Pharmacologic Stress Agents

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Disclosure

Neither I nor my immediate family members have a financial relationship with a commercial organization that may have a direct or indirect interest in the content.
Perfusion Options

- ECG stress
- Echocardiography
- Nuclear
  - SPECT
  - PET
- MRI
- CT
### Perfusion Performance Characteristics *

<table>
<thead>
<tr>
<th>Modality</th>
<th>SEN</th>
<th>SPEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress ECG</td>
<td>61%</td>
<td>70%</td>
</tr>
<tr>
<td>Stress Echo</td>
<td>79%</td>
<td>87%</td>
</tr>
<tr>
<td>SPECT</td>
<td>88%</td>
<td>73%</td>
</tr>
<tr>
<td>MRI</td>
<td>93%</td>
<td>75%</td>
</tr>
<tr>
<td>CCTA</td>
<td>81%</td>
<td>71%</td>
</tr>
<tr>
<td>CT perfusion/viability</td>
<td>89%</td>
<td>96%</td>
</tr>
</tbody>
</table>

Based on Gold standard Of > 50% stenosis on Angiography

*Andrew Bierhals, MD, MPH: “Cardiac Perfusion and Viability Detection with Computed Tomography” July 2011*
Perfusion MRI vs. SPECT

There are many possible justifications for choosing MRI. These include:

- Higher spatial resolution
- Shorter exam time
- Absence of soft tissue attenuation artifacts
- No radiation
- More accurate quantitative assessment of myocardial viability and ventricular/valvular function
- Subendocardial vs. transmural
Our Clinical Experience

Overall, since the CPT code (75563) was introduced in 2008, relatively few cardiac stress perfusion MRI’s have been performed.

We have completed 44 at our site.
Personal Research Perfusion MRI Experience

Since 1999, we have conducted 185 cardiac perfusion MRI studies using either Dobutamine, Adenosine and lastly Lexiscan between 5 different research studies.

- Dobutamine MRI’s- 89
- Adenosine MRI’s- 49
- Lexiscan MRI’s- 47
MR Perfusion Stress Agents: Past and Present

- Dipyridamole (persantine)
  - 0.142-mg/kg/min IV infusion over 4 minutes

- Adenoscan (adenosine)
  - 140-µg/kg/min IV infusion over 4-6 minutes

- Lexiscan (regadenoson)
  - 0.4-mg/5mL IV bolus injection
The stress chemical agents used today in the cardiac MRI setting are Lexiscan, Adenosine and Dobutamine.

Lexiscan and Adenosine are vasodilators that are extremely short acting and easier to use.

Dobutamine is an inotopic vasopressor that requires incremental increases in doses, therefore taking a longer time to stress the heart.
What is Dobutamine?

- Dobutamine is a synthetic chemical with primarily beta 1 adrenergic activity (rocket fuel for the heart).
- Here it is used as an agent to increase heart rate.
- Dobutamine is supplied as Dobutamine HCl, a synthetic inotropic agent related structurally to dopamine. It occurs as white, to off-white, crystalline powder with a pKa of 9.4. Dobutamine is sparingly soluble in water and alcohol.
Dobutamine Stress Protocol--Function

- **Ischemia** – “high dose” dobutamine. Look for development of focal regions of wall abnormality. These regions are ischemic.

- **Viability** – “low dose” dobutamine. Look for segmental improvement in wall thickening or “recovery” in regions of dysfunctional myocardium at rest.
Dobutamine Stress Protocol--Ischemia

- Imaging at rest and then with dobutamine IV, 5, 10, 20, 30, 40 μg/kg per minute for three minutes at each dose level.

- At 40 μg/kg may add atropine (up to 1 mg) to reach submaximal heart rate [(220-age) x 0.85].

- Stop at any dose level when wall motion abnormality is observed.

- At each dose level, acquire 4-chamber LA, 2 chamber LA and 3-5 SA images.
“LOW DOSE” Dobutamine

- Same SA and LA images at rest, 5µg and 10µg/kg/min of IV dobutamine.
- 3 min infusion at each dose level.
- Viable dysfunctional regions show increase in systolic function, improvement in “wall thickening”.
- Analysis: visually or measure myocardial thickness.
Dobutamine Perfusion MRI Monitoring

- 12 lead EKG before and after study.
- Run lead II tracing during study, vital signs, SaO2.
- Fully stocked crash cart and defibrillator should be available.
- ACLS-certified personnel.
Dobutamine Perfusion MRI Monitoring

- Ability to communicate with patient.
- Must watch images as they appear AND be able to compare with images at the lower Dobutamine levels to assess for wall motion abnormalities before going on to next step. Once abnormal wall motion develops – STOP.
- If necessary, effects of dobutamine can be reversed using 0.5 mg/kg of esmolol injected IV as a slow bolus.
What is Adenosine?

- Adenosine is an A2a agonist agent present in all cells of the body (endogenous nucleoside).

- Adenosine is a white crystalline powder soluble in water.

