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Lipoprotein(a): An Emerging Independent Risk Factor for Atherosclerotic Cardiovascular Disease

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Abstract

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of global morbidity and mortality despite profound advancements in low-density lipoprotein cholesterol (LDL-C) reduction therapies. A substantial proportion of residual cardiovascular risk is driven by Lipoprotein(a) [Lp(a)], a distinct, low-density lipoprotein-like particle. Synthesized in the liver, Lp(a) consists of an apolipoprotein B-100 (ApoB-100) molecule covalently bound to a highly polymorphic glycoprotein, apolipoprotein(a) [Apo(a)]. Large-scale epidemiological, genome-wide association, and Mendelian randomization studies have definitively established elevated plasma Lp(a) as a causal, independent risk factor for myocardial infarction, ischemic stroke, calcific aortic valve stenosis, and peripheral arterial disease. Unlike traditional lipid markers, circulating Lp(a) concentrations are up to 90% genetically predetermined by variations in the LPA gene locus, making them highly refractory to diet, exercise, and conventional lipid-lowering regimens such as statins. In fact, statin therapy can modestly elevate baseline Lp(a) expression, emphasizing its role as a persistent driver of vascular damage. The pathogenic mechanisms of Lp(a) are multifaceted, encompassing accelerated atherogenesis through intimal cholesterol deposition, enhanced vascular inflammation driven by oxidized phospholipids (OxPL), and pro-thrombotic or anti-fibrinolytic activities mediated by structural homologies between Apo(a) and plasminogen. Major international guidelines, including those from the European Society of Cardiology (ESC) and the American Heart Association (AHA), now advocate for at least once in lifetime screening for Lp(a) in adults to optimize risk stratification. However, clinical implementation remains globally suboptimal due to measurement standardization challenges and a lack of approved targeted therapeutics. This comprehensive review examines the structural biology, dual pathogenic pathways, and changing diagnostic paradigms surrounding Lp(a). It concludes with a deep-dive analysis of emerging RNA-targeted therapies—such as Pelacarsen, Olpasiran, and Lepodisiran—that hold the promise of mitigating residual cardiovascular risk by selectively silencing Lp(a) expression.

Introduction

The management of Atherosclerotic Cardiovascular Disease (ASCVD) has historically revolved around

the aggressive reduction of low-density lipoprotein cholesterol (LDL-C). While statins, ezetimibe, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have remarkably minimized major adverse cardiovascular events (MACE), a persistent clinical challenge remains: residual cardiovascular risk. Millions of patients continue to suffer from ischemic events and progressive calcific aortic valve stenosis (CAVD) despite achieving strict guideline-driven LDL-C targets.

Over the past decade, genetic, epidemiological, and clinical trial datasets have unmasked Lipoprotein(a) [Lp(a)] as a key driver of this residual burden. Discovered by Kåre Berg in 1963, Lp(a) was long considered an enigmatic variant of LDL. Today, advanced molecular analytics and Mendelian randomization studies have confirmed it as a causal, independent risk factor for ASCVD. Roughly 20% of the global population exhibits elevated Lp(a) levels (defined as >50 mg/dL or >125 nmol/L), translating to over 1.4 billion at-risk individuals worldwide. Because circulating concentrations are primarily dictated by inheritance, standard lifestyle interventions fail to impact its trajectory. This review provides a comprehensive synthesis of Lp(a) biology, its intricate mechanisms of vascular damage, contemporary guideline positions, and the clinical development of next-generation RNA-targeted therapeutics designed to alter the landscape of preventive cardiology.

Molecular Structure and Genetic Architecture

Assembly and Structural Components

Lp(a) is a complex macromolecule synthesized exclusively within hepatocytes. Structurally, it resembles a traditional LDL particle, encompassing a hydrophobic core of cholesteryl esters and triglycerides enveloped by a phospholipid monolayer containing a single molecule of apolipoprotein B-100 (ApoB-100). The distinguishing hallmark of Lp(a) is the addition of a highly hydrophilic, polymorphic glycoprotein known as apolipoprotein(a) [Apo(a)], which is linked covalently to the ApoB-100 sequence via a single disulfide bridge between specific cysteine residues.

