Direct Ischaemia imaging and other Competing technologies

Dr. NATHAN BETTER
Associate Professor of Medicine
University of Melbourne
Departments of Cardiology & Nuclear Medicine
Royal Melbourne Hospital
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CLINICAL CASE

- 34 year old male
- Atypical chest pain. No cardiac risk factors.
- Examination – normal. BP 120/70
- ECG – Normal.
- CXR/Bloods- Normal

- Which test next?
CHOICES

- Nil
- Exercise ECG
- Stress echo
- Stress nuclear
- Cardiac CT
- Coronary angiography
A standard treadmill stress test was performed
Robert Bruce (The AGE 1/3/04)

- 20/11/16 – 12/2/04
- First published 1949
- Multistage test 1963
- Emeritus Professor of Medicine, U of Washington.
- “You would never buy a used car without taking it for a drive and seeing how the engine performed while it was running, and the same is true for evaluating the function of the heart.”
Exercise test

9 minutes Bruce
Ceased due to SOB
No chest pain
HR  Rest - 72   Peak - 162
BP  Rest - 130/75  Peak - 200/80
INDICATIONS FOR Ex ECG

Clear Indications

1. Dx CAD in men with atypical symptoms
2. Assess prognosis and functional capacity in pts with known CAD
3. Assessing exercise-induced arrhythmia
4. Assessment post MI
5. Evaluation post revascularisation
Possible indications

1. **Dx CAD** in women with typical and atypical pain
2. RBBB, Digoxin
3. Known CAD - functional capacity, response to treatment
4. Functional capacity in some pts with valvular heart disease – Moderate to severe AS (ESC 2005)
5. Asymptomatic males > 40 or high risk job with 2+ risk factors or a sedentary pt going to begin a vigorous exercise program
RESULTS

ST depression, ST/HR slope, QRS amplitude and size

HR and BP response, change rhythm - incl VEs

Positive, Negative, Equivocal, Non-diagnostic

Treadmill score

  e.g. DUKE score = ex duration - (5xST deviation) - (4x angina index)

0 = no angina, 1 = non-limiting, 2 = ex limited
## RISK STRATIFICATION

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>68 %</td>
<td>77 %</td>
</tr>
<tr>
<td>Multivessel</td>
<td>81 %</td>
<td>66 %</td>
</tr>
<tr>
<td>Females</td>
<td>76 %</td>
<td>64 %</td>
</tr>
<tr>
<td>Males</td>
<td>78 %</td>
<td>73 %</td>
</tr>
</tbody>
</table>

Weiner et al NEJM 1979...
Where to now?

- Normal – stop

- Abnormal – further tests, depending on results
44 year old female

Past history - HT, NIDDM, Smoke 20/day
Chol 5.6  TG 2.0  LDL 4.1  HDL 0.8
F/H - Positive
P/C – 3/12 exertional SOB and atypical pain
Examination - Unremarkable
CHOICES

- Nil
- Exercise ECG
- Stress echo
- Stress nuclear
- Cardiac CT
- Coronary angiography
Ischaemic Cascade

- Perfusion
- Diastolic Function
- Systolic Function
- ECG changes
- Angina
3 steps

1. Echo at rest

2. Treadmill test

3. Echo immediately post stress with digitisation and sequenced to ECG
## Interpretation

<table>
<thead>
<tr>
<th>Rest</th>
<th>Stress</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>N/Hypo</td>
<td>akinesis/dys</td>
<td>Ischaemia</td>
</tr>
<tr>
<td>Akinesis</td>
<td>Normal/hypo</td>
<td>Viable</td>
</tr>
<tr>
<td>Akinesis/dys</td>
<td>Akinesis/dys</td>
<td>Infarct/Necrosis</td>
</tr>
</tbody>
</table>
Indications

