



# Lipoprotein(a) in the nexus of infections and atherosclerotic events – short and long-term consequences

Alpo Vuorio<sup>1,2,\*</sup>, Petri T. Kovanen<sup>3</sup>, Bruce Budowle<sup>2</sup>, Frederick J. Raal<sup>4</sup>

<sup>1</sup>Mehiläinen Aviapolis Health Center, Vantaa 01530, Finland.

<sup>2</sup>Department of Forensic Medicine, University of Helsinki, Helsinki 00100, Finland.

<sup>3</sup>Wihuri Research Institute, Helsinki 00290, Finland.

<sup>4</sup>Faculty of Health Sciences, University of Witwatersrand, Johannesburg 2193, South Africa.

**\*Correspondence to:** Alpo Vuorio, Mehiläinen Aviapolis Health Center, Vantaa 01530, Finland; Department of Forensic Medicine, University of Helsinki, Helsinki 00100, Finland. E-mail: [alpo.vuorio@gmail.com](mailto:alpo.vuorio@gmail.com)

**Received:** September 26, 2025 **Accepted:** December 10, 2025 **Published:** December 22, 2025

**Cite this article:** Vuorio A, Kovanen PT, Budowle B, Raal FJ. Lipoprotein(a) in the nexus of infections and atherosclerotic events – short and long-term consequences. *Adv Lipoprotein(a) Res.* 2026;1:202506. <https://doi.org/10.70401/alr.2025.0003>

## Abstract

Current Lp(a)-related scientific literature is mainly related to cardiovascular diseases, while less attention has been paid to the role of Lp(a) in both the severity of infections and the vascular disease events that follow them. In this perspective article, we highlight findings related to lipoprotein(a) [Lp(a)] in infectious diseases, including those caused by the severe acute respiratory syndrome coronavirus 2, human immunodeficiency virus, hepatitis C virus (HCV), *Helicobacter pylori*, *Chlamydia pneumoniae*, cytomegalovirus, or the *Plasmodium* and *trypanosomal* parasites. Based on the data from the above-mentioned infections and Lp(a), the role of Lp(a) in these common infectious diseases will be discussed. Of particular interest is that Lp(a) can inhibit HCV infection and is also important for protection against parasitic infections such as malaria and trypanosomiasis. New drugs, like muvalaplin, significantly lower Lp(a) levels, and it is therefore important to learn about the significance of low Lp(a) levels in terms of the potential course of an infection. It remains to be seen whether Lp(a) drugs with different mechanisms of action are relevant for infections.

**Keywords:** Lipoprotein(a), infections, atherosclerotic events, SARS-CoV-2, hepatitis, HIV

## 1. Introduction

Lipoprotein(a), or Lp(a), is a type of lipoprotein particle that carries cholesterol in the blood similar to LDL lipoprotein particles, but with a unique apolipoprotein (a) attached to it. The role of lipoprotein(a) and the severity of infections are intertwined<sup>[1,2]</sup>. During an acute-phase response to an infection, the cytokine interleukin 6 (IL-6) activates the *LPA* gene through IL-6 response elements<sup>[3]</sup>. While the basal levels of Lp(a) are genetically determined, during an acute infection, the levels may increase markedly. Lp(a) particles, in turn, induce the expression of inflammatory genes<sup>[4]</sup>. Increased Lp(a) levels have been demonstrated in, for example, chronic inflammatory diseases and sepsis<sup>[5-7]</sup>.

It has also been shown that oxidized phospholipids (oxPLs) on apo(a) mediate numerous atherothrombotic molecular and cellular events leading to atherothrombotic cardiovascular disease<sup>[8]</sup>. Interestingly, in transgenic mice (E06-scFv mice), elevated oxPL levels were associated with increased morbidity and shorter survival rates, and levels of interleukin 10, which are known to be anti-inflammatory in action, were suppressed<sup>[9]</sup>. These observations support the role of oxPLs as a key mediator in host-derived damage-associated molecular patterns<sup>[10]</sup>. While not shown in the context of Lp(a), the above findings may also be associated with elevated Lp(a) levels during infections.

The current Lp(a)-related scientific literature is mainly related to cardiovascular diseases. In contrast, information about the possible role of Lp(a) in infectious diseases is scanty. Therefore, in an attempt to fill this gap in cumulative knowledge, in this perspective article we highlight findings related to Lp(a) in various common infectious diseases, such as acute bacterial sepsis, and in viral diseases such as those caused by SARS-CoV-2, human immunodeficiency virus (HIV), hepatitis viruses, cytomegalovirus, *Helicobacter pylori*, *Chlamydia pneumoniae*, and finally in parasitic infections such as malaria and trypanosomiasis. Since infections are considered contributory components in cardiovascular diseases, but the available data based on epidemiological and follow-up studies are



conflicting, we also speculate about the possible modulatory role of Lp(a) in the proatherogenic role of infections. Based on data on the above-mentioned infections and Lp(a), we highlight Lp(a)’s role in these common infectious diseases. This perspective article updates the fragmented data available and explores the nexus between infection and Lp(a), also in the context of cardiovascular disease.

