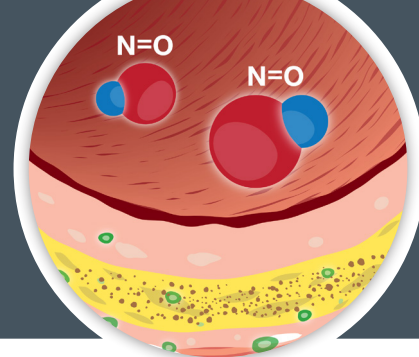


# ADMA/SDMA

CPT Code **82542**  
Sample Type **Serum**

Order Code **C301**  
Tube Type **Tiger Top**



Inflammation

## Elevated ADMA levels may identify:

- Endothelial dysfunction
- Pre-diabetes/diabetes
- Subclinical cardiovascular disease

## Elevated SDMA levels may identify:

- Reduced renal function and progressive kidney failure

## Description

One of the earliest manifestations of endothelial dysfunction is nitric oxide (NO) deficiency, which promotes atherosclerosis. ADMA (asymmetric dimethylarginine) and SDMA (symmetric dimethylarginine), its structural isomer, are metabolites of L-arginine, an amino acid that is catalyzed to L-citrulline and NO by nitric oxide synthase (NOS).

Both ADMA and SDMA have distinct pathophysiologies and manifestations. ADMA is a competitive inhibitor of NOS thereby reducing NO production and promoting endothelial dysfunction. SDMA also interferes with NO production, but does so indirectly by reducing the cellular availability of arginine. ADMA is primarily cleared through enzymatic degradation in the bloodstream and identifies subclinical cardiovascular disease. Conversely, SDMA is primarily excreted in the urine and identifies reduced renal function.

## Clinical Use

ADMA/SDMA may be measured in individuals with multiple risk factors for the development of cardiovascular disease.

## Clinical Significance

### Cardiovascular Significance:

- Elevated ADMA levels are associated with the presence of hypertension<sup>1</sup>, insulin resistance<sup>1</sup>, and hyperlipidemia<sup>2</sup>.
- Elevated ADMA levels are associated with subclinical atherosclerosis:
  - Elevated ADMA concentrations correlate with internal carotid artery bulb intimal media thickness<sup>3</sup>, a hemodynamically unstable region vulnerable to nitric oxide deficiency<sup>4</sup> and plaque formation.
  - Elevated ADMA in young adults has been associated with increased CT coronary artery calcification<sup>5</sup>.
- Individuals with established coronary artery disease and elevated ADMA levels have more than twice the risk for adverse events (MI, stroke) than those with normal ADMA levels<sup>6</sup>.

### Renal Significance:

- Elevated SDMA levels positively correlate with reduced renal function as measured by eGFR<sup>7</sup>.

## Sample Type

The ADMA/SDMA test should be performed on a serum sample, and fasting is recommended, but not required.

## Testing Frequency

The frequency of testing is determined by an individual's medical history, but may be monitored in individuals with hyperlipidemia, hypertension, pre-diabetes/diabetes, or those who are at moderate to high risk for developing cardiovascular disease.

## Commercial Insurance or Medicare Coverage

Coverage guidelines, also known as NCD (National Coverage Determination) or LCD (Local Coverage Determination) have been established or posted by CMS (Medicare & Medicaid). Guidelines should be reviewed for coverage and limitation. Limited information has been provided by the majority of the larger carriers (Aetna, United Healthcare, Cigna, Blues).

## Understanding Medical Necessity

The following ICD-10 codes for ADMA/SDMA are listed as a convenience for the ordering physician. The ordering physician should report the diagnosis code that best describes the reason for performing the test.

Diagnosis	Diagnosis Code
Type 2 Diabetes Mellitus with Hyperglycemia	E11.65
Type 2 Diabetes Mellitus without Complications	E11.9
Other Specified Diabetes Mellitus without Complications	E13.9
Pure Hypercholesterolemia	E78.0
Mixed Hyperlipidemia	E78.2
Other Hyperlipidemia	E78.4
Hyperlipidemia, Unspecified	E78.5
Metabolic Syndrome	E88.81
Essential (primary) Hypertension	I10
Atherosclerotic Heart Disease of Native Coronary Artery without Angina Pectoris	I25.10
Atherosclerotic Heart Disease of Native Coronary Artery with Unstable Angina Pectoris	I25.110
Impaired Fasting Glucose	R73.01
Impaired Glucose Tolerance Test (oral)	R73.02
Abnormal Finding of Blood Chemistry, Unspecified	R79.9



## RELATIVE RISK

ADMA (ng/mL)

<100 Low	100 - 123 Moderate	>123 High
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## REFERENCE RANGE

SDMA (ng/mL)

73 - 135 Low	>135 High
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TEST			Interpretation
ADMA	SDMA		
Low	Low		<ul style="list-style-type: none"> <li>Normal endothelial function</li> </ul>
Med	High	Low	<ul style="list-style-type: none"> <li>Endothelial dysfunction and possible presence of pre-diabetes/diabetes or CVD</li> </ul>
Low	High		<ul style="list-style-type: none"> <li>Reduced renal function</li> </ul>
Med	High	High	<ul style="list-style-type: none"> <li>Endothelial dysfunction and possible presence of pre-diabetes/diabetes or CVD</li> <li>Possible renal failure</li> </ul>

## Treatment Considerations

*These treatment considerations are for educational purposes only. Specific treatment plans should be provided and reviewed by the treating practitioner.*

### ✓ Assess LDL-C levels.

- If not at goal, consider lipid-lowering therapy, ideally with a statin-based regimen if not contraindicated.

### ✓ Assess blood pressure.

- If not at goal, consider initiating, or titrating, antihypertensive therapy.

**Note:** *An elevated blood pressure may contribute to endothelial dysfunction and the development of coronary artery disease and subsequent renal disease.*

- Consider L-Arginine supplementation to improve vasodilation and vascular tone.

**Note:** *L-Arginine enhances the production of nitric oxide which has anti-inflammatory, anti-thrombotic, anti-hypertensive, and anti-oxidant effects.*

### ✓ Assess risk for pre-diabetes/diabetes.

- If abnormal fasting glucose or oral glucose tolerance test, consider PPAR agonists, metformin or DPP-IV inhibitors if not contraindicated.

### ✓ Assess the presence of CAD with imaging techniques such as CIMT or coronary artery calcium scoring.

- Consider aspirin therapy if not contraindicated.
- Consider clopidogrel if history of CAD (i.e. myocardial infarction or revascularization) and/or cerebrovascular disease (i.e. TIA or stroke).

## References

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- Maas R et al. Association of the endogenous nitric oxide synthase inhibitor ADMA with carotid artery intimal media thickness in the Framingham Heart Study offspring cohort. *Stroke*. 2009; 40: 2715-2719.
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- Schnabel R et al. Asymmetric dimethylarginine and the risk of cardiovascular events and death in patients with coronary artery disease: Results from the AtheroGene study. *Circ Res*. 2005; 97: e53-e59.
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