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ASNC STRESS TESTING
PRACTICE POINTS

Pharmacologic Stress Testing – Dipyridamole

OVERVIEW

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

Mechanism of Action

Dipyridamole is an *indirect* coronary vasodilator. It increases the tissue levels of adenosine by preventing the intracellular reuptake and deamination of adenosine. This results in a 3.8- to 7-fold increase in coronary blood flow velocity. Dipyridamole-induced hyperemia lasts for more than 50 minutes; however, the peak vasodilation after dipyridamole administration occurs on average 6.5 minutes after the start of infusion. The half-life of dipyridamole is approximately 30 to 45 minutes. See Figure 1.

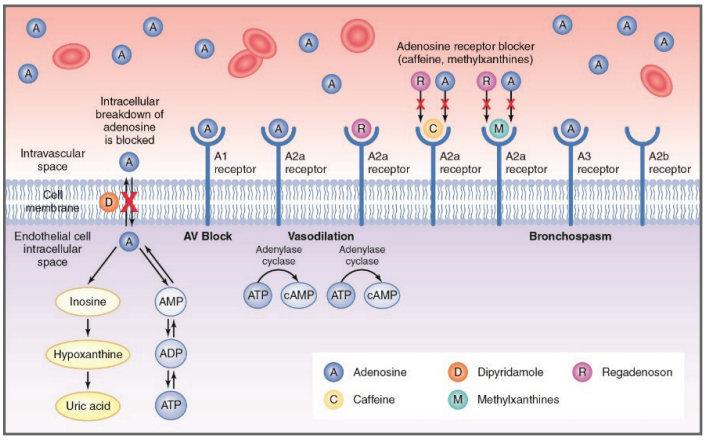

Figure 1: Mechanism of action of coronary vasodilators; ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; AV, atrioventricular; and cAMP, cyclic adenosine monophosphate.

INDICATIONS AND PATIENT SELECTION

Indications for dipyridamole stress imaging are the same as for exercise and in the presence of the following:

- Inability to perform adequate exercise due to noncardiac physical limitations or due to lack of motivation.
- Baseline electrocardiographic (ECG) abnormalities 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 after acute myocardial infarction following presentation to the emergency department with a presumptive acute coronary syndrome.
- Diagnosis or risk stratification following presentation to the emergency department with a presumptive acute coronary syndrome that has been excluded by serial clinical evaluation, ECGs, and serum markers

DOSE

Dipyridamole is administered at 0.56 mg/kg intravenously over a 4-minute period. Weight-based doses are typically used up to the weight of 250 lbs as an upper limit.

HEMODYNAMIC EFFECTS AND SIDE EFFECTS

Dipyridamole results in a modest increase in heart rate (HR), 17± 11 bpm and a decrease in both systolic blood pressure (BP), 14 ± 15 mmHg and a decrease in diastolic BP.

Minor side effects are common and occur in 50% of patients and include:

Chest pain*	20%*
Headache	12%
ST-segment and T-wave changes	8%
Ventricular extrasystoles	5%
Hypotension	5%
Flushing	3%
AV block**	2%**
Systolic BP fall to <90 mmHg	2%

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** Chest pain is not specific and not necessarily indicative of CAD)*
*** The incidence of AV block with dipyridamole is less than observed with adenosine (2% versus 7.6%).*

Symptoms may last for a longer period of time than other vasodilators (15 to 25 minutes) and may vary significantly among patients. Aminophylline (125 mg to 250 mg administered intravenously) is often required to reverse these side effects.

PROCEDURE

- *Patient preparation*: patients should not eat for at least 3 hours prior to testing. Patients may not consume any products containing methylxanthines, included caffeinated coffee, tea, or other caffeinated beverages or theophylline for at least 12 hours prior to testing.
- *Monitoring*: ECG monitoring should be performed as with other forms of stress testing. A 12-lead ECG should be recorded every minute during dipyridamole infusion, and at least every 3 to 5 minutes into recovery or until stable. BP should be monitored every minute during infusion and every 3-to-5 minutes or until stable during recovery.
- Protocol
  - Infusion: Dipyridamole, 0.56 mg/kg, is infused over 4 minutes, ideally via an infusion pump.
  - Radiotracer: The radiotracer is injected 3-to-5 minutes after the completion of dipyridamole infusion. See Figure 2.

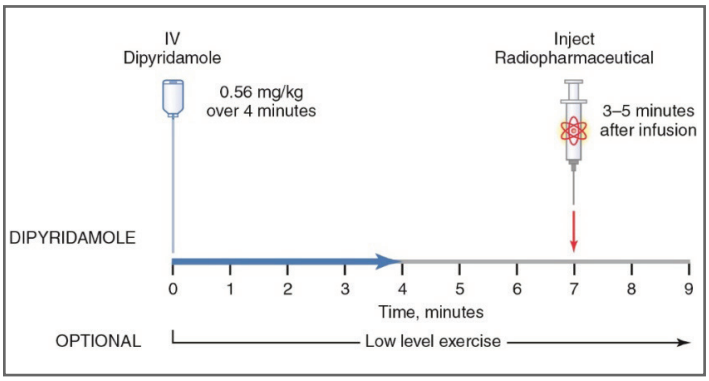

Figure 2. Dipyridamole Protocol

- Combination of Exercise and Dipyridamole
  - Low-level upright treadmill exercise (1.7 mph, 0% grade) has been found safe during dipyridamole infusion. The combination reduces side effects of dipyridamole and improves image quality by decreasing high hepatic and gut radiotracer uptake. Low-level exercise is not recommended for patients with LBBB, pre-excitation, and ventricular pacing due to HR related imaging artifacts.

INDICATIONS FOR EARLY TERMINATION AND REVERSAL

- Severe hypotension (systolic BP < 80 mmHg)
- Development of symptomatic, persistent second-degree or complete heart block or other significant cardiac arrhythmia
- Other significant cardiac arrhythmia
- Wheezing
- Severe chest pain associated with ST depression of 2 mm or greater
- Signs of poor perfusion (pallor, cyanosis, cold skin)
- Technical problems with the monitoring equipment
- Patient's request to stop

Aminophylline (125 mg - 250 mg intravenously) is often required to reverse side effects of dipyridamole infusion.

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CONTRAINDICATIONS

Patients with bronchospastic lung disease with ongoing wheezing or history of significant reactive airway disease
Systolic blood pressure (BP) < 90 mmHg
Uncontrolled hypertension (systolic BP > 200 mmHg or diastolic BP > 110 mmHg)
Ingestion of caffeinated foods or beverages or recent use of methylxanthines (such as aminophylline)
Known hypersensitivity to dipyridamole
Unstable angina, acute coronary syndrome, or less than 2-to-4 days after an acute myocardial infarction

RELATIVE CONTRAINDICATIONS

Profound sinus bradycardia (heart rates <40 bpm)
Second- or third-degree AV block without a functioning pacemaker
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; doi:10.1007/s12350-015-0387-x

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