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MYOCARDIAL PERFUSION IMAGING “WORKSHOP-1”

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DIFFERENT STRESSORS FOR MPI

EXERCISE

PHARMAKOLOGIC STRESSORS:

DIPYRIDAMOLE
ADENOSINE
A2A AGONISTS (Regadenoson; Binodenoson)
DOBUTAMINE
• EXERCISE STRESS TEST (RATIONALE)

• when appropriate, is always to be preferred to pharmacologic stressors

• It provides information regarding exercise capacity and permits the evaluation of exercise-related symptoms

• It explores the Endothelial dysfunction that is a component of the pathogenesis of inducible ischemia and plays a role in the clinical presentation of CAD

Exercise increases coronary flow on the basis of an endothelium-dependent flow-mediated coronary dilatation of the distal coronary resistance vessels.
MECHANISM OF ENDOTHELIUM-DEPENDENT CORONARY DILATION (normal subjects)

EXERCISE

SHEAR STRESS

NO SYNTHESIS

CORONARY VASODILATION

FUNCTIONAL COMPONENT: ENDOTHELIAL DYSFUNCTION (CAD pts)

EXERCISE

SHEAR STRESS

IMPAIRED N.O. SYNTHESIS

CORONARY VASOCONSTRICTION

EXERCISE-DIPYRIDAMOLE MISMATCH

The importance of the Dynamic Component of CAD may reflect differences in epicardial and microvascular coronary dysfunction

36 pts with suspected angina and normal or near normal coronary angiography.

EX and Dip MPI

Intracoronary infusion of Adenosine (End. Indep.) and Achethlecoline (End. Depend.)

Doppler Flow Velocity

HOW TO PERFORM

ISSUES related to Ex Testing:

• The importance of an “Adequate” level of Ex (if Diagnostic):
  - Reproducing symptoms (in symptomatic pts)
  - >85% MPHR in asymptomatic pts

Medications ON/OFF: OFF if Diagnostic;

ON if Assessment of therapy

The extent of ischemia as a key prognostic factor

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Effect of Exercise Level on the Ability of Thallium-201 Tomographic Imaging in Detecting Coronary Artery Disease: Analysis of 461 Patients

VASODILATOR STRESSORS  
NON SELECTIVE ADENOSINE-RECEPTORS AGONISTS  
MECHANISM

ADENOSINE: Is a non specific agonist of A1, A2A, A2B, A3 receptors  
Its vasodilator effect occurs by interacting  
with the A2A receptors of the smooth  
muscle cells of the coronary resistance vessels.  
Rapid onset of vasodilator effect.  
Adenosine is quickly released from the receptors  
therefore its duration is short (few seconds)(No Aminophilline needed)

DIPYRIDAMOLE: acts indirectly by inhibiting the Re-uptake and deamination of Adenosine  
in the membrane of red cells and endothelial cells.  
By this way it increases the adenosine blood levels.  
It has a slower onset of action with a peak  
vasodilatory effect between 3 – 7 min.  
Its vasodilator effect is longer (up to 30 min.)  
Theofilline, Aminophilline, caffeine inhibit the effect  
of Adenosine and dipyridamole by displacing  
Adenosine from the A2A receptors

FLOW ETHEROGENEITY; NOT NECESSERALLY ISCHEMIA
VASODILATOR STRESSORS: SELECTIVE A2a ADENOSIN RECEPTORS

A2A SELECTIVE AGONISTS: REGADENOSON
BINODENOSON

Selective A2a agonists which increase coronary flow with reduced side effects. Can be used in COPD pts and mild to moderate asthma

Simpler to use compared with Adenosine and Dipyridamole (Bolus)

Regadenoson: Approved FDA

Binodenoson: in the late phase of clinical trials

Very good correlation with Adenosine for scintigraphic results
AGREEMENT REGADOXOSON AND ADENOSINE STRESS MPI (ADVANCE TRIAL)

![Short Axis Diagram](image1)

![Vertical Long Axis Diagram](image2)

![Horizontal Long Axis Diagram](image3)


AGREEMENT BINODOSON AND ADENOSINE STRESS MPI

![Stress and Rest Diagram](image4)

CLINICAL IMPLICATIONS RELATED TO VASODILATOR STRESS TESTS vs EXERCISE

Although vasodilator stress SPECT MPI have been found to have similar diagnostic and prognostic values compared with Ex MPI, some differences exist due to the different mechanism by which they generate flow heterogeneity: (Endothelium independent vs endothelium dependent)

Several reports of direct comparison between exercise and vasodilator MPI have shown a greater extent, severity of defects with Ex compared with dipyridamole test in the same subjects

DIAGNOSIS: Potential reduction in sensitivity and accuracy for detecting Ischemia (they do not explore endothelial vasoreactivity)

PROGNOSIS: Worse prognosis for any kind of MPI results (sicker patients)

Comparison of risk stratification with Pharmacologic and Exercise stress M.P.I. : A meta-analysis

HOW TO PERFORM

ISSUES RELATED TO VASODILATOR STRESS MPI

• COMBINED DIPYRIDAMOLE + EX. STRESS TEST
  (POTENTIAL IMPROVEMENT OF ACCURACY* and PROGNOSIS)

*Only 50% of pts achieve maximal vasodilatation with Dipyridamole standard dose
  (in Iskandrian-Garcia Textbook 2008)

• CAFFEINE STOPPING: should we re-schedule pts who
  have assumed caffeine few hrs before?

