Acute Chest Pain Evaluation with SPECT and PET MPS

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Ronald G. Schwartz, MD, MS, FACC, FAHA, FASNC
Professor of Medicine and of Imaging Sciences
Attending in Cardiovascular Medicine, Imaging and Prevention
Director of Nuclear Cardiology and Cardiac PET CT
Paul N. Yu Heart Center and Science Park
University of Rochester Medical Center
Rochester, N.Y.
Disclosures

Ronald G. Schwartz, MD, MS, FACC, FAHA, FASNC

Consulting: Astellas, CV Therapeutics, King, Merck, Merck Schering Plough, Pfizer

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Is Imaging Really Necessary?

- Value of a good history is very substantial.
- Too much imaging is going on for the wrong reasons.
- Medical legal liability.
- Imaging should be performed if incremental to clinical assessment for the individual patient.
3 Questions: When Imaging May Be Helpful to Assess Acute CP

• **Dx ?** (ACS? Dissection? GERD? Non-cardiac CP?)

• **Px ?** (Low, intermediate, high?)

• **Rx ?** Reassurance, Lifestyle, Medications, Revascularization?
SPECT MPS: Gatekeeper of Coronary Angiography

• Substantial incremental value compared to clinical, risk factor, stress testing and coronary arteriographic variables.

• Even if CTA were as diagnostically accurate as the gold standard of invasive angiography to which it aspires, it still would have only ¼ to ½ the incremental prognostic value of SPECT MPS.

• SPECT limits rather than promotes use of diagnostic coronary arteriography because of
  • Strong NPV of normal studies
  • Avoids Pavlovian activation of oculostenotic reflex of invasive cardiologists demonstrated in the literature with CTA

• SPECT is proven more cost effective than gold standard invasive coronary angiography (END).

• Avoids risks of contrast nephropathy, allergic reactions including anaphylaxis, and many inappropriate referrals for re-evaluation of unsuspected, clinically irrelevant “incidental findings”

• Able to assess therapeutic response to medical Rx better than cath findings; improved SPECT / PET findings on serial studies are associated with improved clinical outcomes.
TACTICS TIMI 18

Primary endpoint: death, MI, rehospitalization for ACS at 6 months

- Conservative: 19.4%
- Invasive: 15.9%

OR 0.78
95% CI (0.62, 0.97)
p=0.025
Outcomes in TACTICS/TIMI 18

% reaching primary endpoint at 30 d

- TnT>0.01
- TnT<=0.01

Invasive
Conserv

p<0.001
p<0.013

P=NS

Cannon et al, NEJM 2001

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Value of Troponins in UA/NQWMI

Mortality Relative to Cardiac Troponin I Measurement

Cardiac SPECT Provides Incremental Coronary Event Risk Identification Compared to Exercise Testing with ECG


**Cardiac SPECT**

**Tables**

- **Circulation 93, No 5**
- **March 1, 1996**

**Event Rate**

- **Low (0.9%)**
  - Hi / Lo H.R.
    - Nuc vs. Echo
    - 26 vs 4.3

- **Intermediate (2.5%)**
  - Duke TM Score

- **High (7.7%)**

**Annual Mortality**

- **0, 1 or MV**

*Stress Echo Data Marwick Circulation 2001 (Table 4, annual mortality based on 5 year data 0, 1 or MV*)

Hachamovitch R. et al.
Figure 1. Distribution of coronary angiographic findings in women with chest pain who initially underwent stress myocardial perfusion imaging followed by coronary angiography (MPI + Cath) compared with patients proceeding directly to coronary angiography (Cath).
COST-EFFECTIVENESS OF MPI RISK ASSESSMENT

Shaw L et al. J Am Coll Cardiol 1999; 33:661-669
Acute Rest Imaging for Evaluation of ACS

Short Axis

Vertical Long Axis

Horizontal Long Axis

Gated SPECT

Acute

Rest

End Diastole

End Systole

G. Heller, M.D., not to be reproduced without permission of author.
Diagnostic Accuracy of Acute Rest Imaging for Myocardial Infarction

Comparison of Accuracy for 4 Trials

G. Heller, M.D.
55 year old male with atypical chest pain, injected during symptoms

Short Axis

Vertical Long Axis

Horizontal Long Axis
Diagnostic Accuracy of Acute Rest Imaging for Myocardial Infarction

Comparison of Accuracy for 4 Trials

G. Heller, M.D.
ED Risk Stratification Using Tc-99m Sestamibi SPECT Acute Imaging

- Low Risk
- Intermediate
- High Risk

Cardiac Event Rate

ECG
Clinical and ECG
Tc-99m Sestamibi

* p = 0.07
* p = 0.007
* p = 0.0001

Hilton et al JACC 1994:23;1016

G. Heller, M.D.
Incremental Value of Acute Rest MPI in the Prediction of Cardiac Events

Heller et al JACC 1998:31;2351
ERASE Chest Pain Trial: Study Design

- For evaluation of the presence/absence of ACI (AMI or UA):
  - All admitted patients followed for results of serial ECGs and enzymes, follow-up stress testing with imaging
  - All discharged ED patients followed-up 24-48 hrs for ECG and enzymes, and stress testing with imaging
ERASE Chest Pain Trial: Patient Inclusion