- Ischaemia assessment
- Valvular heart disease – asymptomatic AS (incl. LV function normal or poor), AR and MR.
- Viability
- Advantages – no ionising radiation. Slightly greater specificity
<table>
<thead>
<tr>
<th></th>
<th>Dip (%)</th>
<th>Exercise (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens – 1-vessel</td>
<td>66</td>
<td>72</td>
</tr>
<tr>
<td>multivessel</td>
<td>81</td>
<td>90</td>
</tr>
<tr>
<td>overall</td>
<td>72</td>
<td>79</td>
</tr>
<tr>
<td>Specificity</td>
<td>92</td>
<td>82</td>
</tr>
<tr>
<td>Accuracy</td>
<td>77</td>
<td>80</td>
</tr>
<tr>
<td>Feasibility</td>
<td>97</td>
<td>81</td>
</tr>
</tbody>
</table>

Meta-analysis… 2009
Problems

- Obesity
- Poor lung windows, incl COAD
- Can be difficult if LV not normal at rest
- Reduced sensitivity for single vessel disease
- Operator dependant
- No funding for contrast (perfusion and wall definition)
Clinical case

65 year old male
Diabetic, hypertensive, LDL chol 4.8
Chest pain FI – Exertional, but pleuritic (atypical)
Examination – Well 150/90
ECG – SR. LBBB.
CHOICES

- Nil
- Exercise ECG
- Stress echo
- Stress nuclear
- Cardiac CT
- Coronary angiography
Persantin-exercise Tc-99m sestamibi study

Off caffeine 24 hours
0.568 mg/kg IV Persantin
4 mins SLR
Peak HR 98  Peak BP 120/80
No pain
Equivocal ECG
Rest and stress images
Gating
Management

Risk factor control
Reassurance +++++++++++++++++
INDICATIONS FOR NUCLEAR CARDIOLOGY

DIAGNOSTIC

1. Chest pain FI - Equivocal ex. ECG, baseline ECG changes (LBBB, BBB, old MI, Digoxin, etc)

2. Atypical syndromes - SOB, etc.

3. Acute chest pain syndromes

4. Pharmacological testing
INDICATIONS FOR NUCLEAR CARDIOLOGY

PROGNOSTIC

1. Post MI – early and late (risk stratification)
2. Significance of a specific lesion
3. Myocardial viability
4. Risk of non-cardiac surgery
5. Gated blood pool scans – chemotherapy, congenital, suboptimal echo, accurate LVEF and RVEF. Role with exercise.
Clinical Case

- 50 year old male
- Positive FH
- Slightly atypical pain
- Low-intermediate probability of IHD
- Examination / ECG - Normal
CHOICES

- Nil
- Exercise ECG
- Stress echo
- Stress nuclear
- Cardiac CT
- Coronary angiography
Cardiac CT
POSSIBLE Cardiac CT Indications

- Screening high risk asymptomatic individuals
- Triple rule out in acute chest pain (with PE and dissection)
- Graft and stent patency
- Equivocal diagnostic functional studies (if no known prior CAD)
- Coronary calcium score
- Diagnosis in low-intermediate risk
- Anomalous coronary artery origins
- Evaluating coronary arteries prior to cardiac non-coronary surgery
WG

Minor plaque RCA
Atherosclerosis Is Common in Ancient Humans: Results of the Horus Study of Ancient Egyptian Mummies

Gregory S Thomas, Adel H Allam, Randall C Thompson, Abd el-Halim Nur el-Din, Gomaa Abd el-Maksoud, Ibrahim Badr, Muhammad Al-Tohamy Soliman, Hany Abd el-Amer, M Linda Sutherland, James D Sutherland, Michael I Miyamoto, L Samuel Wann

Presenter: Adel Allam, MD, FASNC
Professor of Cardiology, Al Azhar University, Cairo Egypt
Chief of Nuclear Cardiology Alfa Medical Center, Cairo, Egypt

Simultaneous publication of ACC abstract and in Allam, et al. Journal of the American College of Cardiology: CVImaging April 2011
Djeher - LCA disease
EBCT for Cardiac Risk Assessment in Asymptomatic Subjects