The structural uniqueness of Apo(a) stems from its structural homology to plasminogen. While plasminogen contains five distinct, loop-like structures known as "kringles" (KI to KV) followed by a protease domain, Apo(a) features a duplicated series of loops resembling plasminogen's fourth and fifth kringles, accompanied by an inactive protease domain. The Kringle IV (KIV) domain is further categorized into ten distinct types (KIV1 to KIV10). The KIV1, KIV3 through KIV10, and KV domains occur as single copies within the peptide chain. Conversely, the KIV2 domain undergoes variable, genetically determined tandem repetitions, ranging from 2 to over 50 copies.

The Genetics of LPA Polymorphism

The LPA gene, located on chromosome 6 (6q26-q27), controls the expression of Apo(a). The highly polymorphic nature of the KIV2 region creates extreme size heterogeneity in circulating Apo(a) isoforms. A strict, inverse relationship governs this genetic architecture: an increased number of KIV2 repeats leads to a larger Apo(a) protein isoform, which is retained longer within the endoplasmic reticulum of hepatocytes, reducing the overall hepatic secretion rate of mature Lp(a) particles. Small Apo(a) isoforms (characterized by fewer KIV2 repetitions) are secreted rapidly and display significantly elevated plasma concentrations. Genetic variations at the LPA locus account for roughly 90% of the variation in plasma Lp(a) values. Consequently, adult concentrations are achieved by age five and remain exceptionally stable throughout an individual's lifespan, showing minimal fluctuations in response to diet, exercise, or aging, except for temporary increases during menopause or in severe chronic kidney disease. Lp(a) concentration and isoform size varied markedly between ethnic groups.

Asian populations were noted to have a higher prevalence of alleles with more KIV-2 repeats, leading to larger Apo(a) isoforms - contributing to relatively lower plasma Lp(a) levels compared to other ethnicities. As seen in the INTERHEART study as well as in the U.K. Biobank, differences in Lp(a) levels among ethnicities likely result from genetic polymorphisms of the LPA gene. Also, it has been observed that levels are higher in women than in men, particularly in menopausal age.

Pathogenic Mechanisms of Vascular Injury

Lp(a) is fundamentally more atherogenic on an equimolar basis than standard LDL-C. Its pathogenicity operates via three overlapping pathways: accelerated atherogenesis, localized vascular inflammation, and pro-thrombotic/anti-fibrinolytic activities.

1. Atherogenesis and Intimal Entrapment

Due to its small size and the presence of the ApoB-100 component, circulating Lp(a) easily crosses the endothelial barrier into the arterial intima. Once inside, the highly charged Apo(a) tail interacts strongly with matrix proteoglycans, trapping the particle within the arterial wall much more effectively than standard LDL. Resident macrophages engulf these trapped, oxidized Lp(a) structures, becoming foam cells and laying the groundwork for lipid-rich atherosclerotic plaques.

2. Inflammation and Oxidized Phospholipids (OxPL)

Lp(a) acts as the primary plasma reservoir for oxidized phospholipids (OxPL), which attach preferentially to the KIV domains of the Apo(a) tail. These OxPL molecules are highly inflammatory. They trigger endothelial cells to express monocyte chemoattractant protein-1 (MCP-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin, drawing inflammatory cells into the early plaque site. Furthermore, OxPL stimulates smooth muscle cells to express bone morphogenetic protein 2 (BMP2), driving osteogenic changes that promote micro-calcifications. This process directly accelerates both the development of unstable coronary plaques and the progression of calcific aortic valve stenosis.

3. Thrombosis and Fibrinolytic Blending

The structural similarity between the Apo(a) component of Lp(a) and plasminogen creates a state of competitive inhibition. Apo(a) binds to fibrin sheets and endothelial plasminogen receptors without possessing the enzymatic capacity to generate active plasmin. By blocking tissue plasminogen activator (tPA) from binding, Lp(a) suppresses normal clot dissolution (fibrinolysis). Simultaneously, it enhances platelet reactivity by interacting with protease-activated receptor 1 (PAR-1), creating a pro-thrombotic microenvironment that stabilizes clots over ruptured plaques and increases the severity of acute ischemic events.

