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ASNC STRESS TESTING
PRACTICE POINTS

Pharmacologic Stress Testing - Adenosine

OVERVIEW

The purpose of this document is to provide a guide to the performance of pharmacologic stress testing with adenosine. The critical components of adenosine stress testing will be specifically outlined in this document and will serve as a reference for all nuclear cardiology laboratories. It will cover mechanism of action, indications and patient selection, dosage, side effects, testing procedure and contraindications as well as indications for reversal of infusion.

MECHANISM OF ACTION

Adenosine induces direct coronary arteriolar vasodilation through activation of the adenosine receptors, including the A_{2a} receptor, resulting in a 3.5 to 4-fold increase in myocardial blood flow (Figure 1). Peak vasodilation after administration of adenosine occurs 1 to 2 minutes after the start of the infusion. The pharmacologic half-life of adenosine is approximately 10 seconds.

Myocardial regions supplied by stenotic coronary arteries have an attenuated hyperemic response. Depending on the severity of the coronary stenosis and coronary flow reserve limitation, a relative flow heterogeneity is induced.

Adenosine generally does not cause myocardial ischemia. However, in a small proportion of patients with severe coronary artery disease (CAD), true ischemia is probably due to the coronary steal phenomenon. Myocardial tracer uptake is proportional to the regional myocardial blood flow resulting in a heterogeneous distribution of the radiotracer in the myocardium.

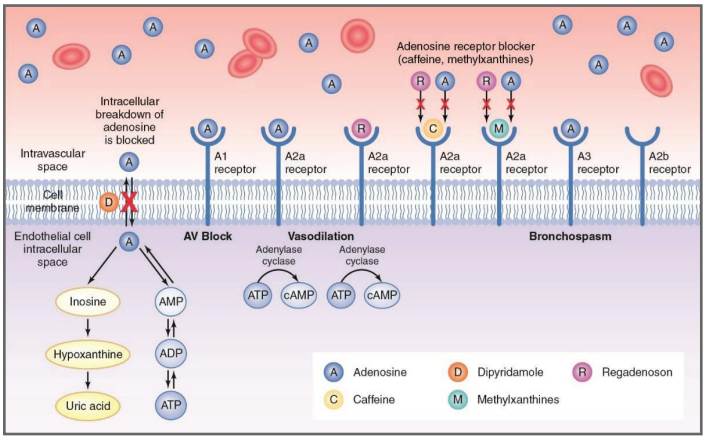

Figure 1: Mechanism of action of the coronary vasodilators; *ADP*, adenosine diphosphate; *AMP*, adenosine monophosphate; *ATP*, adenosine triphosphate; *AV*, atrioventricular; and *cAMP*, cyclic adenosine monophosphate

INDICATIONS AND PATIENT SELECTION

Indications for adenosine stress perfusion imaging are the same as that for exercise myocardial perfusion imaging. In general, exercise is strongly preferred except in the following circumstances:

- Inability to perform adequate exercise (greater than 3' and achievement of target heart rate) due to noncardiac physical limitations or lack of motivation.
- Baseline electrocardiographic abnormalities (ECG) such as left bundle branch block (LBBB), ventricular pre-excitation (Wolff Parkinson White (WPW) syndrome) or permanent ventricular pacing.
- Risk stratification of clinically stable patients into low- and high-risk groups in the period after myocardial infarction when maximal exercise testing is contraindicated (4-6 weeks).
- Diagnosis or risk stratification following presentation to the emergency department with presumptive acute coronary syndrome, exclude by serial clinical evaluation, ECGs, and serum markers.

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DOSE

Adenosine is given as a continuous infusion of 140 mcg/kg/min over a 6-minute period. The perfusion tracer is injected at 3 minutes and the infusion is continued for an additional 3 minutes, see Figure 2. A shorter duration adenosine infusion, lasting 4 minutes, with the perfusion tracer injected at 2 minutes, has been reported as being equally effective as the 6 minute protocol for the detection of coronary artery disease.

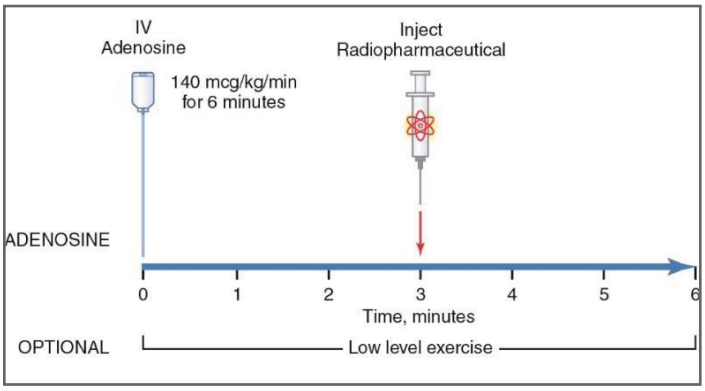

Figure 2: Adenosine protocol.

