



Myeloperoxidase (MPO)

CPT Code **83876***

Order Code **C133**

Sample Type **EDTA Plasma**

Tube Type **Lavender Top**

MPO levels are associated with an increased risk for:

- Cardiovascular disease
- Myocardial infarction

MPO levels may be measured in:

- Individuals with multiple risk factors
- Individuals at risk for pre-diabetes/diabetes
- Individuals with established cardiovascular disease

Description

MPO is a white blood cell-derived inflammatory enzyme that measures disease activity from the luminal aspect of the arterial wall.

When the artery wall is damaged, or inflamed, MPO is released by invading white blood cells where it accumulates.¹ MPO mediates the vascular inflammation that propagates plaque formation² and activates protease cascades that are linked to plaque vulnerability.³ White blood cell activation in the bloodstream, in response to injury of the artery wall including fissures, erosions or a degrading collagen cap, leads to MPO release in the bloodstream.⁴ This combination of detrimental effects demonstrates that MPO is actively involved in the progression of atherosclerosis. The Cleveland HeartLab MPO test measures free MPO in the bloodstream.

Clinical Use

The MPO test may be performed on individuals with multiple risk factors for cardiovascular disease, or those with established disease.

Clinical Significance

- Elevated MPO levels are associated with risk of heart disease in subgroups otherwise considered as low risk.^{5,6}

- Elevated MPO levels are independently associated with risk of future cardiovascular events in patients presenting with an acute coronary syndrome.^{7,8}
- Individuals with elevated MPO levels are more than 2x as likely to experience cardiovascular mortality.⁹
- MPO enhances cardiovascular risk prediction when used independently or alongside standard biomarker testing such as hsCRP.⁹
- Circulating MPO in the blood is a specific marker of vascular inflammation and vulnerable plaque/erosions/fissures.^{4,10}
- The p-ANCA test (anti-MPO antibody test) is not the same as the MPO test performed by Cleveland HeartLab. The p-ANCA test primarily measures the number of antibodies directed against the MPO protein.

Testing Frequency

The frequency of testing is determined by an individual's medical history, but may be monitored more frequently in diabetic, hypertensive, and those patients at moderate to high risk for metabolic syndrome and cardiovascular disease.

Sample Type

The MPO test should be performed on an EDTA plasma sample.

Commercial Insurance or Medicare Coverage

Coverage guidelines, also known as NCD (National Coverage Determination) or LCD (Local Coverage Determination) have not been established or posted by CMS (Medicare and Medicaid). We have reviewed the larger carriers (Aetna, United Healthcare, Cigna, Blues) and information has not been posted or is limited.

RELATIVE RISK

MPO (pmol/L)

<470
Low

470-539
Moderate

≥540
High

Treatment Considerations[†]

