Test Definition: CERAM

MI-Heart Ceramides, Plasma

Overview

Useful For
Evaluating the risk of major adverse cardiovascular events within the next 1 to 5 years

Highlights
Plasma ceramides predict risk of myocardial infarction, coronary revascularization, acute coronary syndrome hospitalization and mortality within 5 years.

Risk conferred by plasma ceramides is independent of low-density lipoprotein (LDL) cholesterol, C-reactive protein, LDL particles, and lipoprotein-associated phospholipase A2.

Plasma ceramides can be lowered by diet, exercise, simvastatin, rosuvastatin, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors.

Method Name
Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Plasma EDTA

Specimen Required
Patient Preparation: Patients should not be receiving Intralipid because it may cause false elevations in measured ceramides.
Collection Container/Tube: Lavender top (EDTA)
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge, aliquot at least 1 mL of plasma into a plastic vial and freeze within 8 hours.

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

Specimen Minimum Volume
0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen (preferred)	30 days	
	Ambient	8 hours	
	Refrigerated	24 hours	

Clinical & Interpretive

Clinical Information

MI-Heart Ceramides is a blood test that measures risk for adverse cardiovascular events and quantifies plasma ceramides. Plasma ceramides are predictors of adverse cardiovascular events resulting from unstable atherosclerotic plaque. Ceramides are complex lipids that play a central role in cell membrane integrity, cellular stress response, inflammatory signaling, and apoptosis. Synthesis of ceramides from saturated fats and sphingosine occurs in all tissues. Metabolic dysfunction and dyslipidemia results in accumulation of ceramides in tissues not suited for lipid storage. Elevated concentrations of circulating ceramides are associated with atherosclerotic plaque formation, ischemic heart disease, myocardial infarction, hypertension, stroke, type 2 diabetes mellitus, insulin resistance, and obesity.

Three specific ceramides have been identified as highly linked to cardiovascular disease and insulin resistance: N-palmitoyl-sphingosine (Cer16:0), N-stearoyl-sphingosine (Cer18:0), and N-nervonoyl-sphingosine(Cer24:1). A fourth ceramide, N-lignoceroyl-sphingosine (Cer24:0), is highly abundant in all individuals and is useful as a normalization factor for intra-individual variability of ceramide concentrations. Individuals with elevated plasma ceramides are at higher risk of major adverse cardiovascular events even after adjusting for age, gender, smoking status, and serum biomarkers such as low-density lipoprotein and high-density lipoprotein cholesterol, C-reactive protein and lipoprotein-associated phospholipase A2. Ceramide concentrations are reduced by current cardiovascular therapies including diet, exercise, statins, and proprotein convertase subtilisin/kexin type inhibitors.

Reference Values

MI-Heart Ceramide Risk Score:
0-2 Lower risk
3-6 Moderate risk
7-9 Increased risk
10-12 Higher risk
Ceramide (16:0): 0.19-0.36 mcmol/L
Ceramide (18:0): 0.05-0.14 mcmol/L
Ceramide (24:1): 0.65-1.65 mcmol/L
Ceramide (16:0)/(24:0): <0.11
Ceramide (18:0)/(24:0): <0.05
Ceramide (24:1)/(24:0): <0.45

Reference values have not been established for patients who are less than 18 years of age.

Note: Ceramide (24:0) alone has not been independently associated with disease and will not be reported.

Interpretation

Elevated plasma ceramides are associated with increased risk of myocardial infarction, acute coronary syndromes, and mortality within 1 to 5 years.

Ceramide Score	Relative Risk	Risk Category
0-2	1.0	Lower
3-6	1.5	Moderate
7-9	2.2	Increased
10-12	3.5	Higher

Score is based on trial data including >4000 subjects.

Cautions

No significant cautionary statements.

Clinical Reference

1 Laaksonen R, Ekroos K, Sysi-Aho M, et al. Plasma ceramides predict cardiovascular death in patients with stable coronary artery disease and acute coronary syndromes beyond LDL-cholesterol. Eur Heart J. 2016;37(25):1967-1976

2. Havulinna AS, Sysi-Aho M, Hilvo M, et al. Circulating ceramides predict cardiovascular outcomes in the population-based FINRISK 2002 cohort. Arterioscler Thromb Vasc Biol. 2016;36(12):2424-2430

3. Wang DD, Toledo E, Hruby A, et al. Plasma ceramides, Mediterranean diet, and incident cardiovascular disease in the PREDIMED trial (Prevenci on con Dieta Mediterranea). Circulation. 2017;135(21):2028-2040. doi:10.1161/CIRCULATIONAHA.116.024261

4. Meeusen JW, Donato LJ, Bryant SC, et al: Plasma Ceramides. Arterioscler Thromb Vasc Biol. 2018;38(8):1933-1939. doi:10.1161/ATVBAHA.118.311199

5. Peterson LR, Xanthakis V, Duncan MS, et al. Ceramide remodeling and risk of cardiovascular events and mortality. J Am Heart Assoc. 2018;7(10). doi:10.1161/JAHA.117.007931

6. Hilvo M, Meikle PJ, Pedersen ER, et al. Development and validation of a ceramide- and phospholipid-based cardiovascular risk estimation score for coronary artery disease patients. Eur Heart J. 2020;41(3):371-380. doi:10.1093/eurheartj/ehz387

7. Alshehry ZH, Mundra PA, Barlow CK, et al. Plasma lipidomic profiles improve on traditional risk factors for the prediction of cardiovascular events in type 2 diabetes mellitus. Circulation. 2016;134(21):1637-1650

8. Anroedh S, Hilvo M, Akkerhuis KM, et al. Plasma concentrations of molecular lipid species predict long-term clinical outcome in coronary artery disease patients. J Lipid Res. 2018;59(9):1729-1737. doi:10.1194/jlr.P081281

9. Lemaitre RN, Jensen PN, Hoofnagle A, et al. Plasma ceramides and sphingomyelins in relation to heart failure risk. Circ Heart Fail. 2019;12(7):e005708. doi:10.1161/CIRCHEARTFAILURE.118.005708

Performance

Method Description

Ceramides are separated and quantified by liquid chromatography tandem mass spectrometry (LC-MS/MS).(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday, Wednesday, Friday

Report Available
2 to 7 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

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

CPT Code Information
0119U

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CERAM	MI-Heart Ceramides, P	93883-7

Result ID	Test Result Name	Result LOINC® Value
42428	Ceramide (16:0)	93882-9
42429	Ceramide (18:0)	93881-1
42430	Ceramide (24:1)	93880-3
42431	Ceramide (16:0)/(24:0) ratio	93879-5
42432	Ceramide (18:0)/(24:0) ratio	93878-7
42433	Ceramide (24:1)/(24:0) ratio	93877-9

42434	MI-Heart Ceramide Risk Score	93876-1