HDL cholesterol particles are considered to be cardioprotective because of their anti-atherogenic properties, which include increasing reverse cholesterol transport, promoting endothelial nitric oxide production, and anti-inflammatory and antithrombotic effects. Low HDL-C, a component of metabolic syndrome, is predictive of cardiovascular risk, but clinical trials have shown therapeutically increased HDL-C levels do not reduce rates of cardiovascular events. These findings led to an understanding that the physiological impact of HDL may be dependent on its functionality, more so than low or high HDL-C levels. The importance of HDL function to CVD is highlighted by findings that patients who have the highest cholesterol efflux capacity (CEC), a marker of HDL function, have a 67% reduction in cardiovascular risk compared to the lowest quartile CEC.

The HDL function test, the HDLfx test, provides additional information about CVD risk. A better understanding of HDL function will add clinical value to the assessment of HDL-C and provide additional insight into CVD risk that is not evident with HDL-C levels alone. The HDLfx test is appropriate for patients who have 1 or more risk factors for the development of CVD.

### Clinical Use
Through assessment of HDL function, the HDLfx test provides additional information about CVD risk. A better understanding of HDL function will add clinical value to the assessment of HDL-C and provide additional insight into CVD risk that is not evident with HDL-C levels alone. The HDLfx test is appropriate for patients who have 1 or more risk factors for the development of CVD.

### Clinical Significance

<table>
<thead>
<tr>
<th>HDLfx Test Subcomponents</th>
<th>Clinical Significance</th>
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<tbody>
<tr>
<td>AALP ApoA-1</td>
<td>Decreased serum levels are associated with CHD</td>
</tr>
<tr>
<td>AALP ApoC-1</td>
<td>Decreased levels in HDL particles of patients with CHD</td>
</tr>
<tr>
<td>AALP ApoC-2</td>
<td>Elevated serum levels in patients with CHD</td>
</tr>
<tr>
<td>AALP ApoC-3</td>
<td>Elevated levels in HDL particles of patients with CAD</td>
</tr>
<tr>
<td>AALP ApoC-4</td>
<td>Elevated levels in HDL particles of patients with CAD</td>
</tr>
</tbody>
</table>

The HDLfx pCAD score is calculated from subcomponents of the HDLfx test and has been validated in clinical studies to identify:
- Patients with CAD, independent of conventional CV risk factors
- Female patients with increased risk of myocardial infarction within 1 to 2 years
- Increased risk of cardiovascular death among those with CAD over a 4-year follow-up
Based on a population of patients diagnosed with CAD (defined as having a coronary lesion consistent with 50% blockage or more; N=149) and a study control group of healthy individuals without CAD (N=69), a pCAD score greater than 0.90 indicates high risk for having atherosclerosis with a clinical sensitivity of 76% and clinical specificity of 75%. Case and control samples were selected from the Fairbanks Institute for Healthy Communities biobank cardiovascular disease study with analysis performed by Cleveland HeartLab.

**Treatment Considerations**

*These treatment considerations are for educational purposes only. Specific treatment plans should be provided and reviewed by the treating practitioner. Therapies that improve CEC or levels of subcomponents of the HDLfx test may improve the HDLfx pCAD score and CAD risk, but further studies are needed to confirm. Most therapies do not directly target CEC, and findings may be confounded by other medications, patient characteristics, or the CEC evaluation test used.*

- **Treatment considerations for CEC**
  - AALP ApoA-1 therapeutics improve CEC
  - Niacin has minimal effects on CEC
  - Fibrates may increase CEC
  - Statins minimally affect or decrease CEC
  - Diet and exercise may improve CEC, but more investigation is needed
  - Omega-3 fatty acids may improve CEC

*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.*

**References**


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