>
<thead>
<tr>
<th>Months after randomization</th>
<th>PCI+MT vs. MT: HR 0.33 (0.03-3.17); p=0.31</th>
<th>PCI+MT vs. Registry: HR 1.12 (0.05-27.33); p=0.54</th>
<th>MT vs. Registry: HR 2.66 (0.14-51.18); p=0.30</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at risk</td>
<td>441 423 390 350 312 281 247 219 188 154 122 90 54</td>
<td>447 423 396 359 318 288 250 220 183 163 122 95 54</td>
<td>166 156 145 134 118 107 96 76 67 55 43 27 13</td>
</tr>
</tbody>
</table>

De Bruyne B et al. *NEJM* 2012
FAME 2: FFR-Guided PCI versus Medical Therapy in Stable CAD

Myocardial Infarction

De Bruyne B et al. NEJM 2012
ISCHEMIA Trial

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches

Study Chair: Judith Hochman
Principal Investigator: David Maron

Sponsor: NHLBI
ISCHEMIA Trial

- >10% Ischemia*
  - LVEF >35%

  - Blinded CCTA
    - Exclude LM/NCA

  - RANDOMIZE
    - Cath (Revasc+ OMT)
      - 3-6 yr. F/U
    - No Cath (OMT)
      - 3-6 yr. F/U

  - *SPECT, PET, echo, CMR
  - Core lab verification

- 8,000 stable CAD patients
- 3-6 yr. F/U

• 3-6 yr. F/U
ISCHEMIA Trial

>10% Ischemia*
LVEF >35%

Blinded CCTA
Exclude LM/NCA

RANDOMIZE

Cedars-Sinai Experience
Nuclear core lab: >1000 patients
Trial site: 0 patients

* SPECT, PET, echo, CMR
Core lab verification

- 8,000 stable CAD patients
- 3-6 yr. F/U

• 3-6 yr. F/U
Suspected/Known Stable CAD
Hypothesis: Value of Ischemia Testing
Depends on Pre-test Risk

Intermediate-to-high

- Outcomes: ↑
- Costs: ↓
- Value: ↑
Yearly Prevalence of Abnormal and Ischemic SPECT Myocardial Perfusion Imaging Studies between 1991 and 2009

Yearly prevalence data showing a decreasing trend from 1991 to 2009 for ischemia (blue line) and abnormal SPECT (red line).

N=39,515

Rozanski, et al JACC 2012
Diamond-Forrester Classification (DFC) overestimates likelihood of angiographically “significant” CAD*

Overall Obstructive CAD prevalence in patients with NonAng, AtypAng, and TypAng (n=8106)

- Expected by using DFC and CASS: 51%
- Observed in CONFIRM: 18%

Cheng, et al Circulation 2011 (CONFIRM)  * In patients referred for CCTA
Why do <10% of patients without known CAD currently undergoing SPECT have ischemia?

• Assume patients sent to SPECT have intermediate likelihood of CAD by Diamond-Forrester classification referred for CCTA (50%)
  – 40% of patients with 50% likelihood of CAD have ≥ 50% stenosis on CCTA*
  – 90% of patients with CCTA stenosis have stenosis on ICA**
  – 57% of patients with stenosis on ICA have FFR ischemia***
  – 90% of patients with FFR ischemia have SPECT ischemia****

• \(0.50 \times 0.40 \times 0.90 \times 0.57 \times 0.90 = 9\%\)

* Cheng (CONFIRM) Circulation 2011  
** Budoff et al (ACCURACY) JACC 2008  
*** Tonino et al (FAME) JACC 2010  
**** best case assumption
Why do <10% of patients currently undergoing SPECT have ischemia?

- Assume patients sent to SPECT have intermediate likelihood of CAD by Diamond-Forrester classification referred for CCTA (50%)
  - 40% of patients with 50% likelihood of CAD have ≥ 50% stenosis on CCTA*
  - 90% of patients with CCTA stenosis have stenosis on ICA**
  - 57% of patients with stenosis on ICA have FFR ischemia***
  - 90% of patients with FFR ischemia have SPECT ischemia

Better selection of patients for stress imaging is needed for stress imaging to provide value

* Cheng (CONFIRM) Circulation 2011
** Budoff et al (ACCURACY) JACC 2008
*** Tonino et al (FAME) JACC 2010
**** best case assumption
Suspected/Known Stable CAD
Hypothesis: Value of Ischemia Testing Depends on Pre-test Risk
Intermediate-to-high

• Outcomes: ↑
• Costs: ↓
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Low
• Outcomes: No Δ
• Costs: ↑
• Value: ↓

Intermediate-to-high
• Outcomes: ↑
• Costs: ↓
• Value: ↑

• Diamond-Forrester: needs update
• Min risk score: Am J Med 2015—potential for adoption
Value-based Cardiac Imaging in CAD

- Technologic improvements
- Applications
  - Prevention
  - Acute coronary syndromes
  - Stable ischemic heart disease
  - Heart failure
- Challenges
PARR-2

F-18-Fluorodeoxyglucose Positron Emission Tomography Imaging-Assisted Management of Patients With Severe Left Ventricular Dysfunction and Suspected Coronary Disease
A Randomized, Controlled Trial (PARR-2)

- 430 pts; HF + CAD; LV EF <35%
- Randomized to Standard care vs PET guided care
- Overall result: Death, MI, Rehosp at 1 y: p=0.15
  - Subset result: Appropriate action taken on PET findings: p=0.019
  - Subset result: Ottawa 5 (experienced PET centers): p=0.005
- Caveat: Imaging trial results depend on: test accuracy, incorporation of results into care, effectiveness of therapy
Value-based Cardiac Imaging in CAD

• Prevention
  – CAC

• Acute coronary syndromes
  – Lower risk: CCTA
  – Higher risk: stress imaging

• Stable ischemic heart disease
  – Lower risk: CCTA
  – Higher risk: stress imaging

• Heart failure
  – MRI, PET/SPECT
Value-based Cardiac Imaging in CAD

- Prevention
  - CAC

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Value-based Cardiac Imaging in CAD

- Technologic improvements
- Applications
  - Prevention
  - Acute coronary syndromes
  - Stable ischemic heart disease
  - Heart failure
- Challenges
Can Cardiac Imaging in CAD Provide Value?

Challenges

- Must improve outcomes or reduce costs
Can Cardiac Imaging in CAD Provide Value?

Challenges

- Must improve outcomes or reduce costs
- Imaging tests cannot improve outcomes unless they result in improved therapy
Value-based Cardiac Imaging in CAD

• Technology/assessments will improve across modalities and clinical settings
• Applications providing value will dominate
• Value
  – Will depend on the clinical setting
  – Requires linkage to therapeutic change
  – Evidence will be required
Thank you very much