Pharmacologic Stress Testing

Pharmacologic Stress With and Without Adjunctive Exercise:

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Question 1

♥ Which agent do you use routinely for vasodilator stress in your laboratory?

1. Dipyridamole
2. Adenosine
3. Regadenoson
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**Question 2**

❤ With vasodilator stress (adenosine, regadenoson, and dipyridamole), do you routinely perform simultaneous low level treadmill exercise?

1. Yes
2. No

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**Question 3**

❤ A husband and wife both present for vasodilator stress MPS.

❤ The husband had a Venti (20 oz) cup of Starbucks coffee 24 hours ago. The wife had a Venti (20 oz) cup of Starbucks decaf coffee 1 hour ago.

❤ Which patient would you reschedule due to caffeine?

1. Husband – Coffee 24 hours ago
2. Wife – Decaf 1 hour ago
3. Both
4. Neither
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CSMC Experience

Adenosine: Mechanism of Action (1)

Verani et al, Am Heart J 1991;122:269-278
Adenosine: Mechanism of Action (2)

- Adenosine activates cell surface receptors:
  - **A\textsubscript{2A}** receptor:
    - Vascular smooth muscle → coronary vasodilation
    - 4-5 fold increase in coronary blood flow
  - **A\textsubscript{1}** receptor:
    - Sinoatrial (SA) and Atrioventricular (AV) nodes
    - Delay in AV conduction (Rx for SVTs)
  - **A\textsubscript{2B}, A\textsubscript{3}** receptors: bronchospasm
  - **Future:** Pure A\textsubscript{2A} agonist would be ideal

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Adenosine: Mechanism of Action (3)

Myocardial Blood Flow

![Graph showing Myocardial Blood Flow](image)

Iskandrian, JNC 1:94-111, 1994
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Adenosine: Mechanism of Action (4)

- Normal Artery: flow ↑ 4-5 fold
- Diseased Artery: smaller flow (↓ coronary flow reserve)
- Regional flow heterogeneity (usually without ischemia) produces reversible defect on SPECT
- 1/3 pts: ischemia (critical stenosis)

Adenosine Stress Protocol (1)

5 Minute Infusion

Inject isotope

Adenosine 140 mcg/kg/min

SPECT

Time (min)

0 1 2 3 4 5

15 min (if adeno walk)
60 min (if no walk)
15 min (if \textsuperscript{201}TI)
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Adenosine Stress Protocol (2)

<table>
<thead>
<tr>
<th>Rate of IV infusion</th>
<th>% achieving max. vasodilation</th>
<th>↑ in coronary blood flow velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>70 µg/kg/min</td>
<td>16%</td>
<td>3.1-fold</td>
</tr>
<tr>
<td>100 µg/kg/min</td>
<td>44%</td>
<td>4.4-fold</td>
</tr>
<tr>
<td>140 µg/kg/min</td>
<td>84%</td>
<td>4.4-fold</td>
</tr>
</tbody>
</table>

♥ Standard dose: 140 µg/kg/min IV

♥ 84% achieve maximal (92% near-maximal) vasodilation at 84 ± 46 sec. (23-125 s.)

♥ Therefore a 2 minute infusion preceding injection of isotope allows ample time for maximal vasodilation.

Wilson, *Circ* 1990;82:1595-1606

Adenosine Stress Protocol (3)

♥ After termination of adenosine infusion:

♥ CBF returns to 50% of maximal change in 37 ± 18 sec.

♥ CBF returns to baseline in 154 ± 88 sec.

♥ Continuing adeno infusion for 3 minutes after injection of sestamibi allows time for complete uptake during maximal CBF

Adenosine Stress Protocol (4)

- Adenosine stress perfusion cardiac MRI
  - 5 minute adenosine infusion

- Adenosine stress perfusion PET (e.g. Rb)
  - 7 minute adenosine infusion

- Selective A2 agonists given by IV bolus will likely simplify stress protocols, e.g. MRI compatible adeno infusion pump not needed

Adenosine Stress Protocol (5)

AdenoWalk and RegWalk Protocols

- Adding low-level treadmill exercise to vasodilator stress:
  - ↓ side effects
  - ↓ symptomatic hypotension and bradycardia
  - Walking induces splanchnic vasoconstriction
    - ↑ target to background ratio
  - Allows for immediate imaging – as would be done with exercise stress.