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

- ✓ **Assess lifestyle habits.**
 - Consider diet,¹⁵ exercise,¹⁶ and weight reduction efforts¹⁶ if appropriate.
- ✓ **Assess level of exercise.**
 - MPO values may be elevated in marathon runners and extreme athletes and may identify those with increased oxidative stress and basal levels of inflammation.¹⁷
- ✓ **Assess smoking habits.**
 - Smoking cessation is essential, as individuals who smoke are at increased risk of heart disease and blood clots.¹⁸
- ✓ **Assess LDL-C levels.**
 - If not at an optimal level,² consider lipid-lowering therapies described in the National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III) Guidelines.¹⁹
- ✓ **Assess HDL-C levels.**
 - If not at an optimal level,²⁰ consider nicotinic acid or omega-3 fatty acids.
 - Assess CoQ10 levels as evidence suggests that low ApoA1 and/or HDL-C levels are associated with low CoQ10 levels.²¹
- ✓ **Assess insulin sensitivity.**
 - If not at an optimal level,¹⁸ consider insulin-sensitizing therapies described in the ADA guidelines for the management of pre-diabetes/diabetes.²²
- ✓ **Assess blood pressure.**
 - If not at an optimal level,²³ consider initiating, or titrating, antihypertensive therapy.
- ✓ **Assess the presence of coronary artery disease (CAD) with imaging techniques such as carotid intima media thickness testing (CIMT)²⁰ or coronary artery calcium (CAC) scoring.²⁴**
- ✓ **Assess clotting risk.**
 - Consider antiplatelet therapy if history of CAD (i.e., myocardial infarction or revascularization) and/or a history of cerebrovascular disease (i.e., transient ischemic attack or stroke).²⁵
- ✓ **Assess dental health (periodontal disease).**
 - Refer to dentist to identify gum disease. Poor dental health may cause significant inflammation and is associated with the presence of atherosclerosis.^{26,27}
- ✓ **Assess, if known to be present, the treatment of inflammatory conditions such as rheumatoid arthritis (RA)¹¹ and systemic lupus erythematosus (SLE).¹²**
- ✓ **Assess the presence of vasculitis.**
 - MPO values may be elevated in individuals with vasculitis as it is characterized by increased vascular inflammation.¹³
- ✓ **Assess the presence of bone marrow dyscrasias.**
 - MPO values may be elevated in individuals with chronic lymphocytic leukemia or other leukemias, that cause increased white blood cell destruction.¹⁴

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

† The treatment considerations are provided for informational purposes only and are not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