- Age > 30 yrs, unless cocaine use
- Chest pain or symptoms suggestive of ACI
- Symptoms ongoing or resolved < 3 hrs prior to consent
- No history of prior AMI
- Normal or non-diagnostic ECG
Results: Patient Inclusion

ED Evaluation

ED pt Sx of ACI
Non-dx ECG

n = 2,889

Informed Consent

n = 2,456
85%

ED Triage

Usual ED Care

n = 1,246

Sestamibi Scan

n = 1,210

Follow-up

ECGs
Enzymes
ETT

Hosp

Home

Hosp

Home

99% complete

n = 1,246

n = 1,210

85%

ED Evaluation

Informed Consent

Usual ED Care

Sestamibi Scan

Follow-up

ECGs
Enzymes
ETT

Hosp

Home

Hosp

Home

2,889

2,456

85%

1,246

1,210

SnM

2008 Annual Meeting

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Cost-Effectiveness of ED Sestamibi Imaging in Suspected ACI

- Usual Care: 683 total hospital admissions
- Sestamibi Scan: 588 total hospital admissions

14% relative reduction

~ $60 - 72/pt savings

AHA Scientific Sessions, 1999
Summary: Acute Rest Imaging in 2008

- Strong predictor of short-term cardiac events
- Very high negative predictive value for acute MI
- Interpretive differences between acute and stress imaging
- Use in clinical decision-making and other acute situations
- Long term risk stratification requires stress imaging
Can CTA function in clinical practice as an effective gatekeeper for coronary angio?

Let us consider a recently published study from a nationally leading CTA group in Royal Oak, Michigan….
A Randomized Controlled Trial of Multi-Slice Coronary Computed Tomography for Evaluation of Acute Chest Pain

James A. Goldstein, MD, FACC, Michael J. Gallagher, MD, William W. O'Neill, MD, FACC, Michael A. Ross, MD, FACEP, Brian J. O’Neil, MD, FACEP, Gilbert L. Raff, MD, FACC

Royal Oak, Michigan

Objectives
This study sought to compare the safety, diagnostic efficacy, and efficiency of multi-slice computed tomography (MSCT) with standard diagnostic evaluation of low-risk acute chest pain patients.

Background
Over 1 million patients have emergency center evaluations for acute chest pain annually, at an estimated diagnostic cost of over $1.0 billion. Multi-slice computed tomography has a high negative predictive value for exclusion of coronary artery stenoses.

Methods
We randomized patients to MSCT (n = 99) versus SOC (n = 98) protocols. The MSCT patients with minimal disease were discharged; those with stenosis >70% underwent catheterization, whereas cases with intermediate lesions or non-diagnostic scans underwent stress testing. Outcomes included: safety (freedom from major adverse events over 6 months), diagnostic efficacy (clinically correct and definitive diagnosis), as well as time and cost of care.

Results
Both approaches were completely (100%) safe. The MSCT alone immediately excluded or identified coronary disease as the source of chest pain in 75% of patients, including 67 with normal coronary arteries and 8 with severe disease referred for invasive evaluation. The remaining 25% of patients required stress testing, owing to intermediate severity lesions or non-diagnostic scans. During the index visit, MSCT evaluation reduced diagnostic time compared with SOC (3.4 h vs. 15.0 h, p < 0.001) and lowered costs ($1,586 vs. $1,872, p < 0.001). Importantly, MSCT patients required fewer repeat evaluations for recurrent chest pain (MSCT, 2 of 99 (2.0%) patients vs. SOC, 7 of 99 (7%) patients, p = 0.10).

Conclusions
Multislice computed tomographic coronary angiography can definitively establish or exclude coronary disease as the cause of chest pain. However, inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations. (Study of Coronary Artery Computed Tomography to Diagnose Emergency Chest Pain CR; http://clinicaltrials.gov/ct/show/NCT00273832?order=1; NCT00273832) (J Am Coll Cardiol 2007;49:863-74) © 2007 by the American College of Cardiology Foundation
CT for gatekeeping in a low risk group? (AKAS: Who’s minding the store? How and Why?)

• EXCLUSIONS:

• 10% patient refused consent for the study.

• Another 46% patients were excluded due to:
  – Pulmonary dz sufficient to exclude B-blocker Rx (18%)
  – Allergy to contrast, iodine, or shellfish (12%)
  – Hx CAD (10%)
  – AF (4%)
  – Other exclusions, unspecified (2%)

Use of CT for gatekeeping: >24% use of Nuclear to risk stratify

Figure 1  Study Algorithm

In this diagnostic algorithm, patients in the multi-slice computed tomography (MSCT) group with normal scans were eligible for immediate discharge. Patients with severe stenosis on MSCT (over 70%) were referred for invasive angiography, whereas those with intermediate lesions or nondiagnostic scans were referred for nuclear stress scans. Patients in the standard diagnostic group underwent nuclear stress scans and were eligible for discharge if normal or referred for invasive angiography if abnormal. SOC = standard of care diagnostic evaluation.
CT for gatekeeping in a low risk group? (AKAS: Who’s minding the store? How and Why?)