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Adenosine Stress Protocol (6)

- Simultaneous with start of adeno infusion, perform a low-level treadmill test for those patients that can tolerate walking slowly.
- Walk patient at 1.7 MPH with 10% incline (Bruce stage 1 as the standard) for entire duration of adenosine infusion. If patient cannot tolerate incline, use 2 MPH. If patient cannot walk fast then use 1 MPH.
- Do not walk patients who have left bundle branch block, pacemakers, abdominal/thoracic aneurysms, or recent MI within last 3 days

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Regadenoson

- A selective A2A adenosine receptor agonist
- Most commonly used coronary vasodilator stress agent
- Equivalent to adenosine in assessing the extent of reversible perfusion defects (two phase III studies)
**Regadenoson**

**Dosage & Administration**

- Recommended IV dose: 0.4 mg.
  - Fixed dose in pre-filled 5 ml syringe
  - No weight adjustment.
  - No infusion pump.
- Administer as a rapid IV injection (10 seconds).
- Administer a 5 mL saline flush immediately after the injection of regadenoson.
- Administer the radionuclide MPI agent 10–20 seconds after the saline flush.

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**Regadenoson**

**RegWalk Protocol**

- Inject isotope
- Low level exercise
- Time (min) 0 1 2 3 4
- SPECT
  - 15 min (if Reg walk)
  - 60 min (if no walk)
  - 15 min (if $^{201}$Tl)

Regadenoson 0.4 mg IV over 10 sec, 5 cc saline flush IV
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Dipyridamole Stress Protocol

- **Inject isotope**
- **SPECT**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Dipy (0.56 mg/kg)</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>15 min (if dipy walk)</th>
<th>60 min (if no walk)</th>
<th>15 min (if 201Tl)</th>
</tr>
</thead>
</table>

Maximal vasodilation occurs at 287 ± 101 seconds. Thus, the radiotracer is not injected until 3 to 5 minutes after the dipyridamole infusion is completed.

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Indications for Vasodilator Stress

- Heart failure
- Inability to exercise (e.g. arthritis, stroke, PVD, chronic lung disease, amputation)
- Inability to achieve ≥ 85% of MPHR (e.g. chronotropic incompetence, beta-blocker)
- Left bundle branch block
- Ventricular paced rhythm
- Early post MI or unstable angina (after medical stabilization)
LBBB and Paced Ventricular Rhythm

- Exercise stress often produces false-positive perfusion defects in the interventricular septum
  - related to $\uparrow$ HR and prolonged septal systole
- Vasodilator stress preferred
- Patients referred for pharm. stress frequently have significant $\uparrow$ HR with even minimal exertion
- Therefore do not use low level treadmill exercise during adenosine stress in these pts

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Early Post-MI

- Brown et al.: 441 patients with first acute MI
  - early (day 2 to 4) dipyridamole $^{99m}$Tc-sestamibi SPECT
  - predischarge (day 6 to 12) submaximal exercise $^{99m}$Tc-sestamibi SPECT
  - early dipy: no adverse events
  - Dipy sestamibi imaging showed better risk stratification than submaximal exercise myocardial perfusion SPECT
- adenosine may be preferable due to its very brief T$_{1/2}$
- substantial cost savings could be realized by early stress testing strategy

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Contraindications

Adenosine/Dipyridamole

- Asthma or active bronchospasm
- Severe COPD with rest hypoxia (e.g. home O₂)
- Advanced AV block
- Sick Sinus Syndrome
- Severe bradycardia (HR < 40 bpm)
- Hypotension (SBP < 90 mmHg)
- < 2 days after acute MI
- Recent use (< 24 hours) of theophylline or caffeine

Regadenoson

- Contraindications:
  - 2° or 3° AV block or sinus node dysfunction
    → unless pt has functioning pacemaker
- Not contraindicated:
  - bronchoconstrictive or bronchospastic lung disease
- Warning: Regadenoson may cause dyspnea, bronchoconstriction, or respiratory compromise. Bronchodilator and resuscitative measures should be available.
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Caffeine

- Caffeine occurs naturally in > 60 plants
  - coffee beans
  - tea leaves
  - kola nuts (soft drinks)
  - cacao pods (chocolate)
- 90% of people in the world use caffeine
- 80% of U.S. adults consume caffeine every day
- Average adult intake = 200 mg/day (two 5 oz cups coffee or four sodas)

