

## Overview

### Useful For

Assessing the likelihood of future coronary events in patients with coronary heart disease, type II diabetes mellitus, or kidney disease

Prompting intervention and assessing improvements among subjects with elevated ADMA and hypercholesterolemia or type II diabetes mellitus

### Method Name

LiquidChromatography-TandemMassSpectrometry(LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA

### Specimen Required

**Patient Preparation:** Fasting-overnight (12 hours)

**Collection Container/Tube:** Lavender top (EDTA)

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 1 mL

### Collection Instructions:

1. Centrifuge and aliquot 1 mL of plasma into plastic vial.
2. Send specimen frozen.

### Forms

If not ordering electronically, complete, print, and send a [Cardiovascular Test Request Form](#) (T724) with the specimen.

### Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

### Specimen Minimum Volume

0.5 mL

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen (preferred)	90 days	
	Ambient	7 days	
	Refrigerated	7 days	

## Clinical & Interpretive

### Clinical Information

Asymmetric dimethylarginine (ADMA) is an independent risk factor for major adverse cardiovascular events.(1-7) ADMA inhibits nitric oxide (NO) synthesis and is elevated in diseases related to endothelial dysfunction including hypertension, hyperlipidemia, and type II diabetes mellitus. Elevation in ADMA and subsequent NO synthesis inhibition leads to vasoconstriction, reduced peripheral blood flow, and reduced cardiac output.

Elevated plasma ADMA confers a 4- to 6-fold increased risk of subsequent cardiovascular events or mortality among patients with acute coronary syndrome,(3) unstable angina,(4) type II diabetes mellitus,(5) end-stage renal disease,(6) coronary heart disease,(7) and peripheral artery disease.(1) Baseline ADMA remained a significant risk factor of adverse events even after adjusting for low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglycerides, creatinine, and high-sensitivity C-reactive protein.

Plasma ADMA concentrations are lowered by rosuvastatin and atorvastatin, but not simvastatin in patients with hypercholesterolemia.(8) Addition of vildagliptin (Galvus) to metformin significantly reduced ADMA concentrations among patients with type II diabetes mellitus.(9)

### Reference Values

> or =18 years: 63-137 ng/mL

Reference values have not been established for patients who are <18 years of age

### Interpretation

In patients with preexisting coronary conditions or at high risk for coronary events (diabetes, renal insufficiency), asymmetric dimethylarginine (ADMA) levels in the upper tertile, above 112 ng/mL, confer an increased risk for future coronary events.

### Cautions

No significant cautionary statements

### Clinical Reference

1. Chu R, Yu D, Chu J, et al: Prognostic efficacy of circulating asymmetric dimethylarginine in patients with peripheral arterial disease: A meta-analysis of prospective cohort studies. *Vascular*. 2018;26:322-330
2. Schulze F, Lenzen H, Hanefeld C, et al.: Asymmetric dimethylarginine is an independent risk factor for coronary heart disease: results from the multicenter Coronary Artery Risk Determination investigating the Influence of ADMA Concentration (CARDIAC) study. *Am Heart J*. 2006 Sep;152(3):493.e1-8
3. Cavusoglu E, Ruwende C, Chopra V, et al: Relationship of baseline plasma ADMA levels to cardiovascular outcomes at 2 years in men with acute coronary syndrome referred for coronary angiography. *Coron Artery Dis*. 2009;20:112-117
4. Krempl TK, Maas R, Sydow K, et al: Elevation of asymmetric dimethylarginine in patients with unstable angina and recurrent cardiovascular events. *Eur Heart J*. 2005;26:1846-1851
5. Cavusoglu E, Ruwende C, Chopra V, et al: Relation of baseline plasma ADMA levels to cardiovascular morbidity and mortality at two years in men with diabetes mellitus referred for coronary angiography. *Atherosclerosis*. 2010 May;210(1):226-231
6. Abedini S, Meinitzer A, Holme I, et al: Asymmetrical dimethylarginine is associated with renal and cardiovascular outcomes and all-cause mortality in renal transplant recipients. *Kidney Int*. 2010 Jan;77(1):44-50
7. Valkonen VP, Paiva H, Salonen JT, et al: Risk of acute coronary events and serum concentration of asymmetrical

dimethylarginine. Lancet. 2001;358:2127-2128

8. Kurtoglu E, Sevket B, Sincer I, et al: Comparison of effects of Rosuvastatin versus Atorvastatin treatment on plasma levels of asymmetric dimethylarginine in patients with hyperlipidemia having coronary artery disease. Angiology. 2014;65:788-793

9. Cakirca M, Karatoprak C, Zorlu M, et al: Effect of vildagliptin add-on treatment to metformin on plasma asymmetric dimethylarginine in type 2 diabetes mellitus patients. Drug Des Devel Ther. 2014;8:239-243

10. Ravani P, Tripepi G, Malberti F, et al: Asymmetrical dimethylarginine predicts progression to dialysis and death in patients with chronic kidney disease: a competing risks modeling approach. J Am Soc Nephrol. 2005;16:2449-2455

11. Elesber AA, Solomon H, Lennon RJ, et al: Coronary endothelial dysfunction is associated with erectile dysfunction and elevated asymmetric dimethylarginine in patients with early atherosclerosis. Eur Heart J. 2006 Apr;27(7):824-31

## Performance

### Method Description

Asymmetric dimethylarginine (ADMA) is separated and quantified by liquid chromatography-tandem mass spectrometry.(Unpublished Mayo method)

### PDF Report

No

### Specimen Retention Time

7 days

### Performing Laboratory Location

Rochester

## Fees & Codes

### Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

82542