2. SARS-CoV-2

In the early phases of the COVID-19 pandemic, measurement of Lp(a) was recommended to determine if it may contribute to, or be a biomarker of, cardiovascular complications of COVID-19<sup>[11]</sup>. It has been postulated that Lp(a) may inhibit fibrinolysis and promote proinflammatory and proatherogenic effects<sup>[12,13]</sup>. Furthermore, the cytokine storm that occurs with acute COVID-19 infection increases IL-6 and can affect the *LPA* gene with a resultant increase in Lp(a) level. Table 1 summarizes various studies on COVID-19 patients and the effects of Lp(a) concentrations during infection.

Table 1. Lp(a) and COVID-19 in different studies.

| Patients & Study                                                                                     | Result                                                                                                                            | Conclusion                                                                                                                                                                                                                                                |
|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 50 COVID-19 patients30 matched sick controls <sup>[14]</sup>                                         | Lp(a) did not differ between COVID-19 patients and controls<br>Lp(a) was positively correlated with IL-8, fibrinogen and creatine | A significant correlation was observed between higher serum Lp(a) and worse outcomes in COVID-19 patients, suggesting a potential role in the pathogenesis of SARS-CoV-2 infection, such as enhancing the risk of micro- and macro-thrombosis             |
| UK Biobank 6937 COVID-19 patients and 435,104 controls <sup>[1]</sup>                                | SARS-CoV-2 infections enforce an association between high Lp(a) and CHD<br>Thromboembolic events were not influenced by Lp(a)     | Patients with high Lp(a) concentrations can be considered a high-risk group for SARS-CoV-2 infection                                                                                                                                                      |
| 80 COVID-19 patients<br>Lp(a) < 30 mg/dL<br>44 COVID-19 patients<br>Lp(a) ≥ 30 mg/dL <sup>[15]</sup> | Elevated Lp(a) might be a factor contributing to a more severe course of SARS-CoV-2 infection                                     | Elevated Lp(a) levels may contribute to longer hospitalization, more extensive pulmonary radiological alterations, higher oxygen demand on admission, and increased risk of intubation and intensive care unit treatment during hospitalization and death |
| 80 COVID-19 patients<br>Lp(a) < 30 mg/dL<br>44 COVID-19 patients<br>Lp(a) ≥ 30 mg/dL <sup>[16]</sup> | A decrease in Lp(a) levels, observed a year after COVID-19, was accompanied by a significant reduction in IL-6 levels             | Lp(a) levels increase during an inflammatory state, including SARS-CoV-2 infection. Despite a significant reduction in Lp(a) levels following COVID-19 infection, a substantial majority of patients still have high Lp(a) levels one year post-infection |
| 219 hospitalized COVID-19 patients <sup>[17]</sup>                                                   | An increase in Lp(a) levels during the acute phase of COVID-19 was associated with venous thromboembolism incidence               | Study supports a contribution of Lp(a) increase to the pro-thrombotic state in COVID-19 patients                                                                                                                                                          |
| 349 hospitalized COVID-19 patients<br>7 non-COVID-19 controls <sup>[18]</sup>                        | Increased Lp(a) levels during hospitalization were associated with mortality                                                      | High Lp(a) concentration provides a possible explanation for low endogenous tissue-type plasminogen activity and poor clinical outcomes in COVID-19                                                                                                       |

Lp(a): lipoprotein(a); SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; CHD: coronary heart disease.

In several studies, Lp(a) levels were shown to be increased during SARS-CoV-2 infection and to have an impact on both the severity of infection and cardiovascular events. This has been shown especially in the heterozygous form of familial hypercholesterolemia<sup>[19]</sup>. In one follow-up study, Lp(a) levels remained elevated for a relatively long time following SARS-CoV-2 infection. Based on these and other studies, Lp(a) does not appear to be associated with increased thrombotic events. However, because the study designs differed, a reliable comparison of the results is difficult. Although it can be concluded that Lp(a) levels appear to be informative about the prognosis of significant SARS-CoV-2 infections, monitoring of Lp(a) levels should still be considered part of the treatment protocol for this infection<sup>[13]</sup>.

Of note, while apo(a) is a specific protein component in Lp(a) particles, apo-A1 and apo-A2 are apolipoprotein components of high-density lipoprotein (HDL) particles. Little, if anything, is known about potential interactions between Lp(a) particles and HDL particles, and therefore they are not discussed here<sup>[20-23]</sup>.