- Competitive inhibitor of adenosine binding
- Can eliminate the effects of dipyridamole or adenosine on coronary vasodilation.
  - Smits, JNM 1991: 6 of 8 pts had false neg. dipy 201Tl.
- Half-life of caffeine is variable (may be > 5-7 hrs):
  - Package insert - no caffeine for:
    - 24 hours prior to dipyridamole or adenosine stress
    - 12 hours prior to regadenoson stress
- The HR and BP response does not provide accurate information regarding whether the pharmacologic effects of adeno or dipy have been blocked by caffeine (Amanullah, et al, AJC 1997;79:1319-1322)
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Caffeine

- 22 men and 8 women, age 64 ± 9 years with reversible defects on adenosine MPS performed while off caffeine.
- Studies repeated with one 8-oz cup of coffee taken 1 hour before adenosine stress.
- No difference in SSS, SDS, or % total defect size.
- Author’s conclusion: “Until further studies become available, we believe that one cup of coffee should not be a reason to cancel a scheduled adenosine study or to change to dobutamine.”

Zoghbi, JACC 2006;47:2296 –302

Caffeine

Regadenoson

- Subjects with ≥ 1 reversible defect returned for 2nd regadenoson MPI (with caffeine vs. placebo).
- 347 subjects (114, placebo; 116, 200 mg caf.; 117, 400 mg caf.); equivalent to 2-4 (5 oz) cups of coffee.
- Results: 26/36 (72%) subjects with 2-4 reversible defects and 5/5 (100%) with ≥ 5 rev. defects shifted to lower ischemia group when received caffeine prior to 2nd study.
- Conclusion: Caffeine reduces # of reversible segments by regadenoson MPI in non-dose dependent manner.

Tejani, JNC 2011; 18:759-60
Caffeine

Regadenoson

Package insert (Oct 2011):

Patients received caffeine or placebo 90 minutes before the second Lexiscan stress MPI. Following caffeine administration (200 or 400 mg), the mean number of reversible defects identified was reduced by approximately 60%. This decrease was statistically significant.

<table>
<thead>
<tr>
<th>Food/beverage/med</th>
<th>Caffeine (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee</td>
<td>85-150 mg/cup</td>
</tr>
<tr>
<td>Decaf</td>
<td>2-4 mg/cup</td>
</tr>
<tr>
<td>Tea</td>
<td>60-75 mg/cup</td>
</tr>
<tr>
<td>Coca-cola</td>
<td>34 mg/12 oz</td>
</tr>
</tbody>
</table>
### Caffeine

| One 5 oz cup of coffee | Caffeine (mg) | | 
|------------------------|---------------|
|                        | Regular Coffee | Decaf |
| 0 hours (0 T\(_{1/2}\)) | 100           | 4     |
| 6 hours (1 T\(_{1/2}\)) | 50            | 2     |
| 12 hours (2 T\(_{1/2}\)) | 25            | 1     |
| 18 hours (3 T\(_{1/2}\)) | 12            | 0.5   |
| 24 hours (4 T\(_{1/2}\)) | 6             | 0.25  |

**Recommendations:**
- Regular coffee – off 24 hours
- Decaf coffee – ok if sure

### Food/beverage/med

<table>
<thead>
<tr>
<th>Food/beverage/med</th>
<th>Caffeine (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee Flavored Yogurt</td>
<td>45 mg/8oz</td>
</tr>
<tr>
<td><strong>Milk Chocolate</strong></td>
<td>3-6 mg/oz</td>
</tr>
<tr>
<td>Bittersweet Chocolate</td>
<td>25 mg/oz</td>
</tr>
<tr>
<td>Anacin</td>
<td>64 mg/2 tab</td>
</tr>
<tr>
<td>Excedrin</td>
<td>130 mg / 2 tab</td>
</tr>
</tbody>
</table>
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Effect of Antianginals on Vasodilator Stress (1)

- 26 pts undergoing 2 dipy studies:
  - the first without and the second with antianginal treatment.
- Anti-anginals:
  - calcium antagonists - 21 pts (81%)
  - nitrates - 19 (73%)
  - beta-blockers - 8 (31%)
- 18 pts underwent cath.
- Quantitative analysis: larger stress perfusion defects off meds
  - LAD territory (25% vs. 17%, p = 0.003)
  - LCx territory (56% vs. 48%, p = 0.03)
  - RCA territory (36% vs. 25%, p = 0.008)