Death / Nonfatal MI (N=632)

Follow-Up 32±7 months

Mean CACS
- Events: 303±441
- No Events: 92±240

Raggi et al. *Circulation* 2000;101:850
## Events by CAC stratification

<table>
<thead>
<tr>
<th>CAC group</th>
<th>Patients, n (%)</th>
<th>Events, n (%)</th>
<th>Event rate (per 1000 person-years)</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary heart disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAC=0</td>
<td>444 (47)</td>
<td>2 (0.5)</td>
<td>0.8</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>CAC 1–100</td>
<td>267 (28)</td>
<td>7 (3)</td>
<td>4.8</td>
<td>4.6 (0.9–23.4)</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td>239 (25)</td>
<td>25 (11)</td>
<td>20.2</td>
<td>24.8 (5.4–11.5)</td>
</tr>
<tr>
<td><strong>Cardiovascular disease events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAC=0</td>
<td>444 (47)</td>
<td>9 (2)</td>
<td>3.7</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>CAC 1–100</td>
<td>267 (28)</td>
<td>12 (5)</td>
<td>8.4</td>
<td>1.8 (0.7–4.6)</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td>239 (25)</td>
<td>32 (13)</td>
<td>26.4</td>
<td>6.0 (2.5–14.6)</td>
</tr>
</tbody>
</table>

CAC score useful in low-int risk Framingham pts, NOT very low probability group
Cumulative rate of stress cardiac imaging (%)

<table>
<thead>
<tr>
<th>CAC score</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10 (n=773)</td>
<td>2.3</td>
<td>7.6</td>
<td>16.8</td>
</tr>
<tr>
<td>11–100 (n=287)</td>
<td>18.0</td>
<td>26.7</td>
<td>33.6</td>
</tr>
<tr>
<td>101–399 (n=187)</td>
<td>16.7</td>
<td>19.8</td>
<td>28.9</td>
</tr>
<tr>
<td>400–999 (n=83)</td>
<td>36.9</td>
<td>41.2</td>
<td>42.3</td>
</tr>
<tr>
<td>≥1000 (n=31)</td>
<td>44.5</td>
<td>58.7</td>
<td>86.8</td>
</tr>
</tbody>
</table>

Objectives: We conducted a prospective randomized trial to compare the clinical impact of conventional risk factor modification to that associated with the addition of coronary artery calcium (CAC) scanning.

Background: Although CAC scanning predicts cardiac events, its impact on subsequent medical management and coronary artery disease risk is not known.

Methods: We assigned 2,137 volunteers to groups that either did undergo CAC scanning or did not undergo CAC scanning before risk factor counselling. The primary end point was 4-year change in coronary artery disease risk factors and Framingham Risk Score. We also compared the groups for differences in downstream medical resource utilization.

Results: Compared with the no-scan group, the scan group showed a net favourable change in systolic blood pressure (p = 0.02), low-density lipoprotein cholesterol (p = 0.04), and waist circumference for those with increased abdominal girth (p = 0.01), and tendency to weight loss among overweight subjects (p = 0.07). While there was a mean rise in Framingham Risk Score (FRS) in the no-scan group, FRS remained static in the scan group (0.7 ± 5.1 vs. 0.002 ± 4.9, p = 0.003). Within the scan group, increasing baseline CAC score was associated with a dose-response improvement in systolic and diastolic blood pressure (p < 0.001), total cholesterol (p < 0.001), low-density lipoprotein cholesterol (p < 0.001), triglycerides (p < 0.001), weight (p < 0.001), and Framingham Risk Score (p = 0.003). Downstream medical testing and costs in the scan group were comparable to those of the no-scan group, balanced by lower and higher resource utilization for subjects with normal CAC scans and CAC scores ≥ 400, respectively.