• HOW TO THE REDUCE SPLANCIC ACTIVITY?

• DO MEDICATIONS AFFECT THE RESULTS?

Symptom-limited exercise combined with dipyridamole stress:
Prognostic value in assessment of known or suspected CAD by use of
gated SPECT imaging

Symptom-limited exercise combined with dipyridamole stress: Incremental Prognostic value in suspected or known or CAD

Prognosis based on the combination of Dip. MPI results and Functional capacity. Six years event free survival based on combined Risk categorization.

Effect of Caffeine on Ischemia Detection by Adenosine SPECT MPI.
Should we re-schedule pts who have assumed caffeine?


CURRENT PERFUSION TRACERS
HOW TO REDUCE SPLANCHNIC ACTIVITY IN VASODILATOR STRESS MPI? Small amount of Soda Water reduce infracardiac intestinal activity.


HOW ANTI-ISCHEMIC MEDICATIONS AFFECT THE RESULTS OF VASODILATOR STRESS MPI?

They may decrease the diagnostic accuracy of the test.

On the other hand the improvement of inducible hypoperfusion in serial tests can be used to Re-assess the individual risk after therapy.

**NITRATES**: reduce the perfusion defects by increasing myocardial blood flow both in epicardial and collateral vessels.

**CALCIUM ANTAGONISTS**: increase myocardial flow by dilating coronary vessels.

**BETA-BLOCKERS**: Their effect on sensitivity of vasodilator MPI is unclear. Conflicting results.

Calcium Channel Blockers and Nitrates should be discontinued 2 days BEFORE A DIAGNOSTIC Vasodilator stress test.

With regard to Beta Blockers: conflicting result, however discontinuation may be advisable.
DOBUTAMINE STRESS TEST : RATIONALE

Like Ex test it acts by increasing the myocardial Oxygen demand
It increases the CFR less than vasodilator and Exercise tests
Overall slightly lower accuracy in diagnosis
Rarely used only in pts who cannot exercise and in whom vasodilator stressors are contraindicated (Asthma)

COMPARISON OF DIFFERENT VASODILATOR STRESSOR FOR MPI:

WHICH STRESSOR FOR WHICH PATIENT?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Test of Choice</th>
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</thead>
<tbody>
<tr>
<td>Can achieve a good exercise</td>
<td>EX</td>
</tr>
<tr>
<td>Bronchospasm present</td>
<td>Dobutamine</td>
</tr>
<tr>
<td>Exercise limitations present</td>
<td></td>
</tr>
<tr>
<td>LBB or pacemaker present</td>
<td></td>
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<tr>
<td>Large AAA present</td>
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<tr>
<td>Within 72 hrs of Acute MI</td>
<td></td>
</tr>
<tr>
<td>Ongoing Beta Blockers</td>
<td>Adenosine or Dipyridamole</td>
</tr>
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</table>

* Patients scheduled for a diagnostic test who are taking beta-blockers (Beta-blockers affect less the detection of perfusion abnormalities with vasodilator stress compared with Exercise)

Muller-Suur et al Cardiology 2001
DIFFERENT TRACERS
CURRENT SPECT MYOCARDIAL PERFUSION TRACERS

LIMITATIONS:

• Disproportionately LOW MYOCARDIAL UPTAKE under Stress conditions with myocardial hyperemia

• SUB-OPTIMAL Heart/Splanchnic Activity

• POOR IMAGE QUALITY IN OBESE PTS

MAJOR LIMITATION OF THE CURRENT PERFUSION TRACERS

With the current SPECT perfusion tracers showing a plateau at flow > 2 ml/min/gr it is hard to detect differences in regional myocardial perfusion above 2 - 2.5 times the resting flow. This limits the sensibility for detecting moderate stenosis.
CURRENT PERFUSION TRACERS: LIMITATIONS (splanchnic activity)

Despite the tremendous growth on SPECT MPI we use the same tracers from 20 yrs.
Little advancements have been performed by industries to overcome artifacts.
We are using the same Anger cameras from 40 years.