Sharir, JACC 1998;31:1540-6
Effect of Antianginals on Vasodilator Stress (2)

<table>
<thead>
<tr>
<th>Vessel Sens.</th>
<th>Off Meds</th>
<th>On Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>93%</td>
<td>64%</td>
</tr>
<tr>
<td>LCx</td>
<td>79%</td>
<td>50%</td>
</tr>
<tr>
<td>RCA</td>
<td>100%</td>
<td>73%</td>
</tr>
<tr>
<td>Overall</td>
<td>92%</td>
<td>62%</td>
</tr>
</tbody>
</table>

❤ CONCLUSION: Antianginal drugs before vasodilator stress reduce the extent/severity of perfusion defects, resulting in underestimation of CAD

Sharir, JACC 1998;31:1540-6

Effect of Beta-Blockers on Diagnostic Accuracy of Vasodilator MPI

❤ 555 pts without known ischemic heart disease
❤ 289 on β-blocker (vs. 266 not on β-blocker)
❤ Vasodilator MPS and cath within 90 days
❤ Retrospective study
❤ Sensitivity (global and per-vessel) and SSS similar between pts taking vs. not taking β-blockers

Figure 1. Global sensitivities and specificities of vasodilator radionuclide MPI for the detection of significant CAD (≥70%) confirmed by angiography, with the normalcy rates for patients with low pretest likelihood of coronary disease. Reported as percentages (%).

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Acute Beta-Blockade Reduces the Extent and Severity of Perfusion Defects with Dipy SPECT

- 21 pts with CAD on cath
  - prospective, double-blind, placebo-controlled study
- The sensitivity of dipy MPI for detection of CAD was 85.7% with placebo vs. 71.4% with metoprolol
  - FN rate 14% -> 29%!
- Conclusions: The presence and severity of CAD are underestimated in pts receiving beta-blocker undergoing dipy stress MPI

Taillefer, JACC 2003;42:1475-83

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Effect of Antianginals on Vasodilator Stress (3)

- Thus, in order to increase vasodilator stress test sensitivity, in Feb 2005 we removed the following sentence from the patient instructions:
  - “if you are undergoing adenosine stress continue all your blood pressure and heart medications”
Pts scheduled for exercise testing frequently have to be converted to pharm stress on the day of the study (e.g. LBBB, paced, unable to achieve 85% of MPHR)

Therefore all pts should receive the same instructions:

• No **caffeine** (sodas, coffee, tea, chocolate, medications) for at least 24 hours prior to stress testing.

• Hold **β-blockers** (48 hours), **calcium blockers** (24 hours), and **long acting nitrates** (6 hours) before stress testing to maximize extent/severity of reversible defects.

Benefit of having all pts be caffeine free:

• allows for immediate conversion to vasodilator (adeno/regadenoson/dipy) stress

Benefit of making cardiology wards and CCU caffeine free:

• Inpatients no longer need to be rescheduled

• Prevents prolonging hospitalization by an extra day (saves time and $$)
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Vasodilator Side Effects

Adenosine

<table>
<thead>
<tr>
<th>Event</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>36.5</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>35.2</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>34.6</td>
</tr>
<tr>
<td>GI Discomfort</td>
<td>14.6</td>
</tr>
<tr>
<td>Headache</td>
<td>14.2</td>
</tr>
<tr>
<td>TMJ discomfort</td>
<td>11.6</td>
</tr>
<tr>
<td>AV Block</td>
<td>7.6</td>
</tr>
</tbody>
</table>


Vasodilator Side Effects

Reversal with Aminophylline

Adenosine:

- very short half-life of 2-10 seconds
- side effects will typically resolve within 1-2 min

Persistent SE or significant adverse events after reg/adeno/dipy can be reversed with:

- Aminophylline 75-125 mg IV given slowly over 30 sec.
- may be repeated up to a total dose of 300 mg.
Safety of Adenosine/Dipy

- 9 cardiac deaths out of 89,973 patients
  - 1 death per 10,000 vasodilator stress MPI studies


Regadenoson: Adverse Reactions (1)