- Each vial contains 3mg/ml.
Adenosine Pharmacology

- A potent vasodilator in vascular beds except in renal afferent arterioles and hepatic veins where it produces vasoconstriction.

- Increases blood flow to normal coronary arteries 4-5 times with little or no increase in stenotic arteries.
Adenosine Hemodynamics

- Adenosine produces negative chronotropic, dromotropic and inotropic (rate, velocity, force) effect on the cardiac muscle fibers and nerves.

- Net effect is a mild to moderate decrease in systolic, diastolic and mean arterial blood pressure associated with a reflex increase in heart rate.

- Rarely significant hypotension or tachycardia have been observed.
Adenosine Pharmacokinetics

- Rapidly cleared from the circulation by cellular uptake. It is degraded by the cell.
- Half life of <10sec. makes this a great drug in the clinical setting.
- Requires no hepatic or renal function for activation.
- Renal or hepatic failure does not alter its effectiveness or tolerability.
Adenosine and Lexiscan Stress Indications

Alternative to exercise stress testing for:
- Patients with Angina Pectoris
- Risk stratification
- Surgical clearance
- Post MI and coronary revascularization procedures
- Patients with risk factors for CAD or atypical chest pain

When exercise stress is not possible or desirable:
- Patients with LBBB
- Paced rhythm
- Concomitant treatment with meds that blunt the heart rate response (beta blockers and calcium channel blockers)
Adenosine Stress
Contraindications

- Second or third degree atrial-ventricular node block
- Sinus node disease, such as sick sinus syndrome or symptomatic bradycardia
- Known or suspected bronchoconstrictive or bronchospastic lung disease (COPD per se is not a contraindication)
- Known sensitivity to adenosine
- Systolic BP<90mm Hg.
- Severe sinus bradycardia (<40/min) is a relative contraindication
Adenosine Dosage and Administration

- Adenosine should be administered through a separate peripheral vein by continuous infusion over 4 minutes.

- The dose for adults is 140μg/kg/min.

- Infusion rate = \( 0.140 \text{(mg/kg/min)} \times \text{body wt. (kg)} \) (ml/min) Adenosine concentration (3mg/ml)
What is Lexiscan?

- An A2a adenosine receptor agonist
- Regadenoson has a 2- to 3-minute biological half-life, as compared with adenosine's 30-second half-life.
- Regadenoson stress protocols using a single bolus have been developed, obviating the need for a second intravenous line.
Lexiscan administration is performed in several steps:

- Administer Lexiscan as an IV injection over approximately 10 seconds into a peripheral vein using a 20-gauge or larger catheter or needle.
- Administer a 5-mL saline flush immediately after the injection of Lexiscan.
- Administer the contrast agent 10-20 seconds after the saline flush. The radionuclide may be injected directly into the same catheter as Lexiscan.
Adenosine and Regadenoson Stress Patient Preparation

- Restriction of Xanthine containing products 24-36 hours before test (Tea, coffee, Uniphyl, Theo-Dur, Slo-Bid, Theophylline etc.) Theophylline is the antidote for Adenosine.
- NPO at least 6, however best if 8 hrs. before test
- No caffeine at least 6, however best if 24 hrs. before test
- No tobacco for 4 hrs. before test
- Any prior studies with results should be available and reviewed by clinician.
- Cardiac enzymes (CK, CK-MB, Troponin) reviewed only in case of angina symptoms
- Prior 12 lead EKG available and reviewed
- Order checked
Stress test explained and informed consent completed

Chest prepared, EKG electrodes placed

IV access obtained with a large bore catheter no smaller than a #20 gauge. (A smaller catheter will result in having to slow down contrast bolus which may result in a less than optimum study.)

Baseline EKG, BP, HR and pulse oximetry

IV sedation PRN. (Versed 1mg. IVP)

With IV sedation -O₂ via nasal cannula at 2L/min
CCTA Perfusion

- Increases performance of CCTA by up to 20%
- Single and dual energy acquisition of data
  - Dual energy improves sensitivity
  - Permit better tissue differentiation based on attenuation
- Optimize timing for peak of contrast in LV blood pool
- Enhancement on delayed (10 min) correlates to functional recovery
CCTA Perfusion

**Advantages**
- One stop shopping
- Incremental gain over CCTA
- Evaluate plaque composition
  - Limited with dual energy
- High spatial resolution
- Delayed enhancement for viability

**Disadvantages**
- Blooming artifact
- Single pass for perfusion
  - Optimize timing
- Medications for image optimization may result in false negative study
- Incidental findings (up to 25% clinically significant)
Food for Thought

- Why haven’t there been more cardiac perfusion MRI’s ordered since it is now reimbursed?

- Should SPECT and perfusion MRI be considered equivalent imaging modalities?
Special Thanks

- Advanced Cardiac Imaging (Cardiac CT/MRI)
- Center for Clinical Imaging Research (CCIR)
- Radiology Dept. at Barnes Hospital
- Cardiovascular Imaging Laboratory