Lp-PLA$_2$ (The PLAC® Test)

Description
Lp-PLA$_2$, or lipoprotein-associated phospholipase-A$_2$, measures disease activity within the artery wall below the collagen or calcified cap due to the activation of macrophages. Lp-PLA$_2$ is not an acute phase reactant. When disease is active in the artery, increased levels of Lp-PLA$_2$ are produced by macrophages and foam cells within the intima of the artery$^1$. Lp-PLA$_2$ also interacts with oxidized LDL, which increases inflammation and enhances a proatherogenic state, as well as plaque vulnerability$^2$. Research suggests that it plays a direct role in the atherosclerotic disease process$^3$.

Clinical Use
The Lp-PLA$_2$ test may be performed on individuals at intermediate or high risk for developing coronary heart disease who are any age with at least two major risk factors, those ≥65 years of age with one major risk factor, smokers, those with a fasting blood glucose of ≥100 mg/dL, or those who have metabolic syndrome.

Clinical Significance
- Lp-PLA$_2$ accumulates within human atherosclerotic plaques and vulnerable lesions$^4$.
- Elevated Lp-PLA$_2$ levels can predict the development of coronary artery disease in apparently healthy individuals$^5$ and the risk of future adverse cardiac and cerebrovascular events$^2$.
- Individuals with normal systolic blood pressure, but high Lp-PLA$_2$ levels, are 2x as likely to have a stroke$^6$, while those with elevated systolic blood pressure and Lp-PLA$_2$ levels are 7x more likely to experience a stroke$^8$.
- Post-menopausal women not using hormone therapy who have an elevated Lp-PLA$_2$ have a 64% increased risk of ischemic stroke$^9$.

Testing Frequency
The frequency of testing is determined by an individual’s medical history, but may be performed alongside a standard lipid panel in patients at moderate to high risk for CHD or ischemic stroke. These patients may have two or more risk factors such as a family history of CVD or hypertension.

Sample Type
The Lp-PLA$_2$ test should be performed on a serum or EDTA plasma sample.

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 limitations. Limited information has been provided by the majority of the larger carriers (Aetna, United HealthCare, Cigna, Blues).

Understanding Medical Necessity
The following ICD-9 codes for Lp-PLA$_2$ are listed as a convenience for the ordering practitioner. The ordering practitioner should report the diagnosis code that best describes the reason for performing the test and provide the 4th and 5th ICD-9 digit as appropriate.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnosis Code</th>
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<tbody>
<tr>
<td>Diabetes Mellitus Type II or Unspecified, Not Stated as Uncontrolled</td>
<td>250.00</td>
</tr>
<tr>
<td>Diabetes Mellitus Type II or Unspecified, Uncontrolled</td>
<td>250.02</td>
</tr>
<tr>
<td>Pure Hypercholesterolemia</td>
<td>272.0</td>
</tr>
<tr>
<td>Mixed Hyperlipidemia</td>
<td>272.2</td>
</tr>
<tr>
<td>Other and Unspecified Hyperlipidemia</td>
<td>272.4</td>
</tr>
<tr>
<td>Benign Essential Hypertension</td>
<td>401.1</td>
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<tr>
<td>Unspecified Essential Hypertension</td>
<td>401.9</td>
</tr>
<tr>
<td>Coronary Atherosclerosis of Unspecified Type of Vessel, Native or Graft</td>
<td>414.00</td>
</tr>
<tr>
<td>Coronary Atherosclerosis of Native Coronary Artery</td>
<td>414.01</td>
</tr>
<tr>
<td>Other Abnormal Blood Chemistry</td>
<td>790.6</td>
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</tbody>
</table>

Increased levels of Lp-PLA$_2$ may lead to increased risk of:
- Coronary heart disease
- Stroke
- Myocardial infarction

Lp-PLA$_2$ levels can be reduced by:
- Treatment with statins
- Supplementation with niacin
- Lifestyle modifications
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 omega-3 fatty acid levels.**
  - Omega-3 fatty acid supplementation, along with statin therapy, may reduce Lp-PLA₂ levels.
- **Assess HDL-C levels.**
  - If not at goal, consider niacin or fenofibrate therapy.
  - Assess CoQ10 levels as recent evidence suggests that low ApoA1 and/or HDL-C levels are associated with low CoQ10 levels.
- **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 a history of cerebrovascular disease (i.e., TIA or stroke).
- **Assess dental health (periodontal disease).**
  - Refer to dentist to identify gum disease.
  - **NOTE:** Periodontal therapy may reduce Lp-PLA₂ levels.
- **Assess smoking habits.**
  - **NOTE:** Smoking cessation is essential as individuals who smoke are at increased risk of heart disease and blood clots.
- **Assess blood pressure.**
  - If not at goal, consider initiating, or titrating, anti-hypertensive therapy.
  - **NOTE:** An elevated blood pressure may contribute to endothelial damage and coronary disease formation.
- **Assess lifestyle habits.**
  - Consider diet/exercise/weight reduction efforts if appropriate.

**References**

11. Toyama K 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.