BMS-747158-02
A novel PET myocardial perfusion imaging agent

Ming Yu et al. J. Nucl. Card. 2007.07.008
BMS-747158-02: A novel PET myocardial perfusion imaging agent

Sequential Whole Body Images of BMS747158
Normal volunteer

"POTENTIALLY NEW" OLD TRACERS: Tc-TEBOROXIME

Introduced in the early nineties

**Favourable properties:** Linear relationship between:
Tebo myocardial activity and Myocardial flow
(better than Thallium and Tc-agents)

**Limitations:** rapid myocardial wash-out

Did not reach a widespread use because of its very rapid myocardial wash-out making the imaging quite difficult with the available cameras

With the new Ultrafast cameras with a reduced imaging time of 3-5 minutes, Teboroxime could be re-introduced with potential Higher Lab. Efficiency, Furthermore, its more favourable Myocardial uptake vs flow Could translate in a better accuracy in detecting moderate stenosis
TRADITIONAL AND NEW GAMMA CAMERAS and ACQUISITION PROTOCOLS

Limitations of current SPECT MPI:

• Long image acquisition time (20 min) favouring motion artifact due to pt. disconfort
• Low spatial resolution
• High Radiation dose

Recently New Imaging Systems have been introduced with:

- Shorter acquisition time and improved patient confort
- Better image quality and resolution
- Lower radiation dose

-Probably the most interesting evolution is represented by a ultrafast camera using CZT solid-state detector technique combined with Multi-Pinhole Colimator approach.

NEW CAMERAS (DIGIRAD CARDIUS)

Acquisition time: 5 min; smaller size; more comfortable; detectors remain fixed; Patient in a rotating chair

Advances in technical aspects of myocardial perfusion SPECT imaging
(CARDIARC)

Detectors and collimators redesigned for cardiac imaging only;
Pt not moving; The detector apparently fixed; the inner part are moving;
Detectors: 3 curved NaI crystals. Imaging time: 2 nìmin


Advances in technical aspects of myocardial perfusion SPECT imaging
(GE ULTRAFAST CARDIAC CAMERA)

Allows ultrafast imaging; 2 min. (Stress); 4 min. (Rest) acquisition
Higher myocardial counts for the same dose
Excellent image quality (85% vs 65% of traditional cameras)

Solid State detector technique
CZT (Cadmio Zinc Telluride detectors): higher resolution and sensitivity

Multipinhole collimator approach: allows simultaneous acquisition of the entire heart
without the need for motion of the detector, collimator or patient. Reduced motion artifacts
GE ULTRAFAST CARDIAC CAMERA vs CONVENTIONAL CAMERA:
NORMAL PATIENT

<table>
<thead>
<tr>
<th>Ultrafast Cardiac Camera</th>
<th>Conventional SPECT Camera</th>
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<tbody>
<tr>
<td>2 min. Stress-4 min Rest</td>
<td>12 min Stress-14 min Rest</td>
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Courtesy E. Garcia Emory Univ.

ADVANTAGES OF CZT Technology

Eliminates scintillation and photomultiplier tubes:
- higher spatial resolution
- higher energy resolution
- smaller size

Provides:
- improved image contrast
- faster scanning / lower dose scans
Detectors

140 keV

• Size
• Energy resolution

~ 1,000 charges

~ 31,000 charges

Nal

PMT PMT PMT PMT

CZT

e

e

Low dose
Female, 61 yr
Atypical angina
Waiting for major abdominal surgery
Hypertension
Wash Out therapy
Dipyridamole stress
No ECG changes
Single day stress/rest protocol
Normal Myocardial Uptake

STRESS: 3mCi
REST: 7mCi

HYBRID IMAGING
PET/CT
Pt with suspected CAD

SPET/CT
Immediate assessment of the functional consequences of coronary lesions assessed by CTA

47 yrs man; Smoking and dyslipidemia
Atypical chest pain

CTA: LAD: 50-70% prox long stenosis
RCA: occluded
LCx: small calcified plaque


POTENTIAL OF HYBRID IMAGING

74 yrs woman; Hypertension; Diabetes, Dyslipidemia
Evaluation of chest pain and syncope

CTA: LM: calcified plaque <50% stenosis
LAD: 70% stenosis in prox. + 50-70% mid stenosis
RCA: 50% mid segment + 50% distal
Cx: free

Difference in regional myocardial uptake vs Quantification of absolute myocardial blood flow (ml/gr/min)

Relative regional myocardial uptake


Better definition of ischemia in MVD

Absolute myocardial Flow (ml/gr/min)

HYBRID CAMERA PET/CT

Microvascular Disease

Pt with effort angina and normal coronary arteries

PET/CT HYBRID IMAGING
BALANCED ISCHEMIA
Anterior view  Posterior view
Pt with MVD

myocardial Perfusion
Relative regional myocardial uptake

Absolute myocardial Flow
(Ml(gr/min)

Conclusion

• Risk of redundancy
• Added value or added costs?
• Appropriateness of pts selection: consider pre-test probability
• Imaging is only one aspect of the evaluation strategy
• Clinical evaluation should remain central
THANK YOU