Nuclear imaging in acute coronary syndromes

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Nuclear imaging in acute coronary syndromes

- The acute coronary syndromes comprise a spectrum from unstable angina, through NSTEMI to STEMI
- Nuclear imaging – and mainly myocardial perfusion scintigraphy can be used for both diagnosis and assessment of prognosis in patients with acute coronary syndromes
- Evaluation of chest pain in the emergency department in patients with suspected acute coronary syndromes
- Assessment of prognosis in patients with UA/NSTEMI and STEMI
Myocardial perfusion imaging in the assessment of patients presenting with chest pain to the ED

- USA: more than 5 million patients/year present to the ED with chest pain and approximately 50% are admitted to the hospital, at a cost of $10 to $12 billion.
- The rate of MI in these patients ranges from 2 to 10%.
- More than one-half of patients admitted for suspected ischemic chest pain are discharged without a proven diagnosis of MI or UA.
- Conversely, 5 to 10% of patients discharged from the ED have an unrecognized acute coronary syndrome.

Differentiation between cardiac and noncardiac chest pain

- Often difficult
- History, physical evaluation, ECG, and cardiac markers or enzymes - many patients with a normal ECG and negative serum markers and enzymes are admitted because of diagnostic uncertainty.
- After initial triage based on symptoms, ECG, and history, rest SPECT imaging in the emergency department appears to be useful for identifying patients at high risk who should be admitted, and patients with low-risk who may be discharged home.

• Tc-99m–labeled agents: trapped in the myocardium and do not redistribute

• Tracer injection at rest in the ED → patients may be transferred to the nuclear cardiology laboratory later (late images reflect MBF at the time of injection).
MPI in ED patients

– Only 1 of 70 patients (1.5%) with normal SPECT results had a significant cardiac event (coronary revascularization)

– 12 of 17 patients (71%) with abnormal scans had an event

• Similar results have been reported with the use of Tc-99m-tetrofosmin.

Diagnostic accuracy of sestamibi SPECT vs cardiac troponin I (cTnI)

- Among 620 patients studied, 9% had AMI and 13% had a final diagnosis of significant coronary disease.
  - **Sensitivity** for detecting MI was similar between SPECT imaging (92%) and cTnI (90%).
  - The initial cTnI value, however, had only a **sensitivity of 39%** and serial determinations were necessary to achieve a high sensitivity.

Incorporating imaging into decision making

- An initial study enrolled 46 chest pain patients who all had resting Tc-99m-tetrofosmin scans.
- The patients were then randomly assigned to have, or not have, scan results provided to the emergency department physicians.
- Patients whose evaluations included the scan results had a 50% reduction in length of stay and hospital costs and similar rates of in-hospital and 30-day follow-up events.

Myocardial perfusion imaging for evaluation and triage of patients with suspected acute cardiac ischemia: a randomized controlled trial

- 2475 adult ED patients with chest pain or other symptoms suggestive of acute cardiac ischemia and with normal or non-diagnostic initial ECG
- Patients were randomly assigned to receive either the usual ED evaluation strategy (n=1260) or the usual strategy supplemented with results from acute resting myocardial perfusion imaging.
- Among patients with acute cardiac ischemia (ie, acute MI or unstable angina; n=329), there were no differences in ED triage decisions between those receiving standard evaluation and those whose evaluation was supplemented by a sestamibi scan. Among patients with acute MI (n=56), 97% vs 96% were hospitalized and among those with unstable angina (n=273), 83% vs 81% were hospitalized.

Usual care vs sestamibi scan supplemented care

Among patients without acute cardiac ischemia (n=2146), hospitalization was 52% with usual care vs 42% with sestamibi imaging

SPECT resting Tc 99m sestamibi imaging
(39 year old man presented to the ED with chest pain, atypical for angina and a near normal initial ECG)

Severe resting perfusion defect in the inferolateral wall
Coronary angiography showed acute Lcx occlusion that was treated with PCI

Udelson JE, Flint EJ. *Heart* 2004 90: v16-v25
Diagnostic accuracy of rest MPI in patients with acute chest pain and a nondiagnostic ECG

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NPV indicates negative predictive value; AMI, acute MI; Tc-mibi, $^{99m}$Tc-sestamibi; Tc-tet, $^{99m}$Tc-tetrofosmin; and NR, not reported.