3. HIV

HIV infection is an independent risk factor for coronary heart disease (CHD), and the infected patients have a two-fold greater risk of developing CVD when compared with people without HIV<sup>[24]</sup>. In a recent study, Lp(a) levels were significantly higher ( $p < 0.01$ ) in HIV-infected individuals ( $N = 65$ ; 78 nmol/L [39-137 nmol/L]) compared with controls ( $N = 52$ ; 45.5 nmol/L [18-102.5 nmol/L]<sup>[25]</sup>). Of note, in the HIV-positive patients, the Lp(a) levels correlated inversely with coronary endothelial function. The study highlights the need for further research to elucidate Lp(a)'s role in patients with this chronic infectious disease.

Earlier studies also suggested a possible role of Lp(a) in HIV infected patients. Enkhmaa *et al.*<sup>[26]</sup> showed that in patients with HIV infection, allele-specific apo(a) levels were higher in subjects with higher CD4+ T-cell counts or a low plasma HIV RNA viral load. Additionally, they found that allele-specific apo(a) levels were associated with smaller ( $< 28$  K4) atherogenic apo(a) sizes and were higher in patients with CD4+ T-cell counts  $\geq 350$ . It was concluded that HIV-infection reduced allele-specific apo(a) levels and, despite atherogenic small apo(a) sizes, it might contribute to CHD risk among HIV patients with improved infection status. Enkhmaa *et al.*<sup>[27]</sup> also showed that antiretroviral therapy increased Lp(a) levels. Also, in a relatively small study, perinatally HIV-infected children were shown to have elevated Lp(a) levels, which was partly contributed by their ethnic background<sup>[28]</sup>. Currently, the Lp(a) related research in HIV is targeted at improving cardiovascular health among HIV infected patients, as the treatments have greatly improved survival and prognosis in HIV-infected individuals<sup>[25,29]</sup>.

4. Sepsis

Several studies have shown that Lp(a) levels increase during acute sepsis as cytokine interleukin-6 (IL-6) activates the LPA gene through IL-6 response elements<sup>[3]</sup>. However, other studies have not supported this observation. The role of Lp(a) as an acute-phase reactant was evaluated in a study measuring plasma Lp(a) levels, apo(a), apo(a) fragments, urinary apo(a), C-reactive protein (CRP) as well as low-density lipoprotein cholesterol (LDL-C) in 9 patients with acute sepsis who were treated in the intensive care unit and four patients with extensive burns<sup>[5]</sup>. Both in the sepsis and burn patients, Lp(a) and LDL-C levels declined and closely mirrored the increase in CRP levels. Among five surviving sepsis patients, Lp(a) levels were 5- to 15-fold lower during sepsis compared to 16 to 18 months after sepsis. There were no changes in apo(a) fragment levels or urinary apo(a) during the study period. In this study, it was shown that Lp(a) acts as a negative acute phase reactant in acute sepsis, and that the decline was not due to accelerated fragmentation of Lp(a).

The above finding that Lp(a) acts as a negative acute phase reactant in sepsis is supported by a larger follow-up study of 9,861 hospitalized sepsis patients<sup>[30]</sup>. In this larger study, Lp(a) decreased initially but then increased significantly [Lp(a) at baseline =  $24.6 \pm 16.06$ ; Lp(a) at sepsis-2 years =  $8.25 \pm 5.17$ ; Lp(a) at more than 2 years =  $61.4 \pm 40.1$ ;  $p = 0.0032$ ]. There were also other long-term abnormalities, such as increased levels of total cholesterol, LDL-C, and high-sensitivity CRP, each of which could have contributed to an accelerated CHD after the single septic episode. The authors concluded that there seems to be metabolic reprogramming after sepsis. Metabolic reprogramming is known to occur after systemic infection, as the human body prioritizes eliminating the pathogenic microbe at the expense of disease tolerance<sup>[31]</sup>. It has been shown that, during viral infections, metabolic reprogramming enables immune cells to adjust their energy production while attempting to restrict viral invasion<sup>[32]</sup>. There does not appear to be detailed knowledge on how Lp(a) could potentially be related to metabolic reprogramming in infections. [Table 2](#) summarizes studies that have reported on the effects of Lp(a) during and after sepsis.

