reported in ASPREE.[70] We recommend having a risk–benefit discussion about aspirin in primary prevention patients with elevated Lp(a), for use as a risk-lowering—not a lipid-lowering—agent, although some studies have reported Lp(a) reduction with high doses of aspirin.[71] As noted, aspirin may also be used in children with high Lp(a) and prior stroke.[31]

Lipoprotein apheresis

Currently, the only FDA-approved therapy for treating high Lp(a) is lipoprotein apheresis, based on observational data (see Table 1; COR IIa, LOE B-NR). In addition to indications defined by LDL-C levels, apheresis is now also approved for use in high-risk patients with FH and ASCVD (coronary or peripheral arteries) whose Lp(a) level remains ≥60 mg/dL [~150 nmol/L)] and LDL-C ≥ 100 mg/dL on maximally tolerated lipid-lowering therapy.[72] Because lipoprotein apheresis removes all apoB-containing lipoproteins, both LDL-C and Lp(a) are substantially reduced acutely but return toward pretreatment levels between procedures. However, apheresis is not available at all centers and can be expensive and time-consuming. A need remains for additional treatment options to address Lp(a)-related residual risk.

New therapies under investigation

Pelacarsen is an antisense oligonucleotide targeting the mRNA transcribed from the *LPA* gene and can reduce Lp(a) levels by >80 %.[73] Olpasiran is an siRNA that also prevents the translation of the apo(a) protein with up to ~100 % reduction in circulating Lp(a) levels.[74] However, whether these therapies can reduce MACE has not yet been established and is currently being tested in large ongoing cardiovascular outcome trials in secondary prevention patients with elevated Lp(a) levels: pelacarsen in Assessing the Impact of Lipoprotein (a) Lowering with Pelacarsen (TQJ230) on Major Cardiovascular Events in Patients with CVD (Lp(a)HORIZON)[75] and olpasiran in Olpasiran Trials of Cardiovascular Events and Lipoprotein(a) Reduction (OCEAN(a))–Outcomes Trial.[76] Other siRNA therapies targeting Lp(a) (zerlasiran [SLN360][77] and lepodisiran [LY3819469])[78] are being tested in phase 2 trials.[79] Additionally, an oral agent (muvalaplin [LY3473329]) that works by a different mechanism of disrupting the formation of Lp(a), by interfering with the apo(a) and apoB interaction, is being tested in early-phase trials.[80]

Challenges in increasing rates of Lp(a) testing

Despite the knowledge that Lp(a) elevation is common and affects at least ~1/5 of individuals worldwide, current rates of testing for Lp(a) in clinical practice remain extremely low.[81,82] Several studies have examined the prevalence of Lp(a) testing across single centers and large health systems.

In the US, the prevalence of Lp(a) testing across 6 centers in the University of California health system in 2012–2021 (5,553,654 patients) was only 0.3 %, with low Lp(a) testing rates observed in patients with ischemic heart disease (2.9 %), peripheral vascular disease (2 %), and stroke (1.8 %).[81] A similar study examined the prevalence of Lp(a) testing across 11 US health systems (PCORnet) in 2015–2019 and found that Lp(a) was measured in only 0.06 % of patients per year.[83]

Thus, while rates of Lp(a) testing are low when examining large health systems, heterogeneity exists in the prevalence of Lp(a) testing among single centers, specific patient populations, and differing healthcare reimbursement policies. For example, the prevalence of Lp(a) testing may be higher at individual centers, among patients with conditions known

Table 3 Take home points.

- The relationship between Lp(a) level and cardiovascular disease risk is continuous and log-linear
- Rather than a single dichotomous cutpoint defining a risk threshold, Lp(a) levels represent a continuum of cardiovascular disease risk spanning low, intermediate, and high risk
- Individuals with Lp(a) levels <75 nmol/L (30 mg/dL) may be considered low risk, individuals with Lp(a) levels ≥125 nmol/L (50 mg/dL) may be considered high risk, and individuals with Lp(a) levels in the "gray zone" between 75 and 125 nmol/L (30–50 mg/dL) are at intermediate risk and may warrant repeat measurement
- Lp(a) risk categories apply across races and ethnicities
- Lp(a) should be measured at least once in every adult for cardiovascular risk assessment
- Lp(a) should be measured and reported in nmol/L; Lp(a) values should not be converted between mg/dL and nmol/L using a fixed conversion factor
- The previously proposed correction factor for Lp(a)-C used to adjust LDL-C calculation may lead to the undertreatment of high-risk patients and therefore should not be used
- Although statins may increase Lp(a) levels, concerns about Lp(a) elevation should not be a reason to discourage or discontinue statins
- In high-risk patients with elevated Lp(a) who need additional LDL-C lowering after maximally tolerated statin therapy, a PCSK9 inhibitor may address residual risk from both LDL-C and Lp(a)
- Lipoprotein apheresis was approved by the FDA for use in patients with clinically diagnosed heterozygous familial hypercholesterolemia and either documented coronary artery disease or documented peripheral artery disease who have Lp(a) level ≥60 mg/dL (~150 nmol/L) and LDL-C ≥ 100 mg/dL despite maximally tolerated lipid-lowering therapy

Abbreviations: FDA, United States Food and Drug Administration; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); Lp(a)-C, lipoprotein(a) cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.