Conclusions: Compared with no scanning, randomization to CAC scanning was associated with superior coronary artery disease risk factor control without increasing downstream medical testing. Further study of CAC scanning, including pre-specified treatment recommendations, to assess its impact of cardiovascular outcomes is warranted. (Early Identification of Subclinical Atherosclerosis Using Non-Invasive Imaging Research [EISNER]; NCT00927693)
MSCT

- Multi-slice CT coronary angiography
- 64 slice
- 128 slice
- Dual source
- 256 slice
- 320 slice

- Use prospective gating – keep dose down!!!
Summary of PPV/NPV of MSCT status… Hachamovitch and Di Carli JNC 10/07
CONFIRM trial...Min et al...AHA 11/10

n = 24775 pts. 12 centres in 5 countries. 2.3 year follow-up
Risk-adjusted hazards ratio for all-cause mortality per patient

<table>
<thead>
<tr>
<th>Patient type</th>
<th>Adjusted hazard ratio</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vessel</td>
<td>1</td>
<td>Reference</td>
</tr>
<tr>
<td>Nonobstructive CAD (&lt;50%)</td>
<td>1.60</td>
<td>0.0023</td>
</tr>
<tr>
<td>Obstructive CAD (&gt;50%)</td>
<td>2.60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Type</td>
<td>Adjusted hazard ratio</td>
<td>p</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Normal</td>
<td>1</td>
<td>Reference</td>
</tr>
<tr>
<td>Nonobstructive CAD</td>
<td>1.62</td>
<td>0.0018</td>
</tr>
<tr>
<td>One-vessel obstructive CAD</td>
<td>2.00</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Two-vessel obstructive CAD</td>
<td>2.92</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Three-vessel or LM obst CAD</td>
<td>3.70</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Review of CTCA v. MPI in U.S. – 300,000 medicare pts

Shreibati et al…. JAMA 11/11

Significant findings included the following:

1. Compared to patients who underwent MPS, those who underwent CCTA were nearly twice as likely to undergo subsequent cardiac catheterization (22.9% versus 12.1% for MPS).

2. CCTA patients were more than twice as likely to undergo coronary artery bypass graft surgery (3.71%) compared to MPS patients (1.29%).

3. CCTA patients remained a little healthier over time, with a slightly lower likelihood of hospitalization for acute heart attack (0.19%) in the first 180 days after their first test than patients undergoing MPS (0.43%). But patients undergoing CCTA had a similar likelihood of all-cause mortality (1.05%) compared to patients whose testing began with MPS (1.28%).

4. As for costs, both average total spending ($29,719) and spending related to coronary artery disease ($14,943) over the 180-day follow-up period were significantly higher among patients undergoing CCTA, who had nearly 50% higher CAD-related average expenditures than patients undergoing MPS.

5. However, CCTA patients had lower associated spending with echocardiography (-$4,981) and exercise ECG (-$7,449) versus MPS patients.

6. Overall spending related to coronary artery disease was $11,437 for CCTA versus $7,430 for MPS. Average total spending was also significantly lower for patients undergoing MPS ($29,719 for CCTA versus $14,943 for MPS).

Conclusion – costs escalate if you do inappropriate pts
Fused images…. Rispler et al JACC 3/07
Adding SPECT to MSCT to predict events

Rispler et al JACC 3/07
CTCA future

- Myocardial perfusion – 2 studies
  - Excellent correlation JACC Imaging 11/12

- CTCA FFR

- In U.S., MPI = CTCA x 52. heart.org 12/12
Cardiac MRI

- “One stop shop”
- Not routine in Australia -……yet!
- Perfusion and function imaging
- Coronary angiography
- Beware pacemakers
- Can’t exercise
- Excellent for viability with late enhancement to detect MI. Also for congenital heart disease and infiltrative diseases (eg sarcoid)
Tissue Characterisation

Late Gadolinium Enhancement (LGE)