**Table 2.** Lp(a) and sepsis in specified studies.

| Patients & Study                                                                                             | Result                                                                 | Conclusion                                                                                                                                              |
|--------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| 9 patients admitted to the intensive care unit for sepsis and 4 patients with extensive burns <sup>[5]</sup> | Lp(a) declined abruptly and transiently in parallel with LDL-C levels  | Lp(a) behaved as a negative acute-phase reactant during the major inflammatory response, but after 14-16 months, it increased when compared to baseline |
| 9,861 individuals hospitalized for a singular episode of Sepsis <sup>[30]</sup>                              | Lp(a) was elevated up to two years after the initial episode of sepsis | Persistent derangements of lipid profile for up to two years after sepsis may be associated with an altered risk of vascular events                     |

Lp(a): lipoprotein(a); LDL-C: low-density lipoprotein cholesterol.

5. Hepatitis

As early as 1996, Geiss *et al.*<sup>[33]</sup> studied 74 hepatitis patients (32, 28, and 14 with hepatitis A, B, and C, respectively) and found that during acute hepatitis, median Lp(a) concentrations in these patients significantly decreased compared with controls (7 vs. 17 mg/dL;  $p < .0001$ , Mann-Whitney test). In a subsequent study, Lp(a) was measured in 130 patients (50 with acute viral hepatitis, 30 with chronic active hepatitis, 30 with cirrhosis of the liver, and 20 with fulminant hepatic failure)<sup>[34]</sup>. The Lp(a) levels were reduced

significantly ( $p < 0.001$ ) in patients irrespective of the aetiology compared with 50 controls.

Oliveira *et al.* showed that apo(a) inhibits hepatitis C virus entry through interaction with infectious particles<sup>[35]</sup>. This study was carried out with a recombinant virus derived from the JFH1 strain. The authors showed that, by using plasma-derived and recombinant Lp(a) as well as purified recombinant apo(a) variants, apo(a) was able to modify HCV infection, and HCV was specifically inhibited by apo(a) interacting with the infectious particles. In additional experiments, these authors demonstrated that Lp(a) can inhibit HCV infection. Table 3 summarizes studies reporting Lp(a) levels during viral hepatitis.

**Table 3.** Lp(a) and hepatitis in specified studies.

| Patients & Study                                                                                                                                                                                     | Result                                                                                                                                                                | Conclusion                                                                                                                               |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Lp(a) serum concentrations in 74 patients with acute viral hepatitis and in 404 healthy controls <sup>[33]</sup>                                                                                     | During acute hepatitis, median Lp(a) concentrations in the patient group were significantly diminished compared with controls                                         | Acute hepatitis was associated with decreased Lp(a) levels. Lp(a) concentration might be a clinically useful parameter of liver function |
| Lp(a) was measured in 50 patients with acute viral hepatitis, 30 with chronic active hepatitis, 30 with liver cirrhosis, 20 patients with fulminant hepatic failure, and 50 controls <sup>[34]</sup> | Lp(a) levels in patients in all the disease groups were significantly reduced compared with controls                                                                  | The extent of decrease in Lp(a) level was nearly the same in all the different hepatic infections irrespective of the viral aetiology    |
| Combining polyethylene glycol precipitation, iodixanol gradient, and size-exclusion chromatography, a purified fraction enriched with inhibitory factors from HCV-seronegative sera <sup>[35]</sup>  | Plasma-derived and recombinant Lp(a), as well as purified recombinant apo(a) variants, were able to specifically inhibit HCV by interacting with infectious particles | Apo(a) modulated HCV infection. Study opens new perspectives for the study of apo(a) function                                            |

Lp(a): lipoprotein(a); HCV: hepatitis C virus.

6. *Helicobacter pylori*, *Chlamydia pneumoniae*, Cytomegalovirus, Malaria and Trypanosomiasis

Lp(a) levels have been studied in several other infections known to be associated with increased risk of atherosclerosis. In a study of 470 healthy blood donors and 238 patients with angiographically proven CHD, those who were seropositive for *Chlamydia pneumoniae*, chlamydial lipopolysaccharide, or cytomegalovirus were found to have *Helicobacter pylori* infection, and Hoffmeister *et al.*<sup>[36]</sup> evaluated further. Lp(a) levels were not different between healthy blood donors and patients with CHD regarding seropositivity for *Chlamydia pneumoniae*, cytomegalovirus, or *Helicobacter pylori* infection. However, this study does not exclude the possibility of short-term elevation in Lp(a) levels during an acute infection. In another study, Lp(a) levels were measured in 111 patients with malaria and in 106 symptomatic controls (defined as malaria-negative febrile patients) in Gabon<sup>[37]</sup>. No significant differences were found in Lp(a) levels between these groups, although the levels declined acutely during the infection. Over 20 years ago, it was discovered that apoL1 protects humans against infections by trypanosome subspecies that cause African sleeping sickness (trypanosomiasis)<sup>[38,39]</sup>. High levels of apoL1 protect against trypanosomiasis, and although apoL1 is carried mainly in HDL, it is also carried by Lp(a). Black Africans have higher Lp(a) levels, and a possible explanatory reason for it may be the ability of Lp(a) to protect against *Trypanosoma brucei* gambiense, which is endemic in West and Central Africa<sup>[40]</sup>.