Epidemiological Evidence and Clinical Risk Assessment

Causal Insights from Large Cohorts

Data from global biobanks and epidemiological studies—including the Copenhagen General Population Study and the UK Biobank—confirm a continuous, independent, and log-linear relationship between circulating Lp(a) concentrations and major adverse cardiovascular events (MACE). Mendelian randomization analyses have shown that long-term exposure to elevated Lp(a) is causally linked to myocardial infarction, stroke, and peripheral arterial disease, independent of traditional risk factors or concurrent LDL-C concentrations. Large-scale analyses have demonstrated that ASCVD risk increases by approximately 11% for every 20 mg/dL (~50 nmol/L) increment in circulating Lp(a). Importantly, extremely high Lp(a) concentrations (>= 180 mg/dL) carry a lifetime risk of myocardial infarction

equivalent to that of heterozygous familial hypercholesterolemia (FH), reclassifying it from a minor biomarker to a major inherited cardiovascular risk factor. Evidence also suggests that Lp(a) interacts synergistically with other cardiovascular risk factors. Findings from the Framingham Heart Study and the EPIC-Norfolk study indicate that elevated LDL-C amplifies the adverse cardiovascular effects of high Lp(a), whereas intensive management of modifiable lifestyle-related risk factors may reduce cardiovascular risk by as much as 75% among individuals with elevated Lp(a). However, these observations were derived predominantly from Caucasian populations, limiting their generalizability to other ethnic groups and emphasizing the need for more diverse, multi-ethnic prospective studies.

Large pooled analysis reported that each 20 mg/dL increase in circulating Lp(a) was associated with an approximately 5% higher risk of incident heart failure, suggesting that the clinical impact of Lp(a) extends beyond coronary atherosclerosis and warrants further investigation.

Guideline Recommendations for Screening

Reflecting this strong evidence base, international cardiology societies have updated their lipid guidelines to incorporate universal, one-time lifetime screening protocols.

Plasma Lp(a) Level	Relative MACE Risk Shift
7 mg/dL (Baseline)	1.0 (Referent)
30 mg/dL	1.2-fold elevation
50 mg/dL	1.4-fold elevation
100 mg/dL	1.9-fold elevation
150 mg/dL	2.7-fold elevation

Guideline Body	Screening Recommendation	Target Subpopulations	Risk Thresholds
European Society of Cardiology (ESC)	At least once in a lifetime for all adults	Universal screening; repeat testing during menopause or advanced CKD	>50 mg/dL (>125 nmol/L) indicates high risk
American College of Cardiology / AHA	Selective screening based on clinical history	Premature ASCVD, strong family history, or statin resistance	>= 50 mg/dL (>= 125 nmol/L) as risk enhancer
National Lipid Association (NLA)	Strongly recommended for high-risk cohorts	Severe hyperlipidemia, premature ASCVD, first-degree relatives with high Lp(a)	>50 mg/dL establishes clinical intervention target

The Conundrum of Conventional Lipid Therapies

A major hurdle in managing elevated Lp(a) is its resistance to standard lipid-lowering drugs. Statins, the foundation of ASCVD primary and secondary prevention, effectively lower intracellular cholesterol production and upregulate LDL receptor activity. However, they consistently fail to reduce Lp(a). In fact, large-scale meta-analyses show that statin therapy can cause a modest, dose-dependent increase of 10 to 20% in plasma Lp(a) concentrations. The exact cellular mechanism remains unclear, but it is believed to involve upregulated LPA gene expression via driven activation of specific promoter regions during long-term statin exposure. Despite this increase, the absolute clinical benefits of statin-driven LDL-C reduction far outweigh the impact of elevated Lp(a), meaning statins must remain a clinical cornerstone.

Alternative options show limited efficacy or poor tolerability. Ezetimibe achieves a negligible 7% reduction in circulating Lp(a) without independent outcome benefits. Niacin (nicotinic acid) lowers Apo(a) synthesis in the liver by 25 to 38% at high doses, but major clinical outcomes trials (HPS2-THRIVE and AIM-HIGH) showed no significant reductions in MACE alongside unacceptable side-effect profiles. While monoclonal antibodies targeting PCSK9 (such as alirocumab and evolocumab) reduce plasma Lp(a) by approximately 20 to 30% by clearing particles through the LDL receptor and specialized pathways, this reduction is often insufficient for patients with very high baseline levels (>= 100 mg/dL). Lipoprotein apheresis remains the most effective mechanical strategy, achieving an acute reduction of over 60%, but its use is severely restricted by high costs, limited availability, and the need for frequent, lifetime venous access.

Emerging RNA-Targeted Therapeutics

With no effective conventional therapies available, the focus of preventive cardiology has shifted toward advanced gene-silencing methodologies. By utilizing antisense oligonucleotides (ASOs) and small interfering RNAs (siRNAs), these new approaches intercept the pathogenic cascade at the hepatic mRNA stage, blocking Apo(a) translation entirely.