References

- Tavora F, Ripple M, Li Ling, Burke AP. Monocytes and neutrophils expressing myeloperoxidase occur in fibrous caps and thrombi in unstable coronary plaques. *BMC Cardiovascular Disord.* 2009; 9: 27-33.
- Hazen SL and Heinecke JW. 3-chlorotyrosine, a specific marker of myeloperoxidase-catalyzed oxidation, is markedly elevated in low density lipoprotein isolated from human atherosclerotic intima. *J Clin Invest.* 1997; 99: 2075-2081.
- Fu X, Kassim SY, Parks WC, Heinecke JW. Hypochlorous acid oxygenates the cysteine switch domain of pro-matrix metalloproteinase (MMP-7). A mechanism for matrix metalloproteinase activation and atherosclerotic plaque rupture by myeloperoxidase. *J Biol Chem.* 2001; 276: 41279-41287.
- Ferrante G, Nakano M, Prati F, et al. High Levels of Systemic Myeloperoxidase Are Associated With Coronary Plaque Erosion in Patients With Acute Coronary Syndromes: A Clinicopathological Study. *Circulation.* 2010; 122: 2505-2513.
- Meuwese MC, Stroes ESG, Hazen SL, et al. Serum myeloperoxidase levels are associated with the future risk of coronary artery disease in apparently healthy individuals: The EPIC-Norfolk Prospective Population Study. *J Am Coll Cardiol.* 2007; 50: 159-165.
- Karakas M, Koenig W, Zierler A, et al. Myeloperoxidase is associated with incident coronary heart disease independently of traditional risk factors: Results from the MONICA/KORA Augsburg study. *J Intern Med.* 2012; 271: 43-50.
- Baldus S, Heeschen C, Meinertz T, et al. Myeloperoxidase serum levels predict risk in patients with acute coronary syndromes. *Circulation.* 2003; 108: 1440-1445.
- Cavusoglu E, Ruwende C, Eng C, et al. Usefulness of baseline plasma myeloperoxidase levels as an independent predictor of myocardial infarction at two years in patients presenting with acute coronary syndrome. *Am J Cardiol.* 2007; 99: 1364-1368.
- Heslop CL, Frohlich JJ, Hill JS. Myeloperoxidase and C-reactive protein have combined utility for long-term prediction of cardiovascular mortality after coronary angiography. *J Am Coll Cardiol.* 2010; 55: 1102-1109.
- Penn MS and Klemes AB. Multimarker approach for identifying and documenting mitigation of cardiovascular risk. *Future Cardiol.* 2013; 9(4): 497-506.
- Maradit-Kremers H, Crowson CS, Nicola PJ, et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: A population-based cohort study. *Arthritis Rheum.* 2005; 52: 402-211.
- Telles RW, Ferreira GA, da Silva NP, Sato EI. Increased plasma myeloperoxidase levels in systemic lupus erythematosus. *Rheumatol Int.* 2010; 30: 779-784.
- Melikoglu MA, Kacar C, Cort A, Yucel G, Aslan M. Oxidases and oxygenases in regulation of neutrophil redox pathways in Behcet's disease patients. *J Enzyme Inhib Med Chem.* 2012; 27(1): 12-17.
- Burgos, RCR Ramautar R, Van Wijk EPA, Hankemeier T, Van Der Greef J, Mashaghi A. Pharmacological targeting of ROS reaction network in myeloid leukemia cells monitored by ultra-weak photon emission. *Oncotarget.* 2018; 9(2): 2028-2034.
- Loke WM, Proudfoot JM, McKinley AJ, et al. Quercetin and Its In Vivo Metabolites Inhibit Neutrophil-Mediated Low-Density Lipoprotein Oxidation. *J Agric Food Chem.* 2008; 56: 3609-3615.
- Richter B, Niessner A, Penka M, et al. Endurance training reduces circulating asymmetric dimethylarginine and myeloperoxidase levels in persons at risk of coronary events. *Thromb Haemost.* 2005; 94(06): 1306-1311.
- Melanson SE, Green SM, Wood MJ, Neilan TG, Lewandrowski EL. Elevation of myeloperoxidase in conjunction with cardiac-specific markers after marathon running. *Am J Clin Pathol.* 2006; 126: 888-893.
- Weirsmas JJ, Meuwese MC, van Miert JN, et al. Diabetes mellitus type 2 is associated with higher levels of myeloperoxidase. *Med Sci Monit.* 2008; 14(8): CR406-410.
- Third report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). National Institutes of Health. September 2002. *NIH Publication No.* 02-5215.
- Exner M, Minar E, Mlekusch W, et al. Myeloperoxidase Predicts Progression of Carotid Stenosis in States of Low High-Density Lipoprotein Cholesterol. *J Am Coll Cardiol.* 2006; 11: 2212-2218.
- Toyama K, Sugiyama S, Oka H, et al. Rosuvastatin combined with regular exercise preserves coenzyme Q10 levels associated with a significant increase in high-density lipoprotein cholesterol in patients with coronary artery disease. *Atherosclerosis.* 2011; 217: 158-164.
- American Diabetes Association: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018; 41(Supplement 1).
- Van der Zwan LP, Scheffer PG, Dekker JM, Stehouwer CDA, Heine RJ, Teerlink T. Hyperglycemia and Oxidative Stress Strengthen the Association Between Myeloperoxidase and Blood Pressure. *Hypertension.* 2010; 55: 1366-1372.
- Wong ND, Gransar H, Narula J, et al. Myeloperoxidase, Subclinical Atherosclerosis, and Cardiovascular Disease Events. *J Am Coll Cardiol.* 2009; 2(9): 1093-1099.
- Mayyas FA, Al-Jarrah MI, Ibrahim KS, Alzoubi KH. Level and significance of plasma myeloperoxidase and the neutrophil to lymphocyte ratio in patients with coronary artery disease. *Exp Ther Med.* 2014; 8: 1951-1957.
- Ramirez JH, Parra B, Gutierrez S, et al. Biomarkers of cardiovascular disease are increased in untreated chronic periodontitis: a case control study. *Aust Dent J.* 2014; 59: 29-36.
- Buhlin K, Mantyla P, Paju S, et al. Periodontitis is associated with angiographically verified coronary artery disease. *J Clin Periodontol.* 2011; 38: 1107-1014.

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