MYELOPEROXIDASE (MPO) TESTING
Overview, Clinical Significance & Treatment Summary

TEST NAME Myeloperoxidase (MPO)

TEST CODE 604

ASSAY DESCRIPTION[1] One-step enzyme immunoassay

Specimen Requirement: 1.0 mL plasma collected in an EDTA plasma separator tube (pearl top)

Please report the ICD-10 code(s) that best describes the reason for ordering the test. A few commonly used ICD-10 codes are listed below.

R07.9 Chest pain
125.10 Coronary Artery Disease
Patients at high risk for developing coronary heart disease

MPO is an enzyme produced by activated cholesterol laden macrophages in the artery wall. Elevated values have been associated with the presence of unstable plaque in the artery wall and a high risk for cardiovascular disease (CVD) events over the next one to six months. CVD events may include: myocardial infarction (MI), cerebrovascular accident (CVA), need for coronary revascularization or death.[1-9]

Plasma levels of MPO are used in conjunction with clinical history, electrocardiogram, and other cardiac biomarkers to evaluate patients presenting with chest pain (CP) or other signs of acute coronary syndrome (ACS) to assess their risk for major adverse cardiac events (MACE) over the next one to six months.

LAB VALUES AND CVD RISK[1,2]

Optimal	Borderline	High Risk
pmol/L		
<350	350 – 633	>633

Alert: >1658 pmol/L

CLINICAL SIGNIFICANCE OF ELEVATED PLASMA LEVELS OF MPO

- Elevated MPO levels >633 pmol/L have been shown to be a significant independent risk factor for MACE over the ensuing one to six months in patients presenting with CP who have normal levels of troponin.[1,2]
- This is especially the case if levels of high sensitivity C-reactive protein (hs-CRP) are also elevated (>2 mg/L), along with increased (>235 ng/mL) lipoprotein associated phospholipase A_2 ($LpPLA_2$).[2-9,10,11]
  - Elevated serum levels of CRP are a marker of generalized and liver inflammation.
  - Elevated levels of $LpPLA_2$ are a marker of inflammation and plaque in the arterial wall.[9]
- Simultaneous elevated levels of MPO (>633 pmol/L), hs-CRP (>2.0 mg/L), and $LpPLA_2$ (>235 ng/mL) are associated with a markedly increased risk of a MACE within one to six months.[2-9,10,11]
- MPO may be elevated due to other factors including:
  - Kidney disease[12]
  - Dialysis[13]
  - Myeloproliferative disorders[14]
  - Heart failure[4]
  - Fabry disease[15]
  - Cystic fibrosis[16]
  - Inflammatory bowel disease[17]
  - Heparin treatment[1]
  - Acute infections[18]
  - Alzheimer's disease[19]
  - Connective tissue disorders[20]

CLINICAL SIGNIFICANCE OF UNDETECTABLE PLASMA LEVELS OF MPO[21–22]

MPO may be undetectable due to an underlying genetic condition seen in about 1:2000 individuals. This genetic condition has been associated with an increased risk for systemic candidiasis.

TREATMENT CONSIDERATIONS[23]

- Evaluate CVD status with physical exam, stress testing and other CVD diagnostic modalities.
- Modify all existing CVD risk factors.
- Reduce elevated MPO levels with medications:
  - Statins
  - Beta-blockers
  - Angiotensin enzyme converting (ACE) inhibitors

ROLES OF INFLAMMATION

Inflammation is a basic way in which the body reacts to infection, irritation or other injury. Increased cholesterol build up in the artery wall leads to inflammation at that site, which leads to the narrowing or blockage of the artery. Inflammatory factors can also contribute to destabilizing the plaque, which can lead to plaque rupture in the arteries.

- Progression of CVD risk over 6 months:
  - Early: hs-CRP >2.0 mg/L[24]
  - Plaque forms: $LpPLA_2$ >235 ng/mL[9]
  - Point of rupture: Especially if MPO >633 pmol/L[1,2]

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PHYSIOLOGIC ACTIVITY OF MPO[25-27]

- MPO is an enzyme produced by foam cells in the artery wall, and elevated values indicate the presence of unstable plaque in the artery wall, and high risk for future near term cardiovascular risk.
- Several lines of evidence indicate that MPO participates in atherosclerotic progression and contributes to plaque vulnerability.
  - MPO is present in atherosclerotic plaques and oxidizes LDL cholesterol, leading to the production of foam cells, a precursor to atherosclerotic plaque.
  - MPO activates proteases that can lead to unstable plaque formation and thrombosis.
- MPO consumes nitric oxide contributing to endothelial depletion of nitric oxide in atherosclerotic vessels and vasoconstriction.
- MPO modifies the apolipoprotein A-I (apoA-I), the major protein of HDL, causing it to become less functional in removing cholesterol from cells.
  - ApoA-I modification leads to a marked excess of cholesterol rich plaque in the artery wall.
  - Cholesterol rich plaques are much more susceptible to rupture than fibrous.
- Elevated MPO levels indicate an increased risk of plaque rupture in arteries, especially in terms of coronary heart disease (CHD).

CLINICAL STUDY OF MPO ASSAY FOR MACE[1,2]

- Plasma samples were obtained from 400 patients who presented to the Emergency Department or to out-patient facilities with CP or equivalent symptoms suggestive of ACS.
- Patients enrolled in the study were assessed for MACE defined as MI, coronary revascularization [defined as coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), or placement of cardiac stent] or death.
- Incidence of MACE was assessed at 30 days and 180 days.
  - Patients at risk for MACE were identified significantly more often for MPO >633 pmol/L (values >95th percentile found in normal subjects) than for MPO < 633 pmol/L in patients with troponin I values <0.07 ng/mL. 14% of patients having MACE in the high MPO group and about 5% in the low MPO group (relative risk increase 2.8 fold).

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