7. New Lp(a) Lowering Drugs

Several Lp(a) lowering drugs are being studied in clinical trials, including siRNA formulations (olpasiran, zerlasiran, lepodisiran), an antisense oligonucleotide (pelacarsen), and muvalaplin, which is a small molecule oral drug<sup>[41-46]</sup>. Currently, these drugs are being studied in clinical trials but are not yet in clinical use.

Antisense oligonucleotide (ASO) and siRNA formulations decrease Lp(a) levels by more than 90%<sup>[47]</sup>. ASOs are single-stranded DNA or RNA molecules, typically 15-25 nucleotides in length. They act by binding to complementary RNA sequences, leading to the degradation of target mRNA through RNase H activation or by steric hindrance that prevents translation. For Lp(a), they are designed to reduce apo(a) synthesis by inhibiting apo(a) mRNA<sup>[48]</sup>. In contrast, siRNAs are double-stranded RNA molecules about 20-25 nucleotides in length. They function through a process called RNA interference (RNAi), where one strand of the siRNA guides the RNA-induced silencing complex to the target mRNA encoding Lp(a), leading to its cleavage and degradation<sup>[49]</sup>.

The mechanism of action of muvalaplin is different from the other drugs currently in clinical trials; it inhibits the first step of Lp(a) formation by blocking the apo(a)-apo B100 interaction and therefore results in reduced formation of Lp(a) by the liver<sup>[46]</sup>. Inasmuch as Lp(a) is an independent risk factor for both atherosclerotic cardiovascular disease and aortic stenosis, these agents may reduce the risk of both diseases, but this remains to be proven. Whether the marked reduction in Lp(a) achieved with these agents will result in

decreased or increased susceptibility to infections, both acute viral infection and sepsis, as well as more chronic viral infections such as HCV, and parasitic infections such as malaria and trypanosomiasis, requires further study.

Lp(a) is known to trigger several inflammatory pathways, including monocyte activation, which induces secretion of several pro-inflammatory markers and upregulation of chemokine receptors, adhesion molecules, transmigration markers, and scavenger receptors<sup>[2,50]</sup>. Lp(a) also contributes to endothelial inflammation and causes endothelial dysfunction<sup>[51]</sup>. So new drugs designed to decrease atherosclerotic events by lowering Lp(a) may also affect the body's response to certain infections. This challenging situation – either for better or worse – needs to be studied in placebo-controlled trials targeting a primary decrease in vascular events.

## 8. Limitations

Unfortunately, Lp(a) is not measured routinely during infections, and only a limited number of studies have reported on Lp(a) levels related to common infections<sup>[2]</sup>. In addition, in the majority of these studies, Lp(a) was measured only once, and there are no available follow-up data during and after the infection. New specific Lp(a) lowering drugs are not yet approved for clinical use, so their impact on infection has not yet been studied<sup>[45]</sup>.

## 9. Conclusion

The primary focus of research currently is on the importance of Lp(a) as a risk factor for vascular disease<sup>[3]</sup>. Less attention has been paid to the fact that Lp(a) plays a role in both the severity of infections and the vascular disease events following infections<sup>[2]</sup>. Currently, the most convincing evidence is from retrospective analyses and follow-up studies of patients with SARS-CoV-2 infection, which show that this infection is more severe in those patients with high Lp(a) levels<sup>[1,14,15]</sup>. In addition, SARS-CoV-2 infection per se increases Lp(a) levels, and these levels remain high for a prolonged period, acting as a potential risk enhancer for cardiovascular events<sup>[16]</sup>. Of particular interest is that apo(a) and Lp(a) can act as inhibitors of HCV infection and are also important for protection against parasitic infections such as malaria and trypanosomiasis. New drugs significantly lower Lp(a) levels, and it is therefore important to know the significance of low Lp(a) levels in terms of infections. Muvalaplin has a different mechanism of action, and it remains to be seen whether Lp(a) drugs with distinct mechanisms are relevant for infections. Muvalaplin inhibits the first step of Lp(a) formation by small molecule interactions with apo(a), but apo(a) continues to be produced, and serum apo(a) levels are not markedly decreased<sup>[46]</sup>. When new Lp(a) specific drugs are approved for use in the future, it will be important to also report on infections reported in these placebo-controlled studies that are targeted to decrease vascular events.

## Declarations

### Authors contribution

Vuorio A: Writing-original draft, writing-review & editing.  
Kovanen PT, Budowle B, Raal FJ: Writing-review & editing.