• 10 minutes after gadolinium
• White - myocardial necrosis or scar
• Ischaemic and non-ischaemic conditions
  – Differentiated by pattern of LGE

Subendocardial involvement

Subendocardial sparing
LGE Viability Imaging

Subendocardial scar only - viable

Transmural scar Non-viable
Stress Perfusion MRI

- Pharmacological stress
- Adenosine/dipyridamole or dobutamine
- In magnet during stress
- Limited patient monitoring

- Robust technique
- Technical expertise essential

- Qualitative or quantitative assessment
Stress Perfusion MRI vs SPECT

- **CE-MARC Study**
  - 752 patients, cath as gold standard
  - Comprehensive MRI including LGE
  - MRI more accurate than SPECT
    - SPECT sensitivity 66.5 %
    - MRI sensitivity 86.5 %

- **MR IMPACT I and II**
  - Similar overall accuracy
  - SPECT sensitivity poor - 59 %

1. CE-MARC. Lancet 2011
2. MR IMPACT I EHJ 2008
3. MR IMPACT II EHJ 2012
After STICH is Viability Imaging Dead?

• Viability did not predict mortality benefit from CAGS
• Nuclear, stress echo (no MRI)
• Not randomized based on viability
• Viability may have affected enrollment
• Await LV function data

• However, is there enough other evidence to deny surgery based on lack of viability?

Bonow. NEJM 2011
Coronary MR Angiography

- Non contrast
- Coronary anomalies
- Follow up aneurysms
DCM - Aetiology

Myocarditis

- T2 weighted image (STIR)
  - Evidence of acute inflammation
- ? Recovery more likely
Hypertrophic Cardiomyopathy (HCM)

- Prevalence 1:500
- Most common cause of sudden death in young adults
- Autosomal dominant
  - Sarcomeric proteins
- Diagnosis based largely on imaging
- Hypertrophy in absence of other underlying case
CMR Diagnosis of HCM

Hypertrophy Missed on Echocardiography

• Regions frequently missed on echo:
  – Apical
  – Anterolateral
  – Inferoseptal

• Comprises 12% of all HCM patients
Arrhythmogenic Right Ventricular Dysplasia (ARVD)

- RV cardiomyopathy
- Arrhythmias, sudden death
- Autosomal dominant

- New criteria place greater emphasis on volumes and RV ejection fraction

- Fat in RV free wall no longer part of criteria
  - Also good for SARCOID!!!
Putting it all together....
CT for equivocal MPI

[Diagram showing decision-making process involving various outcomes and interventions based on myocardial perfusion imaging (MPI) results and cardiac computed tomographic angiography (CCTA).]

Abidov et al. JNC 12/10
Hecht...JNC 2/11

Typical Angina

- MPI
  - Abnormal: Consider cath if % ischemia and symptoms warrant
  - Normal
    - 50%-75% stenosis
    - ≥75% stenosis
      - Consider MPI if not already normal
      - Cath if symptoms or stenosis severity warrant
    - Normal: No Further Tests
Algorithm to reduce radiation exposure

Cerqueira et al… JNC 8/10

Aim = < 10 mSv in 50 % studies by 2014
Imaging algorithm 2012

Clinical – Hx, exam, ECG

Asymptomatic – ca score (???), exercise ECG (???) v. nothing

Low risk – exercise ECG

Low-intermediate risk – Stress echo, cardiac CT (?stress MRI)

Intermediate to Intermediate – high – Stress nuclear MPI

  Negative – risk factor control
  Equivocal – another test – CT v. functional v. cath
  Positive – medical (mild ischaemia) v. cath (mod-large ischaemia)
    This depends on test result, symptoms and clinical status!!!

High probability – Cath – if equivocal lesion – Stress nuclear / echo or FFR
CONCLUSION

In 2012, we have choices with variety in availability, cost, radiation, ability to exercise, sensitivity v. specificity and prognostic power.

9/05 – Time Magazine – “Use the test that is done best in your institution”

P. Douglas ACC president.