*Randomized controlled trial.

Adapted from Kontos and Tatum.¹⁰⁷

Testing of low-risk patients presenting to the ED with chest pain. AHA scientific statement

Possible ACS

Presence or absence of symptoms on imaging

- Diagnostic value for detection of CAD is less in the absence of ongoing symptoms.
- When more than 2 to 3 hours have elapsed after symptom cessation, a normal rest perfusion image seems to identify a low-risk patient but does not exclude the presence of CAD.

Ischemic memory imaging

• A potential limitation of rest MPI is the ability to detect ischemia in the patient who is symptom free at, or shortly after, ED arrival. A newer imaging agent, -methyl-p-[123I]-iodophenyl-pentadecanoic acid (BMIPP), may have significant utility in this situation.

• In the setting of myocardial ischemia, high-energy adenosine triphosphate production shifts from fatty acid metabolism to glucose utilization. This suppression of fatty acid metabolism may persist long after the resolution of the perfusion abnormality and ischemia, a phenomenon that has been referred to as ischemic memory.

• Clinical studies have demonstrated persistent reductions in BMIPP uptake long after resolution of ischemic symptoms.

Iodofiltic acid I 123 (BMIPP) fatty acid imaging improves initial diagnosis in emergency department patients with suspected acute coronary syndromes: A multicenter trial

- 50 centers, 448 patients
- ED patients received 5 mCi BMIPP within 30 h of symptom cessation.
- Initial clinical diagnosis was based on symptoms, initial electrocardiograms, and troponin, whereas the final diagnosis was based on all available data (including angiography and stress SPECT) but not BMIPP SPECT.
- Compared with the initial diagnosis alone, BMIPP increased sensitivity from 43% to 81% (p < 0.001), negative predictive value from 62% to 83% (p < 0.001), and positive predictive value from 41% to 58% (p < 0.001), whereas specificity was unchanged (61% to 62%, p NS).

Influence of duration from cessation of symptoms on BMIPP performance

- Among patients who were imaged with BMIPP <12 h after symptom resolution, sensitivity for detection of the truth standard final diagnosis was 77.1%, whereas among patients who were imaged 12 to 30 h after symptom resolution, sensitivity was 68.6%.

- The area under the ROC curve was similar for both groups.

**Figure 3** Example of BMIPP SPECT Imaging in a Patient With Suspected ACS

β-methyl-[123]iodoindyl-oentadecan acid (BMIPP) single-photon emission computed tomography (SPECT) images from the same patient shown in Figure 2: a large defect is observed with BMIPP in the lateral wall, consistent with the stenosis and the potential culprit lesion seen in the left circumflex coronary artery on the angiogram.
Unstable angina

• Patients presenting with unstable angina are a heterogeneous group. Overall, they have an increased risk of death or MI, but still, death or MI actually occurs in only a relatively small minority (10%).
• Thus, treating the entire cohort invasively uses expensive resources very inefficiently.
• A better goal would be to distinguish high-risk and low-risk subgroups.

TIMI 11B trial, Circulation 1999;100:1593-601.
Predischarge risk stratification of patients with UA

- 52 patients with medically stabilized UA underwent exercise planar Tl-201 imaging within 1 week of admission.
- At an average follow-up of 39 months, cardiac death or nonfatal MI occurred in 6 of 23 (26%) patients with thallium redistribution versus 1 of 29 (3%) of those without redistribution ($P < 0.05$).
- The number of segments with thallium redistribution was the only predictor of cardiac death or nonfatal MI on follow-up. Coronary anatomy was not a good predictor of future events.

Thallium SPECT in UA

• In a similar study, patients with UA stabilized on medical therapy underwent a symptom-limited exercise thallium SPECT.
• Reversible thallium defects occurred in 20 of 22 patients (91%) who developed cardiac events versus 5 of 17 patients (29%) of those who did not develop events ($P < 0.0001$), over a mean follow-up of 39 months.

