

The Coming Shift in Lp(a) Management: What to Know Now

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What is Lp(a)?

Lipoprotein(a), or Lp(a), is a lipoprotein that—like LDL—carries cholesterol and one apolipoprotein B (apoB) molecule (Figure 1). Lp(a) also carries an additional molecule called apolipoprotein(a), or apo(a), which is covalently bound to apoB. Each apo(a) molecule contains a section of repeated structures that varies widely between unrelated people; this section is often called the “tail.”

A longer tail is associated with lower Lp(a) production while a shorter tail is associated with higher production. The structure of a person’s apo(a)—and therefore their Lp(a) level—is genetically determined. Lifestyle interventions such as diet and exercise do not affect Lp(a) levels.

Why is Lp(a) harmful?

Lp(a) deposition in the arterial wall attracts monocytes, leading to inflammation, plaque development and calcification. Extensive studies show that elevated Lp(a) is a major contributor to atherosclerotic cardiovascular disease (ASCVD) and aortic valve stenosis (AVS).

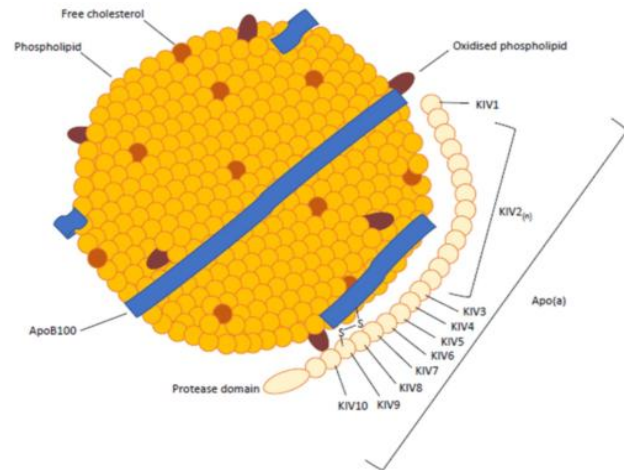


Figure 1

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This risk persists even in patients on statin therapy who have an LDL less than 70mg/dL.¹

How is Lp(a) measured?

Lp(a) should be measured in nmol/L, which counts each Lp(a) particle as one unit. When measured in mg/dL, each particle may be counted multiple times because apo(a) contains repeated structures. Elevated Lp(a) is defined as greater than 125 nmol/L or 50mg/DL.²

A conversion factor of 2-2.5 has been proposed to convert mg/dl to nmol/L, but

this estimate is imprecise and prone to error.

Are there any treatments?

The only treatment available in the United States that lowers Lp(a) is lipoprotein apheresis. Statins do not reduce Lp(a) concentrations, although they should still be used to lower global ASCVD risk.

The PCSK9 monoclonal antibodies alirocumab and evolocumab can reduce Lp(a) by up to 27%.^{3,4} Inclisiran, a small interfering RNA therapy, can reduce Lp(a) by up to 21.9%.⁵ None of these medications are approved by the Food and Drug Administration to lower Lp(a), and it is not yet known whether these reductions translate into lower risk of ASCVD or AVS.

What is pelacarsen?

Pelacarsen is an investigational antisense oligonucleotide (ASO) that targets apo(a) mRNA production in hepatic cells. A phase 2 randomized, double-blind, dose-ranging study was conducted in 286 people with established cardiovascular disease.⁶ Two-thirds of the patients were taking statins.

Baseline Lp(a) concentrations ranged from 205-247 nmol/L, and LDL levels were 67-89 mg/dL. The primary endpoint was percent change in Lp(a) concentration. At six months, all

pelacarsen dose groups showed reductions. The highest dose of 20 mg subcutaneously every week yielded an 80% change from baseline.

A four-year phase 3 trial is complete, and results are expected in 2026. The primary endpoint is time to first major cardiovascular event. If pelacarsen demonstrates a significant benefit over placebo, it will be essential to assess the degree of Lp(a) reduction linked to the benefit.

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AHA/ACC 2026 Lipid Guideline⁷
In all adults, measurement of Lp(a) concentration is recommended at least once for ASCVD risk assessment.
In all individuals with elevated Lp(a), optimal early control of modifiable cardiovascular risk factors is recommended to reduce ASCVD risk.
In individuals with clinical ASCVD and elevated Lp(a) who have not achieved LDL and non-HDL treatment goals on maximally tolerated statin therapy, the addition of a PCSK9 monoclonal antibody with proven cardiovascular benefit is recommended to achieve treatment goals and reduce ASCVD risk.

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