- Adverse reactions occurred at similar rates between the study groups in Phase 3 studies
  - Regadenoson group, 80%; Adenosine group, 83%.
- Aminophylline use for reactions:
  - Regadenoson group, 3%. Adenosine group, 2%.
- Most adverse reactions began soon after dosing, and generally resolved within approximately 15 minutes, except for headache which resolved in most patients within 30 minutes.
Regadenoson: Adverse Reactions (2)

Table 1 Adverse Reactions in Studies 1 and 2 Pooled (Frequency ≥ 5%)

<table>
<thead>
<tr>
<th></th>
<th>Lexiscan N = 1,337</th>
<th>Adenoscan N = 678</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>28%</td>
<td>26%</td>
</tr>
<tr>
<td>Headache</td>
<td>26%</td>
<td>17%</td>
</tr>
<tr>
<td>Flushing</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>Chest Discomfort</td>
<td>13%</td>
<td>18%</td>
</tr>
<tr>
<td>Angina Pectoris or ST Segment Depression</td>
<td>12%</td>
<td>18%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>7%</td>
<td>10%</td>
</tr>
<tr>
<td>Nausea</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Abdominal Discomfort</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Feeling Hot</td>
<td>5%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Advance MPI 1 and 2

Clinical & ECG Response to Adeno

♥ Chest Pain
  ♥ very non-specific and does not implicate presence of CAD.
  ♥ + CP → clinical response: Nondiagnostic

♥ ST Depression
  ♥ Low Sensitivity: only 1/3 of patients with reversible defects have ST-segment depression during adeno infusion
  ♥ High Specificity (not frequently occurring in normal pts)
    ♥ thus the presence of ST depression has a high positive predictive value for CAD, which is frequently severe and often correlates with presence of coronary collaterals.
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Ischemic ECG with Normal Adeno MPS

- Klodas et al., J Nucl Cardiol 2003;10:4-8
  - Mayo, 5526 pts with vasodilator stress, mean F/U 28 mo.
  - 49 (1%) normal MPS, but ischemic ECG
  - 11 of 12 with cath: multivessel CAD \([11/49 = 22\%]\)
  - Rate of CD or nonfatal MI: 4%/1 yr, 10%/2 yrs, 14%/3 yrs

- Abbott et al., J Nucl Cardiol 2003;10:9-16
  - Yale, 3231 pts adeno MPS, mean F/U 29 mo.
  - 228 ischemic ECG (7%): 66 (2%) normal MPS
  - normal adeno MPS, ischemic vs. nonischemic ECG:
    - Risk of nonfatal MI: 7.6% vs. 0.5%, \(p = 0.004\)
    - Risk of CD: 3.0% vs. 1.0%, \(p = 0.25\)
    - Risk of death or MI: 10.6% vs. 1.5%, \(p=0.00006\)

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Transient Ischemic Dilation (TID)

- the left ventricular cavity appears to be significantly larger in the post-stress images than in the resting images
- may actually be an apparent cavity dilation secondary to diffuse subendocardial ischemia (obscuring the endocardial border)
- marker for severe and extensive coronary artery disease
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Adenosine: TID

- TID 1.62
- LM 80%
- RCA 65%


Severe and extensive CAD (≥ 90% in prox LAD or ≥ 2 vessels)

<table>
<thead>
<tr>
<th>Normal perfusion</th>
<th>TID - No</th>
<th>TID - Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/79 (1%)</td>
<td>3/11 (27%)</td>
</tr>
<tr>
<td>Abnormal perfusion</td>
<td>23/182 (13%)</td>
<td>55/84 (65%)</td>
</tr>
</tbody>
</table>

Abidov, JACC 2003;42:1818-1825

Normal Ex or Adeno MPS with TID: Intermediate risk

Recommend cath if other high risk features, e.g. typical angina, DM, age > 75.
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Adenosine vs. Exercise for CAD detection

Adenosine is superior to submaximal exercise MPS and similar to that of maximal exercise:

<table>
<thead>
<tr>
<th>(n = 144)</th>
<th>Exercise (%)</th>
<th>Adenosine (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>Specificity</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>PPV</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>NPV</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Accuracy</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>


Regadenoson: Image Agreement

Advance MPI 1 and 2 each demonstrated that regadenoson (Lexiscan) is similar to adenosine (Adenoscan) in assessing the extent of reversible perfusion abnormalities.