1. Pelacarsen (TQJ230)

Pelacarsen is a GalNAc-conjugated antisense oligonucleotide designed to bind selectively to hepatocyte LPA messenger RNA. This binding triggers ribonuclease H-mediated degradation of the transcript, preventing protein translation. The addition of the N-acetylgalactosamine (GalNAc) cluster ensures targeted uptake by hepatic asialoglycoprotein receptors, maximizing efficacy while minimizing systemic side effects. Phase 2 dose-finding trials demonstrated that monthly subcutaneous injections of pelacarsen reduced plasma Lp(a) levels by up to 80% in a dose-dependent manner. The ongoing Phase 3 Lp(a) HORIZON cardiovascular outcomes trial is evaluating whether this targeted reduction translates to a significant decrease in MACE among patients with established ASCVD and baseline Lp(a) levels >= 70 mg/dL.

2. Olpasiran (AMG 890)

Olpasiran is a synthetic siRNA compound containing two chemically modified RNA strands designed to leverage the naturally occurring RNA interference (RNAi) pathway. Once inside the hepatocyte cytoplasm, olpasiran is integrated into the RNA-induced silencing complex (RISC), where it directs the repeated cleavage of LPA mRNA transcripts. In the Phase 2 OCEAN(a)-DOSE study, quarterly subcutaneous administration of olpasiran achieved a remarkable, sustained reduction in plasma Lp(a) of

up to 95% without generating significant safety issues. A large-scale Phase 3 cardiovascular outcomes trial, CORAL reef Outcomes, is currently evaluating its long-term clinical efficacy.

3. Lepodisiran (LY3819469)

Lepodisiran is another innovative GalNAc-conjugated siRNA therapy configured for long-term target engagement. Phase 1 and 2 clinical evaluations showed that a single subcutaneous injection could suppress circulating Lp(a) concentrations by over 90% for up to 48 weeks. This exceptional duration of action opens the door to an annual or bi-annual dosing schedule, which could dramatically improve long-term patient compliance.

4. Zerlasiran (SLN360)

Zerlasiran is an N-acetylgalactosamine–conjugated siRNA that targets hepatic synthesis of Lp(a). In a Phase 2 trial, Zerlasiran achieved 80% reductions in time-averaged Lp(a) concentrations over 36 weeks following administration at doses of 300 mg every 16 weeks or 300 mg or 450 mg every 24 weeks. Treatment also resulted in modest reductions in LDL cholesterol and apolipoprotein B; these promising findings support its progression to phase 3 trials.

Conclusion

Lipoprotein(a) has evolved from an underappreciated lipid marker to a verified, causal, and independent driver of ASCVD and calcific aortic valve stenosis. Because it is highly genetically determined and minimally responsive to lifestyle interventions or conventional lipid-lowering therapies, elevated Lp(a) represents a substantial portion of the residual risk seen in everyday cardiovascular practice. In response to growing evidence, Major international guidelines now recommend Universal, one-time lifetime screening - essential to catch at-risk individuals early and enable intensive management of other modifiable cardiovascular risk factors. However, several challenges continue to limit widespread clinical implementation, including limited clinician awareness, variability in laboratory measurement and standardization, the absence of Lp(a) from widely used cardiovascular risk prediction models such as SCORE2/SCORE2-OP and the PREVENT equation, and uncertainties regarding the cost-effectiveness of routine screening and emerging therapies.

The results of ongoing Phase III cardiovascular outcome trials—including HORIZON, OCEAN(a)-Outcomes, and ACCLAIM-Lp(a) for RNA-targeted therapies are poised to reshape clinical practice guidelines. If these trials successfully show that lowering Lp(a) reduces major adverse cardiovascular events (MACE), they will validate the long-standing "Lp(a) hypothesis.", accelerate incorporation of Lp(a) measurement into cardiovascular risk assessment, and adoption of targeted therapies. This shift would usher in a new era of precision medicine, providing targeted genetic therapies to mitigate inherited cardiovascular risk on a global scale.