- How well did CTA vs. SPECT MPS Standard of Care Work?

Findings:

- No clinical events in either group (Obviously, it’s a low risk group!)
- >24% use of Nuclear to risk stratify still required in CTA group
- 11 vs. 3 referrals for angiography (p value by chi square…. A little help, please Rory?)
- 5 (for CTA) vs 1 (for SPECT) in-hospital revascularizations in this low risk group!
- 6 (for CTA) vs 1 (for SPECT) revascularizations by 6 mos in this low risk group!
- We may ponder, which approach (SPECT vs CTA) better matched the level of diagnostic and therapeutic intervention in this low risk group?

Invasive coronary angiography is the gold standard for localizing stenoses in patients with suspected myocardial ischemia (1). Because this test is invasive and costly and has risks, professional organizations have defined indications for it (1). An expert panel gives a class I recommendation only when it finds strong evidence or general agreement of effectiveness, and the most recent guideline from the American College of Cardiology and the American Heart Association contains few class I indications (1). In patients with asymptomatic or stable angina and known or suspected coronary artery disease (CAD), the class I recommendations are for patients with severe grades of angina (Canadian Classification System classes III and IV) despite intensive medical treatment; patients who, regardless of angina severity, are at high risk for severe ischemia or sudden cardiac death according to noninvasive functional testing; and patients who survived an episode of sudden cardiac death or have a high-risk arrhythmia. Invasive coronary angiography is appropriate in each of these situations because of the high pretest probability of finding high-grade stenoses that will often result in a clinical recommendation for revascularization.

Class I recommendations for invasive coronary angiography had multislice CT (invasive coronary angiography was the gold standard test). The weighted average sensitivity and specificity of MRI for detection of high-grade stenoses were 72% and 87%, respectively, with narrow confidence intervals. Weighted sensitivity and specificity of multislice CT were 85% and 95%, respectively, also with narrow confidence intervals. The data suggest that multislice CT is more accurate, but few if any studies directly compared multislice CT and MRI results in patients who had both tests (head-to-head comparison).

The paper by Dewey and colleagues (3) in this issue presents important new information about the accuracy of multislice CT and MRI for detecting coronary stenoses. In this carefully done study, the authors obtained both multislice CT and MRI in patients presenting to a single tertiary care center in Germany for suspected CAD. Both noninvasive tests were performed within a median of 1 day of the invasive coronary angiography. Direct comparisons in the same patient were possible in 108 of the 129 patients. In per-patient analyses, CT outperformed MRI with higher sensitivity (92% vs. 74%) while specificity was comparable for the 2 tests (79% vs. 75%; P = 0.643). In analyses of specific coronary arteries, both tests performed less

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What is the bottom line for clinicians? Clinicians should not use multislice CT routinely in the evaluation of patients with suspected myocardial ischemia. Multislice CT is not useful in patients with a high pretest probability of CAD and may be harmful. It is useful when the diagnosis is uncertain after a careful chest pain history and equivocal results on functional testing for CAD.”

Cardiac CT

**Strengths**

- **CT coronary calcium** proven for screening and long term risk assessment
- **Coronary CTA**
  - Rapid, easily performed
  - Reassuring when negative
  - High sensitivity and specificity for CAD
  - Unlikely to underestimate or miss high-risk CAD

**Weaknesses**

- Densely calcified plaques: nondiagnostic
- Dependence on low HR and regular rhythm
- Radiation (Einstein A JAMA July 2007), iodinated contrast
- Limited regarding plaque “activity”
- Limited prognostic data of CTA
Myocardial-Perfusion SPECT (MPS)

Strengths

• High technical success rate
• Objective measurements of perfusion and function
• Documented for risk-stratification/management
• Simultaneous multitracer imaging

Limitations

• Does not detect early atherosclerosis
• Currently only “relative” perfusion quantitation
• Frequently underestimates extent of ischemia/CAD

Myocardial PET

**Strengths**

- Routine attenuation correction
- Peak-stress function and perfusion
- Potential to quantify absolute flow and flow reserve
- Proven for viability
- Ease of labeling biologic molecules
- Cost effectiveness (Merhige JNM 2007)

**Limitations**

- Same as SPECT for early atherosclerosis
- Capital expense
- High tracer costs
- Single energy: 1 tracer at a time
Imaging for Acute CP Management

- **Goals:** Manage both symptoms and risk
  - Diagnostic: Is ischemia causing the symptom?
  - Prognostic and Therapeutic Guidance: What is the risk of CAD events (CD, MI, CVA) and what is the best treatment for the patient?
    - No disease: Reassurance, and focus on the Dx and Rx of the symptoms.
    - Small to medium risk: (“Mild to moderate disease”) Aggressive lifestyle and medical therapy
    - High Risk: (“Severe and extensive disease”): Mechanical revascularization.

- **Angiographic stenosis severity vs. outcomes**
  - Mild or non-stenotic disease is frequently unstable and dangerous
  - High grade stenotic disease is frequently stable and poses little risk.

- **Hybrid imaging is the best way to identify both symptoms and risk of CAD and optimize management.**