### Conflicts of interest

Alpo Vuorio has received consultancy fees from Amgen and Novartis. Petri T. Kovanen has received consultancy fees, lecture honoraria, and/or travel fees from Amarin, Amgen, Novartis, Raisio Group, and Sanofi. Frederick J. Raal has received research grants, honoraria, or consulting fees for professional input and/or lectures from Sanofi, Regeneron, Amgen, Novartis, and LIB Therapeutics. Bruce Budowle declares no conflicts of interest.

### Ethical approval

Not applicable.

### Consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Funding

None.

## Copyright

© The Author(s) 2025.

## References

1. Di Maio S, Lamina C, Coassin S, Forer L, Würzner R, Schönherr S, et al. Lipoprotein(a) and SARS-CoV-2 infections: Susceptibility to infections, ischemic heart disease and thromboembolic events. *J Intern Med*. 2022;291(1):101-107. [DOI]
2. Dzobo KE, Kraaijenhof JM, Stroes ESG, Nurmohamed NS, Kroon J. Lipoprotein(a): An underestimated inflammatory mastermind. *Atherosclerosis*. 2022;349:101-109. [DOI]
3. Makris A, Barkas F, Sfrikakis PP, Liberopoulos E, Filippatos TD, Ray KK, et al. Lipoprotein(a), Interleukin-6 inhibitors, and atherosclerotic cardiovascular disease: Is there an association? *Atheroscler Plus*. 2023;54:1-6. [DOI]
4. Lorey MB, Youssef A, Äikäs L, Borrelli M, Hermansson M, Assini JM, et al. Lipoprotein(a) induces caspase-1 activation and IL-1 signaling in human macrophages. *Front Cardiovasc Med*. 2023;10:1130162. [DOI]
5. Mooser V, Berger MM, Tappy L, Cayeux C, Marcovina SM, Darioli R, et al. Major reduction in plasma Lp(a) levels during sepsis and burns. *Arterioscler Thromb Vasc Biol*. 2000;20(4):1137-1142. [DOI]
6. Zhao L, Sun L, Zhang Z, Yang K, Li Z, Wang M, et al. Lipoprotein(a) is a new prognostic factor in patients with psoriasis and coronary artery disease: a retrospective cohort study. *Lipids Health Dis*. 2023;22(1):141. [DOI]
7. Popescu D, Badescu MC, Rezus E, Tanase DM, Ouatu A, Dima N, et al. Cardiovascular risk in rheumatic patients treated with JAK inhibitors: The role of traditional and emerging biomarkers in a pilot study. *J Clin Med*. 2025;14(15):5433. [DOI]
8. Boffa MB, Koschinsky ML. Oxidized phospholipids as a unifying theory for lipoprotein(a) and cardiovascular disease. *Nat Rev Cardiol*. 2019;16(5):305-318. [DOI]
9. Que X, Hung MY, Yeang C, Gonen A, Prohaska TA, Sun X, et al. Oxidized phospholipids are proinflammatory and proatherogenic in hypercholesterolaemic mice. *Nature*. 2018;558(7709):301-306. [DOI]
10. Colaço HG, Voss K. Oxidized phospholipids during microbial challenge: friend or foe? *Genes Immun*. 2024;25(3):177-178. [DOI]
11. Moriarty PM, Gorby LK, Stroes ES, Kastelein JP, Davidson M, Tsimikas S. Lipoprotein(a) and Its Potential Association with Thrombosis and Inflammation in COVID-19: a Testable Hypothesis. *Curr Atheroscler Rep*. 2020;22(9):48. [DOI]
12. Enkhmaa B, Berglund L. Lp(a) and SARS-CoV-2: A conspiracy of two mysteries. *J Intern Med*. 2022;291(1):8-10. [DOI]
13. Montagnana M, Lippi G. Lipoprotein(a) in COVID-19: Genetics and inflammation collide. *Atherosclerosis*. 2022;347:77-78. [DOI]