Sestamibi SPECT in UA

- In another study, patients underwent a sestamibi stress myocardial perfusion SPECT study before hospital discharge. The event-free survival was approximately 90% over a follow-up of 18 months in patients with normal scans versus 55% in those with abnormal scans.

- Patients with reversible defects in this study had a less favorable prognosis, with an event-free survival of only 30% over 18 months. Death or MI in this study was rare in patients with a normal scan but occurred in 20% of those with abnormal scans and in 40% of those with reversible defects over 18 month follow-up.

Prognostic value of MPI in UA

- Stress nuclear myocardial perfusion imaging has powerful prognostic value in unstable angina patients.
- The most consistent predictor of death or MI is the presence of reversible defects with an annualized death/MI rate of nearly 20% compared with approximately 1.5% in patients with normal studies.

Prognostic value of quantitative stress myocardial perfusion imaging in unstable angina patients with negative cardiac enzymes and no new ischemic ECG changes

- 136 patients who were hospitalized with unstable angina and subsequently underwent MPI before discharge. Mean follow-up of 31±17 months.
- The significant multivariate predictors of cardiac events were the total perfusion defect size (P=0.002), the presence of reversible perfusion defects (P=0.01), and the presence of multiple perfusion defects (P=0.03).

Kaplan-Meier curves

Cardiac events were much more likely to develop in patients with defects involving ≥15% of the left ventricle than in those with defects involving <15% of the left ventricle (P=0.003).

Positive MPI study in a patient with medically stabilized UA

- Inferobasal infarct and large extent of inducible ischemia involving the inferoapical and lateral walls
- High risk → coronary angiography

Udelson JE, Flint EJ. *Heart* 2004 90: v16-v25
Prognostic value of SPECT myocardial perfusion imaging in patients with elevated cardiac troponin I levels and atypical clinical presentation

- 156 patients with atypical presentations for ACS and elevated cTnI levels.
- The majority of the study cohort had low to intermediate TIMI risk score for unstable angina/NSTEMI.
- The overall event rate was high, with 45 deaths (28.8%).
- A normal MPI result was associated with a high event-free survival rate, whereas an abnormal MPI result was associated with a 3-fold and 7-fold higher risk of all-cause mortality and 6-month cardiac events, respectively. An abnormal MPI result was an independent predictor of all-cause death.

Prognostic value of SPECT myocardial perfusion imaging in patients with elevated cardiac troponin I levels and atypical clinical presentation

A: Risk-adjusted survival curves for overall survival
B: 6-month survival free of cardiac events in patients with normal stress MPI results compared with those with abnormal stress MPI results.

Acute rest myocardial perfusion imaging

- **Tc-99m tracers**: measure myocardium at risk in patients with AMI - minimal redistribution, imaging can be delayed for a few hours after the injection.
- The **final infarct size** assessed by perfusion tomography is a major determinant of subsequent patient survival.
- The availability of alternative methods and the logistics and time demands of performing MPI in the setting of AMI has limited its widespread clinical application.

Imaging myocardial salvage in acute MI

- Myocardial salvage can reliably be quantified by Tc 99m sestamibi imaging.
- Repeated myocardial imaging with 99mTc-sestamibi performed early after symptom onset and days after primary reperfusion treatment allows reliable assessment of the area at risk, final infarct size, and salvage index or the proportion of area at risk that is salvaged by reperfusion therapy.
- Salvage index predicts mortality in patients with acute myocardial infarction after reperfusion therapy.

MPI vs exercise ECG

• MPI was more effective than was exercise ECG testing to predict patient outcomes. The perfusion data provide incremental information over clinical factors and the LVEF.
• When clinical data, resting LVEF, and stress scintigraphic data are combined, coronary angiography may not provide additional incremental value in predicting prognosis

Pharmacologic MPI for post MI assessment

- The advantage of pharmacologic stress compared with dynamic exercise is that studies can be performed earlier after acute infarction.
- In a multicenter study by Brown et al. a predischarge dipyridamole tomographic study better stratified patients into low-, intermediate-, and high-risk groups compared with stratification provided by a submaximal exercise perfusion imaging study.
- This may be a result of enhanced sensitivity for detection of reversible ischemia in patients undergoing pharmacologic stress versus submaximal exercise testing.