HEMODYNAMIC EFFECTS AND SIDE EFFECTS

Adenosine results in a decrease in systolic blood pressure (BP) by 10 ± 37 mmHg, and a decrease in diastolic BP by 8 ± 19 mmHg. Heart rate (HR) increases by 14 ± 30 bpm. Maximum hemodynamic changes after adenosine administration occurs with a decrease in systolic BP of >35 mmHg in 8% of patients, a decrease in diastolic BP >25 mmHg in 5% of patients, and an increase in HR of >40 bpm in 3 % of patients.

Side effects of adenosine due to non-target receptor activation:

A_1 receptor	Atrioventricular (AV) block
A_{2B} receptor	Peripheral vasodilation, bronchospasm
A_3 receptor	Bronchospasm

Minor side effects, which occur in approximately 80% of patients, include:

Flushing	35-40%
Chest pain (usually non-specific for CAD)	25-30%
Dyspnea	20%
Dizziness	7%
Nausea	5%
Symptomatic hypotension	5%

Other side effects of adenosine include:

Common Side Effects

AV block	8%
Second degree AV block	4%
Complete heart block	<1%
ST-T depression of ≥ 1 mm	5-7%

Very Rare Side Effects

Fatal and nonfatal myocardial infarction	Extremely rare, but has been reported
Atrial fibrillation	Reported within several minutes of initiation of adenosine infusion
New onset or recurrence of convulsive seizures	Infrequent but reported following adenosine administration
Hemorrhage and ischemic cerebrovascular events	Reported following adenosine infusion

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PROCEDURE

- Patients should not eat for at least 3 hours before the test. Patients may not consume anything containing methylxanthines (caffeine, theophylline, aminophylline or theobromine) for at least 12 hours prior to testing.
- This test requires an infusion pump to administer adenosine at a constant rate and an intravenous (IV) line with a dual-port Y-connect which should be as close to the intravenous (IV) catheter as possible to avoid a bolus of adenosine with administration of the isotope.
- Adenosine infusion should be given at a rate of 140 mcg/kg/min.
  - Patients who are at a high risk for complications adenosine infusion may be started at a lower dose (70-100 mcg/kg/min). The dose may then be increased to 140 mcg/kg/min as tolerated and the injection of the radiotracer given at the halfway point of the infusion.
  - During the infusion, patient's BP and 12-lead ECG should be monitored continuously until stable
  - The patient should be monitored in recovery until symptoms have resolved and there is no evidence of ischemia.
- Combination of low-level exercise and adenosine. (Optional)
  - Low-level treadmill exercise (e.g.1.7 mph, 0% grade) during adenosine infusion is safe and is helpful in reducing side effects and also attenuates the relative hypotension seen with adenosine. Image quality is also improved as exercise reduces high hepatobiliary and gut radiotracer uptake.
  - Low-level exercise in combination with pharmacologic stress test is not recommended in patients with left bundle branch block (LBBB) or patients with pacemakers.

INDICATIONS FOR REVERSAL OF ADENOSINE

Most side effects are self-limiting due to the short half-life adenosine (<10 seconds) and resolve within 30-60 seconds of stopping the infusion. IV aminophylline administration (50 to 250 mg) can be given but is only rarely required.

Indications for reversal using IV aminophylline (50 to 250 mg) include:

Persistent hypotension with systolic BP < 80 mmHg
Symptomatic, persistent second degree AV block or complete heart block
Other significant cardiac arrhythmia
Wheezing
Evidence of persistent ischemia manifested by chest pain or ECG changes
Signs of poor peripheral perfusion such as pallor, cyanosis or cold skin
Patient's requests to stop the test

Aminophylline administration should be delayed for at least one minute post-radionuclide administration. Administration of aminophylline less than one minute after radioisotope injection is likely to reduce the sensitivity of the test.

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CONTRAINDICATIONS

Patients with bronchospastic lung disease particularly with ongoing wheezing or bronchospasm.
Mobitz type II or third degree AV block without a functioning pacemaker
Sinus node disease (i.e. sick sinus syndrome or symptomatic bradycardia) without a functioning pacemaker
Systolic BP ≤ 90 mmHg
Uncontrolled hypertension (systolic BP >200 mmHg or diastolic BP >110 mmHg
Recent (<48 hours) use of dipyridamole or dipyridamole-containing medications
Hypersensitivity to adenosine
Unstable angina, acute coronary syndromes, or less than 2-to-4 days after acute myocardial infarction

RELATIVE CONTRAINDICATIONS

Profound sinus bradycardia with HR <40 bpm.
Mobitz Type 1 second-degree AV block (Wenckebach)
Severe aortic stenosis
Seizure disorder

SUGGESTED READING

Henzlova MJ, et al. ASNC Imaging Guidelines for SPECT nuclear cardiology procedures: Stress, protocols and tracers. J. Nucl Cardiol 2016; 23:606-639.

ASNC thanks the following members for their contributions to this document:

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