<table>
<thead>
<tr>
<th>Table 4 Agreement Rates in Studies 1 and 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Adenoscan – Adenoscan Agreement Rate (± SE)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td></td>
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<tr>
<td>Adenoscan – Lexiscan Agreement Rate (± SE)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Rate Difference (Lexiscan – Adenoscan) (± SE)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
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<td></td>
</tr>
</tbody>
</table>
Regadenoson: Quant Analysis

<table>
<thead>
<tr>
<th></th>
<th>Regadenoson</th>
<th>Adenosine</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total defect size</td>
<td>11.5%</td>
<td>11.4%</td>
<td>0.88</td>
</tr>
<tr>
<td>Ischemic defect size</td>
<td>4.8%</td>
<td>4.6%</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Close correlation between adenosine and regadenoson:
- Total defect size, $r = 0.97$, $p < 0.001$
- Ischemic defect size, $r = 0.95$, $p < 0.001$


Regadenoson: Selected Populations

Patients with Renal Impairment
- 504 pts, random., double-blind, placebo-control.
  - 432 stage 3 CKD (GFR 30-59) (287 reg, 145 placebo)
  - 72 stage 4 CKD (GFR 15-29) (47 reg, 25 placebo)
- Overall AE high in Reg (62.6% vs. 21.2%).
  - H/A, CP, nausea, flushing, dizziness
- No serious AE or deaths at 24 h.
- Conclusion: Reg. safe and well tolerated in pts with stage 3 or stage 4 renal impairment.

Regadenoson: Selected Populations

❤ Patients with End Stage Renal Disease
❤ 277 pts with ESRD compared to 134 pts with normal renal function
❤ All underwent regadenoson gated SPECT
❤ Side effect profile similar
❤ No medication-related hospitalizations, serious events, or deaths occurred within 30 d.

Am J Cardiol 2010;105:133-135

❤ LBBB and Pacemaker
❤ HR increases more with regadenoson than adeno
❤ Thomas, JNM 2010; 51:1730
  ❤ Advance MPI I and II
  ❤ LBBB (n=64) and Pacemaker (n=93)
  ❤ Regadenoson: no increase in septal or LAD ischemia

❤ COPD/Asthma
❤ Two small studies (50 patients each)
  ❤ Thomas, JNC. 2008;15:319-328
  ❤ Leaker, JNC. 2008;15;329-336
Regadenoson: Selected Populations

**COPD/Asthma**
- Phase 4 Study (999 pts)
- Multicenter, randomized, double-blind, placebo-cont.
  - 532 asthma, 467 COPD
  - Stable, no recent change in asthma/COPD meds
  - Known CAD or ≥ 2 CAD risk factors
- Reg 0.4 mg vs. placebo IV over 10 seconds
- No difference in proportion of pts with > 15% drop in FEV1 from baseline to 2 h post-dose.

*J Nucl Cardiol 2012;19:681-92*

**PET**
- One manuscript
- Cullom/Bateman: 32 pt
  - 26 with reversible PD on dipy PET
  - 6 low LK (<5%)
- Conclusion: Regadenoson PET visually and quant. equivalent to dipy PET

*J Nucl Cardiol 2012 (online)*
Universal Stress Protocol

- SPECT patients ordered for:
  - Exercise
  - Pharm stress
    - no LBBB/PM or contraindication to TM Ex
- Attempt symptom-limited TM Ex
- Achieve 85% MPHR or other end-point?
  - Yes – inject stress isotope
  - No – slow TM to 1.7 MPH, 0% gr., inject regadenoson and isotope

Survival by Exercise Duration

Rozanski, JNC 2010;17:999-1008
Pharmacologic Stress Testing

ASNC Imaging Guidelines

Stress Protocols and Tracers – 2009

- Exercise
- Adenosine
- Regadenoson
- Dipyridamole
- Dobutamine

Guidelines available at:

http://www.asnc.org/content_184.cfm

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Pharmacologic Stress Testing

Question 4

A husband and wife both present for vasodilator stress MPS.

The husband had a Venti (20 oz) cup of Starbucks coffee 6 hours ago. The wife had a Venti (20 oz) cup of Starbucks decaf coffee 1 hour ago.

Which patient would you reschedule due to caffeine?

1. Husband – Coffee 6 hours ago
2. Wife – Decaf 1 hour ago
3. Both
4. Neither
Pharmacologic Stress Testing

Thank you!