Diagnostic Tests

What Physicians Need to Know

Lipoprotein(a) Testing for Atherosclerotic Cardiovascular Disease

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Test	Indication	Population	Cost*
Lipoprotein(a)	Refine ASCVD risk	Adults at risk of ASCVD	$39 to $177

ASCVD = atherosclerotic cardiovascular disease.

*—Information obtained at https://www.findlabtest.com/lab-test/blood-tests-for-heart-disease/lipoprotein-a-labcorp-120188 (accessed February 9, 2023).

Lipoprotein(a), or Lp(a), is a genetically determined low-density lipoprotein (LDL) subtype, which has been identified as a causal risk factor for atherosclerotic cardiovascular disease (ASCVD).[1-3] The Lp(a) test is approved by the U.S. Food and Drug Administration; however, there are no universally accepted screening indications. The American College of Cardiology/American Heart Association (ACC/AHA) recommends screening for adults who have a family or personal history of premature ASCVD.[4] The ACC/AHA further considers Lp(a) levels greater than 50 mg per dL (125 nmol per L) to be risk-enhancing for ASCVD.[1-12]

Accuracy

A large prospective cohort study including 460,506 patients demonstrated a modest association between Lp(a) level and ASCVD risk.[8] The average patient age was 57 years, 45% were men, 94.3% were White, and 3.8% had a history of documented ASCVD at the time of enrollment. Median Lp(a) levels were 7.8 mg per dL (19.6 nmol per L), with high risk defined as a level greater than 70 mg per dL (150 nmol per L). In the subset of patients with pre-existing ASCVD, 20% had high-risk Lp(a) levels. Over the 11-year study, patients with high-risk Lp(a) levels had a greater likelihood of developing coronary artery disease (hazard ratio [HR] = 1.63; 95% CI, 1.56 to 1.70) or having a secondary event in the setting of known disease (HR = 1.23; 95% CI, 1.10 to 1.37).[8]

A 2019 randomized controlled trial of 25,096 patients with known ASCVD and LDL cholesterol greater than 70 mg per dL (1.81 mmol per L) or non–high-density lipoprotein cholesterol greater than 100 mg per dL (2.59 mmol per L) studied the value of measuring Lp(a) to determine ASCVD risk.[9] The average patient age was 62 years, 75% were men, and 85% were White. The population was divided into quartiles based on Lp(a) levels (less than 5.2 mg per dL [13 nmol per L], 5.2 to 14.8 mg per dL [13 to 37 nmol per L], 14.8 to 66 mg per dL [37 to 165 nmol per L], and greater than 66 mg per dL [165 nmol per L]). Being in the highest two quartiles was associated with a history of myocardial infarction at the time of enrollment. Compared with those in the lowest quartile, patients with Lp(a) levels of 14.8 to 66 mg per dL had an increased risk of death from coronary artery disease, clinical myocardial infarction, or need for urgent revascularization (HR = 1.24; 95% CI, 1.02 to 1.50). Those with Lp(a) levels greater than 66 mg per dL had an even higher risk (HR = 1.33; 95% CI, 1.1 to 1.6). This risk persisted after multivariate adjustments for age, sex, race, comorbidities, and LDL cholesterol or apolipoprotein B, with an increased risk of major coronary events in the entire population (adjusted HR = 1.06; 95% CI, 1.02 to 1.09) and highest quartile (adjusted HR = 1.22; 95% CI, 1.01 to 1.48).

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Benefit

Lp(a) levels are primarily genetic, inexpensive to quantify, remain stable after five years of age, and do not require fasting for accuracy.[1-5] Elevated Lp(a) levels may enable physicians to have a more patient-centered conversation about treatment approaches.[2-11]

Harms

Lifestyle changes and medications, including statins, have little direct effect on Lp(a).[6] Although proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and lipoprotein apheresis both lower Lp(a), PCSK9 inhibitors are not approved by the U.S. Food and Drug Administration for this indication. There are no data from randomized trials

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showing that direct Lp(a) reduction improves cardiovascular outcomes.[2-6,9] Lp(a) risk thresholds have predominantly been studied in White populations.[5,8,9]

Standardization of Lp(a) laboratory assays remains a specific challenge to widespread testing implementation due to varying particle sizes (nmol per L) among patients.[5,6,8] Studies have also shown varying high-risk Lp(a) thresholds, which may differ from laboratory-reported normal ranges. Inflammatory processes and impaired renal function may also increase Lp(a) levels.[6]

Cost

Advanced lipoprotein and apolipoprotein testing is not covered by Medicare or Medicaid.[13] Most major U.S. health insurance companies also do not cover testing. The Lp(a) test is available at many commercial laboratories throughout the United States, and out-of-pocket costs range from $39 to $177.[14]

Bottom Line

Lp(a) measurement can characterize a patient's risk of ASCVD beyond conventional risk calculators, but there are no data from randomized trials showing that direct Lp(a) reduction decreases ASCVD events.[9,15] For patients with high Lp(a) levels, family physicians should continue to recommend a heart-healthy lifestyle and may use this information to individualize how aggressively to treat other ASCVD risk factors.

The opinions and assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the U.S. Air Force Medical Corps or the U.S. Air Force at large.

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