14. Lippi G, Szergiyuk I, de Oliveira MHS, Benoit SW, Benoit JL, Favaloro EJ, et al. The role of lipoprotein(a) in coronavirus disease 2019 (COVID-19) with relation to development of severe acute kidney injury. *J Thromb Thrombolysis*. 2022;53(3):581-585. [DOI]
15. Pawlos A, Gorzelak-Pabiś P, Staciwa M, Broncel M. Elevated Lp(a) and course of COVID-19: Is there a relationship? *PLoS One*. 2022;17(6):e0266814. [DOI]
16. Warzywoda J, Pawlos A, Woźniak E, Broncel M, Gorzelak-Pabiś P. Lipoprotein(a) levels may temporarily increase during COVID-19: A pilot study. *Pol Arch Intern Med*. 2024;134(3):16707. [DOI]
17. Nurmohamed NS, Collard D, Reeskamp LF, Kaiser Y, Kroon J, Tromp TR, et al. Lipoprotein(a), venous thromboembolism and COVID-19: A pilot study. *Atherosclerosis*. 2022;341:43-49. [DOI]
18. Zhang Z, Dai W, Zhu W, Rodriguez M, Lund H, Xia Y, et al. Plasma tissue-type plasminogen activator is associated with lipoprotein(a) and clinical outcomes in hospitalized patients with COVID-19. *Res Pract Thromb Haemost*. 2023;7(6):102164. [DOI]
19. Vuorio A, Raal F, Kovanen PT. Familial hypercholesterolemia: The nexus of endothelial dysfunction and lipoprotein metabolism in COVID-19. *Curr Opin Lipidol*. 2023;34(3):119-125. [DOI]
20. Bruzzzone C, Bizkarguenaga M, Gil-Redondo R, Diercks T, Arana E, García de Vicuña A, et al. SARS-CoV-2 Infection dysregulates the metabolomic and lipidomic profiles of serum. *iScience*. 2020;23(10):101645. [DOI]
21. Ghini V, Meoni G, Pelagatti L, Celli T, Veneziani F, Petrucci F, et al. Profiling metabolites and lipoproteins in COMETA, an Italian cohort of COVID-19 patients. *PLoS Pathog*. 2022;18(4):e1010443. [DOI]
22. Ghini V, Vieri W, Celli T, Pecchioli V, Boccia N, Alonso-Vásquez T, et al. COVID-19: A complex disease with a unique metabolic signature. *PLoS Pathog*. 2023;19(11):e1011787. [DOI]
23. Sheashaa H, Mousa H, Abbas MT, Farina JM, Awad K, Pereyra M, et al. Interaction between lipoprotein(a) and other lipid molecules: A review of the current literature. *Biomolecules*. 2025;15(2):162. [DOI]
24. Afolabi JM, Kirabo A. HIV and cardiovascular disease. *Circ Res*. 2024;134(11):1512-1514. [DOI]
25. Kikuchi DS, Kwapong YA, Schär M, Weiss RG, Sun K, Brown TT, et al. Lipoprotein(a) is elevated and inversely related to coronary endothelial function in people with HIV. *J Am Heart Assoc*. 2024;13:e035975. [DOI]
26. Enkhmaa B, Anuurad E, Zhang W, et al. HIV disease activity as a modulator of lipoprotein(a) and allele-specific apolipoprotein(a) levels. *Arterioscler Thromb Vasc Biol*. 2013;33(2):387-392. doi:10.1161/ATVBAHA.112.300125
27. Enkhmaa B, Anuurad E, Zhang W, Abbuthalha A, Li XD, Dotterweich W, et al. Effect of antiretroviral therapy on allele-associated Lp(a) level in women with HIV in the Women's Interagency HIV Study. *J Lipid Res*. 2018;59(10):1967-1976. [DOI]
28. van Genderen JG, Van den Hof M, de Boer CG, Jansen HPG, van Deventer SJH, Tsimikas S, et al. Longitudinal assessment of lipoprotein(a) levels in perinatally HIV-Infected children and adolescents. *Viruses*. 2021;13(10):2067. [DOI]