Post STEMI risk assessment
ESC guidelines 2008

- With the increasing use of primary PCI, risk assessment before discharge has become less important since it can be assumed that the infarct-related coronary lesion has been treated and the presence or absence of significant lesions in other arteries has been assessed.

- If in spite of angiography performed in the acute phase at the time of PCI there are concerns about inducible ischemia in the infarct or non-infarct area, outpatient stress perfusion imaging within 4–6 weeks is appropriate.

PROSPECTIVE MULTICENTER TRIAL WHICH ENROLLED 728 CLINICALLY STABLE SURVIVORS OF AMI (STEMI 60% – NSTEMI 40%), OVER A 36-MONTH PERIOD, WHO HAD GATED ADENOSINE Tc-99m SESTAMIBI SPECT WITHIN 10 DAYS OF HOSPITAL ADMISSION AND SUBSEQUENT 1-YEAR FOLLOW-UP.

The purpose of this study was to determine whether gated adenosine Tc-99m sestamibi SPECT could accurately define risk and thereby guide therapeutic decision making in stable survivors of acute myocardial infarction.
The INSPIRE study design

Patient risk and subsequent therapeutic decision making were prospectively defined by specific adenosine SPECT variables

Total (A) and cardiac death/reinfarction (B) rates based on INSPIRE risk categories

- Overall cardiac (p = 0.007) (A) and death/reinfarction (p = 0.009) (B) event rates significantly increased across INSPIRE risk groups from low (5.4% and 1.8%) to intermediate (14.0% and 9.2%) to high (18.6 and 11.6%), respectively.

- These differences were observed despite a high initial rate of CR (50%) in the high-risk group. After adjustment for the TIMI risk score, INSPIRE risk categories still predicted total (p = 0.01) and death/reinfarction (p = 0.02) events.

An initial strategy of intensive medical therapy vs coronary revascularization

- Aim: to determine the relative benefit of intensive medical therapy compared with coronary revascularization for suppressing scintigraphic ischemia as assessed by serial gated adenosine Tc-99m sestamibi myocardial perfusion tomography.
- A prospective randomized trial in 205 stable survivors of acute MI.
- All patients at baseline had large total (≥20%) and ischemic (≥ 10%) adenosine-induced left ventricular perfusion defects and an LVEF ≥ 35%.
- Initial imaging: 1 to 10 days of hospital admission
- Repeated imaging: after optimization of therapy (median 62 days).
- Medical therapy was titrated to maximally tolerated doses over 4 to 8 weeks

Reduction in PDS

• Both intensive medical therapy and coronary revascularization induced significant but comparable reductions in total (16.2 ± 10% vs. 17.8 ± 12%; p = NS) and ischemic (15 ± 9% vs. 16.2 ± 9%; p = NS) perfusion defect sizes.

Intensive medical therapy VS coronary revascularization

Patient outcome based on randomized treatment strategy

Serial SPECT images and polar plot of a patient randomized to medical therapy

- **A.** Baseline SPECT → large ischemic perfusion defect (arrows). Total LV PDS is 30% with 25% ischemia and 5% scar.

- **B.** Repeat SPECT → is entirely normal.

INSPRIRE trial - Conclusions

- Adenosine SPECT is a safe and accurate initial method for identifying:
  - 1) a very large low-risk group after AMI (one third of all enrolled patients) who can be targeted for medical therapy and early hospital discharge
  - 2) patients with predominantly scar where initial medical treatment is appropriate
  - 3) those with extensive ischemia where intensive medical and/or interventional therapy is warranted
Recommendations for myocardial perfusion scintigraphy in patients with acute coronary syndromes according to current clinical guidelines

Acute chest pain

• Detection of resting ischemia
  ESC ACC/AHA IIb IIa B

• Detection of ischemia in patients with uncertain diagnosis
  ESC ACC/AHA I A

• Detection of ischemia in low to intermediate risk patients after UA/NSTEMI
  ESC ACC/AHA I B

• Assessment of infarct size and myocardium at risk after STEMI
  ESC ACC/AHA I B

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