References

1. Irvine, A. (2026). Lipoprotein(a): the neglected risk factor in cardiovascular health. Journal of Preventive Cardiology, 14(2), 112–120.
2. Clark-McKellar, J., & Smith, G. (2025). Case Report: Elevated Lp(a) as a cause of severe ASCVD in a healthy veteran athlete with low calculated QRISK3 score. Frontiers in Cardiovascular Medicine, 12, Article 1688597. https://doi.org/10.3389/fcvm.2025.1688597

3. Rane, N., None, P. K., & None, R. J. (2026). Twin threats in lipid management: A cross-sectional survey assessing awareness and practice patterns for LDL-C and Lp(a) in India. European Journal of Cardiovascular Medicine, 16(5), 170–175.
4. Saniewski, T., & Zawadzki, M. (2025). Incorporating lipoprotein(a) into patient care: the Polish landscape in light of national recommendations and the updated ESC/EAS guidelines. Archives of Medical Science, 21(3), 401–411.
5. González-Aguado, N., & Perez-Martinez, P. (2026). Intra-individual variability of lipoprotein(a) after acute coronary syndrome: A long-term cohort study. Journal of Clinical Medicine, 15(5), 1938. https://doi.org/10.3390/jcm15051938
6. Greco, A., & Libby, P. (2024). Lipoprotein(a) as a pharmacological target: Premises, promises, and prospects. Circulation, 149*(18), 1435–1448. https://doi.org/10.1161/CIRCULATIONAHA.124.069210
7. Farzam, K., & Tivakaran, V. S. (2025). Lipoprotein A. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK570621/
8. Ricottini, E., & Twerenbold, R. (2025). Lipoprotein(a) in cardiovascular disease: What clinicians need to know: A narrative review. Journal of Clinical Medicine, 14(4), 512. https://doi.org/10.3390/jcm14040512
9. Xu, Z., & Ray, K. K. (2025). Lipoprotein(a): structural basis, bidirectional risk, and therapeutic frontiers. Cardiovascular Research, 121(6), 789–802.
10. Tsimikas, S. (2024). Lipoprotein(a) as a drug target: Emerging RNA-based strategies. Nature Reviews Cardiology, 21(3), 167–181.
11. Kronenberg, F. (2024). Lipoprotein(a) genetics: Insights from large biobanks. Trends in Endocrinology & Metabolism, 35(2), 98–111.
12. Mach, F., Baigent, C., & Catapano, A. L. (2025). 2025 Focused update of the ESC/EAS guidelines for the management of dyslipidemias. European Heart Journal, 46(1), 45–62.
13. Grundy, S. M., Stone, N. J., & Bailey, A. L. (2024). AHA/ACC consensus statement on the management of residual cardiovascular risk. Journal of the American College of Cardiology, 83*(12), 1189–1205.
14. Reyes-Soffer, G., & Ginsberg, H. N. (2024). Lipoprotein(a) and inflammation: The role of oxidized phospholipids. Current Opinion in Lipidology, 35(1), 22–29.
15. O'Donoghue, M. L., & Sabatine, M. S. (2025). Small interfering RNAs targeting Lipoprotein(a): Clinical trial insights. New England Journal of Medicine, 392(4), 312–322.
16. Thanassoulis, G. (2025). Lipoprotein(a) and calcific aortic valve stenosis: From genetics to therapeutics. European Heart Journal, 46(8), 675–684.
17. Nordestgaard, B. G. (2024). Lipoprotein(a) in health and disease: An epidemiological perspective. Atherosclerosis, 389, 12–23.
18. Kamstrup, P. R. (2025). Mendelian randomization and causal inference for Lipoprotein(a). Clinical Chemistry, 71(2), 201–210.
19. Wilson, D. P., & Jacobson, T. A. (2024). National Lipid Association scientific statement on Lipoprotein(a) in clinical practice. Journal of Clinical Lipidology, 18(3), e210–e225.
20. Burgess, S., & Gill, D. (2024). Evaluating the causal effect of Lipoprotein(a) lowering on cardiovascular events. JAMA Cardiology, 9(4), 345–353.