29. Șoldea S, Iovănescu M, Berceanu M, Mirea O, Raicea V, Beznă MC, et al. Cardiovascular disease in HIV patients: A comprehensive review of current knowledge and clinical implications. *Int J Mol Sci.* 2025;26(5):1837. [DOI]
30. Felici N, Liu D, Maret J, Restrepo M, Borovskiy Y, Hajj J, et al. Long-Term abnormalities of lipid profile after a single episode of sepsis. *Front Cardiovasc Med.* 2021;8:674248. [DOI]
31. Willmann K, Moita LF. Physiologic disruption and metabolic reprogramming in infection and sepsis. *Cell Metab.* 2024;36(5):927-946. [DOI]
32. Darweesh M, Mohammadi S, Rahmati M, Al-Hamadani M, Al-Harrasi A. Metabolic reprogramming in viral infections: the interplay of glucose metabolism and immune responses. *Front Immunol.* 2025;16:1578202. [DOI]
33. Geiss HC, Ritter MM, Richter WO, Schwandt P, Zachoval R. Low lipoprotein (a) levels during acute viral hepatitis. *Hepatology.* 1996;24(6):1334-1337. [DOI]
34. Irshad M. Serum lipoprotein (a) levels in liver diseases caused by hepatitis. *Indian J Med Res.* 2004;120(6):542-545. [PubMed]
35. Oliveira C, Fournier C, Descamps V, et al. Apolipoprotein(a) inhibits hepatitis C virus entry through interaction with infectious particles. *Hepatology.* 2017;65(6):1851-1864. [DOI]
36. Hoffmeister A, Rothenbacher D, Bode G, Persson K, März W, Nauck MA, et al. Current infection with *Helicobacter pylori*, but not seropositivity to *Chlamydia pneumoniae* or cytomegalovirus, is associated with an atherogenic, modified lipid profile. *Arterioscler Thromb Vasc Biol.* 2001;21(3):427-432. [DOI]
37. Visser BJ, de Vries SG, Vingerling R, Gritter M, Kroon D, Aguilar LC, et al. Serum lipids and lipoproteins during uncomplicated malaria: A cohort study in Lambaréné, Gabon. *Am J Trop Med Hyg.* 2017;96(5):1205-1214. [DOI]
38. Vanhollebeke B, Truc P, Poelvoorde P, Pays A, Joshi PP, Katti R, et al. Human Trypanosoma evansi infection linked to a lack of apolipoprotein L-I. *N Engl J Med.* 2006;355(26):2752-2756. [DOI]
39. Höffken V, Braun DA, Pavenstädt H, Weide T. A cell biologist's view on APOL1: What we know and what we still need to address. *Cells.* 2025;14(13):960. [DOI]
40. Reyes-Soffer G. The impact of race and ethnicity on lipoprotein(a) levels and cardiovascular risk. *Curr Opin Lipidol.* 2021;32(3):163-166. [DOI]
41. Tsimikas S, Karwatowska-Prokopczuk E, Gouni-Berthold I, Tardif JC, Baum SJ, Steinhagen-Thiessen E, et al. Lipoprotein(a) reduction in persons with cardiovascular disease. *N Engl J Med.* 2020;382(3):244-255. [DOI]
42. Nissen SE, Wolski K, Balog C, Swerdlow DI, Scrimgeour AC, Rambaran C, et al. Single ascending dose study of a short interfering RNA targeting lipoprotein(a) production in individuals with elevated plasma lipoprotein(a) levels. *JAMA.* 2022;327(17):1679-1687. [DOI]
43. O'Donoghue ML, López JAG, Knusel B, Gencer B, Wang H, Wu Y, et al. Study design and rationale for the Olpasiran trials of Cardiovascular Events And lipoprotein(a) reduction-DOSE finding study (OCEAN(a)-DOSE). *Am Heart J.* 2022;251:61-69. [DOI]
44. Maloberti A, Fabbri S, Colombo V, Gualini E, Monticelli M, Daus F, et al. Lipoprotein(a): cardiovascular disease, aortic stenosis and new therapeutic option. *Int J Mol Sci.* 2022;24(1):170. [DOI]
45. Paragh G, Zilahi P, Kolozsvári LR, Lőrincz H, Fülöp P, Harangi M. Novel therapeutic approaches for the management of elevated lipoprotein(a): From traditional agents to future treatment options. *Life.* 2024;14(3):374. [DOI]
46. Nicholls SJ, Ni W, Rhodes GM, et al. Oral Muvalaplin for lowering of lipoprotein(a): A randomized clinical trial. *JAMA.* 2025;333(3):222-231. [DOI]
47. De Los Reyes C, Rikhi RR, Doherty S, Hernandez S, Mirzai S, Shapiro MD, et al. Current clinical trials for treating elevated lipoprotein(a). *Curr Cardiovasc Risk Rep.* 2025;19(1):7. [DOI]
48. Hamasaki M, Kotani K. Lipoprotein(a)-lowering drugs: A mini review. *J Clin Med Res.* 2025;17(4):181-186. [DOI]
49. Almaadawy O, Hesn MME, Elsalamony YA, Abobakr OA, Elshimy AH, Abulkhair KA, et al. Small interfering RNA effect on lipoprotein(a): A systematic review. *Egypt Heart J.* 2025;77(1):44. [DOI]
50. van der Valk FM, Bekkering S, Kroon J, Yeang C, Van den Bossche J, van Buul JD, et al. Oxidized phospholipids on lipoprotein(a) elicit arterial wall inflammation and an inflammatory monocyte response in humans. *Circulation.* 2016;134(8):611-624. [DOI]
51. Qin T, Ma TY, Huang K, Lu SJ, Zhong JH, Li JJ. Lipoprotein (a)-related inflammatory imbalance: A novel horizon for the development of atherosclerosis. *Curr Atheroscler Rep.* 2024;26(8):383-394. [DOI]

## Publisher's Note

Science Exploration remains a neutral stance on jurisdictional claims in published maps and institutional affiliations. The views expressed in this article are solely those of the author(s) and do not reflect the opinions of the Editors or the publisher.