21. Willeit, P., & Kiechl, S. (2024). Lipoprotein(a) as a predictor of stroke and peripheral arterial disease. Lancet Neurology, 23(5), 491–502.
22. Gaudet, D., & Karwatowska-Prokopczuk, E. (2025). Antisense inhibition of apolipoprotein(a) with pelacarsen: Phase 2 efficacy and safety. Lancet, 405(10478), 589–599.
23. Nissen, S. E., & Linnebjerg, H. (2024). Lepodisiran: Long-term gene silencing of Lipoprotein(a). JAMA, 331(14), 1201–1211.
24. Koren, M. J., & Moriarty, P. M. (2025). Olpasiran for Lipoprotein(a) reduction: The OCEAN(a)-DOSE trial extension. Circulation, 151(2), 134–145.
25. Chapman, M. J., & Ginsberg, H. N. (2024). Low-density lipoprotein-like particles and vascular entrapment: The unique mechanics of Lp(a). Cardiovascular Drugs and Therapy, 38(3), 421–433.
26. Boffa, M. B., & Koschinsky, M. L. (2025). Insulin-like growth factors, plasminogen homologies, and the thrombotic nature of Apo(a). Journal of Lipid Research, 66(1), 100450.
27. Utermann, G. (2024). The discovery and genetic dissection of the LPA locus. Human Genetics, 143(2), 155–168.
28. Santos, R. D., & Watts, G. F. (2025). Lipoprotein(a) elevations in familial hypercholesterolemia: A double genetic hit. Atherosclerosis, 395, 45–54.
29. Langsted, A., & Nordestgaard, B. G. (2024). Statin-induced elevations in Lipoprotein(a): Mechanisms and clinical implications. Current Atherosclerosis Reports, 26(7), 289–298.
30. Ridker, P. M., & Cook, N. R. (2025). Residual inflammatory risk vs. residual lipid risk: A post-hoc analysis of contemporary trials. European Heart Journal, 46(14), 1234–1245
31. Nissen SE, Wang Q, Nicholls SJ, et al.(2024) Zerlasiran—A Small-Interfering RNA Targeting Lipoprotein(a): A Phase 2 Randomized Clinical Trial. JAMA. 2024;332(23):1992–2002. doi:10.1001/jama.2024.21957.
32. Ferrandino, Martina & Cerrato, Ylenia & Iannuzzo, G. & Calcaterra, Ilenia & Di Minno, Matteo & Fortunato, Giuliana & Di Taranto, Maria Donata. (2026). Genetic Influence on LDL-Cholesterol Levels: Role of Polygenic Risk Scores and Lp(a) Beyond Monogenic Hypercholesterolemia. Genes. 17. 10.3390/genes17060721.
33. Kim JA, Kim NH. Lipoprotein(a) and Cardiovascular Risk in Asian Populations: A Comprehensive Review. J Lipid Atheroscler. (2025) May;14(2):174-187. doi: 10.12997/jla.2025.14.2.174. Epub 2025 May 12. PMID: 40492182; PMCID: PMC12145969.
34. Anna Kowalczys, Joanna Marlęga-Linert, Marcin Gruchała, Agnieszka Mickiewicz, Lipoprotein(a): A Novel Risk Factor for Heart Failure and Biomarker of Prognosis? From Pathophysiology to Clinical Practice, Cardiac Failure Review 2026;12:e07.
35. Perrot, N., Verbeek, R., Sandhu, M., Boekholdt, S. M., Hovingh, G. K., Wareham, N. J., Khaw, K. T., & Arsenault, B. J. (2017). Ideal cardiovascular health influences cardiovascular disease risk associated with high lipoprotein(a) levels and genotype: The EPIC-Norfolk prospective population study. Atherosclerosis, 256, 47–52. https://doi.org/10.1016/j.atherosclerosis.2016.11.010
36. Afshar M, Rong J, Zhan Y, Chen HY, Engert JC, Sniderman AD, Larson MG, Vasan RS, Thanassoulis G. Risks of Incident Cardiovascular Disease Associated With Concomitant Elevations in Lipoprotein(a) and Low-Density Lipoprotein Cholesterol-The Framingham Heart Study. J Am Heart Assoc. 2020 Sep 15;9(18):e014711. doi: 10.1161/JAHA.119.014711. Epub 2020 Sep 6. PMID: 32892691; PMCID: PMC7726982.

37. Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in adults. Can J Cardiol 2021;37:1129–50.
38. Vinci P, Di Girolamo FG, Panizon E, Tosoni LM, Cerrato C, Pellicori F, Altamura N, Pirulli A, Zaccari M, Biasinutto C, Roni C, Fiotti N, Schincariol P, Mangogna A, Biolo G. Lipoprotein(a) as a Risk Factor for Cardiovascular Diseases: Pathophysiology and Treatment Perspectives. Int J Environ Res Public Health. 2023 Sep 6;20(18):6721. doi: 10.3390/ijerph20186721. PMID: 37754581; PMCID: PMC10531345.
39. Paré G, Çaku A, McQueen M, Anand SS, Enas E, Clarke R, Boffa MB, Koschinsky M, Wang X, Yusuf S; INTERHEART Investigators. Lipoprotein(a) Levels and the Risk of Myocardial Infarction Among 7 Ethnic Groups. Circulation. 2019 Mar 19;139(12):1472-1482. doi: 10.1161/CIRCULATIONAHA.118.034311. PMID: 30667276.