REVIEW ARTICLE

The Adiponectin/Leptin Ratio and Lipoprotein(a) in Cardiovascular Disease: Is There an Overlooked Link? A Scoping Review

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ABSTRACT

The adiponectin/leptin (A/L) ratio and lipoprotein(a) or Lp(a) are independent predictors of cardiovascular disease (CVD), as they represent an example of distinct biological pathways spanning metabolic inflammation and atherothrombosis. Adiponectin is recognized as having an anti-inflammatory, insulin-sensitizing effect, while leptin facilitates vascular inflammation and endothelial dysfunction; the ratio of adiponectin: leptin is a surrogate marker of fat tissue health and balance of metabolic control. However, it is unclear whether there is an unnoticed interplay between the A/L ratio and Lp(a) in the CVD pathogenesis processes or whether risk classification is unclear. The scoping review sought to examine human studies on the A/L ratio and Lp(a) that are currently available in the literature and to determine whether research and evidence obtained in the past exist to suggest a synergistic or additive clinical utility using both markers in the context of CVD. Keywords were used to perform a systematic search in ScienceDirect, PubMed, Scopus, and Web of Science from its inception through May 2025. After consideration of relevance, ten eligible studies were included, and the data were organized into themes. Although both biomarkers are closely associated with cardiovascular risk factor-low A/L ratios with insulin resistance, vascular inflammation, and elevated Lp(a) in the prothrombotic state, no research has examined their impact of them together. The lack of integrative analysis implies a major lack of knowledge. Discussion: This review suggests that future studies are required to determine the ability of dual profiling of the A/L ratio and Lp(a) to improve CVD prediction models and guide more personalized therapy classes. As these markers pending for more confirmatory evidence, we suggest considering the A/L ratio and Lp(a) in future cardiovascular risk-stratification protocols.
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INTRODUCTION

Cardiovascular disease is still the most common reason for death in the world, which is why risk management is an important aim in preventive cardiology. More interest is developing in certain new markers as well, since they could give us more accurate ways to calculate heart disease risk and find out what causes these illnesses. These two biomarkers, the adiponectin/leptin ratio and lipoprotein(a), since they are formed in different parts of the body (adipose tissue and the liver), and have usually been explored individually. Two hormones, adiponectin and leptin work differently, where adiponectin works against inflammation and heart damage, while leptin, which controls hunger levels, may lead to inflammation and affect the heart negatively [1]. A rise in leptin and fall in adiponectin in obesity and metabolic syndrome predisposes the body to atherosclerosis [2]. Analysts suggest that A/L ratio is a more integrative marker of adipose tissue dysfunction and risk of insulin resistance than using just one of the two hormones on its own [3, 4]. Conventional risk scores (e.g., Framingham, ASCVD) may underperform in individuals with metabolic inflammation or genetically elevated Lp(a), because these tools do not incorporate adipokine profiles or Lp(a). This omission can leave substantial residual risk unrecognized.

Meanwhile, recently, researchers have shown that lipoprotein(a) or Lp(a) is a key independent factor that causes CVD. Through the attachment of apolipoprotein(a) to an LDL-like particle, lp(a) is formed, and its structure is very similar to that of plasminogen [5]. Genetic factors

tend to make people's plasma Lp(a) levels high, especially if they are >30 mg/dL. Such high levels are known to contribute to premature coronary artery disease and stroke. For many years, since lipid-controlling ways do not work well on Lp(a), it was regarded as difficult to treat and wasn't given much attention in medicine. Still, present-day guidelines suggest checking Lp(a) levels at least once in a person's adult life to recognize those who have high values [6]. Elevated levels of Lp(a) increase the risk of atherosclerosis because its LDL part causes cholesterol buildup in arteries and its apolipoprotein (a) part gives the blood increased chances of clotting and inflammation [5, 7]. Likewise, apo(a) prevents fibrinolysis from working properly by affecting plasminogen, and Lp(a) brings oxidized phospholipids (OxPLs) that may start inflammation in the vessels.

This scoping review summarizes and brings together information about the A/L ratio and Lp(a) in regard to CVD, in order to notice any overlay, areas that need to be explored, and synergies. We would like this to encourage studies on how different biomarkers could be combined and lead to a wider view of cardiovascular risk by joining research on fatty tissue and lipoproteins.

METHODS

Following the recommendations of a scoping review, we examined existing studies on the adiponectin/leptin ratio, Lp(a), and cardiovascular disease to determine whether there is any evidence of a connection. A detailed search approach was then developed. Our search from inception to May 2025 included the topics adiponectin, leptin, their ratio, lipoprotein(a), and results related to cardiovascular disease in ScienceDirect, PubMed, Scopus, and Web of Science. Specific terms entered in our search were combinations such as "adiponectin," "leptin," "leptin-to-adiponectin ratio" (also abbreviated to "LAR") or "lipoprotein(a)," and "Lp(a)" along with mentions of these terms in relation to "coronary" events, "heart disease," "atherosclerosis," and as a "biomarker." We also included a list of references from similar studies. We included: (a) observational studies, (b) interventions, (c) reviews, and (d) meta-analyses offering information on the relationship between adiponectin, leptin, and any elements of cardiovascular risk or concerns. Because few studies have shown a direct link, we wanted to find any information that highlights a correlation or considers the two biomarkers at the same time. We included human studies; animal or in-vitro studies were excluded unless they directly elucidated mechanistic cross-talk relevant to human CVD. We have read only publications written in English. The literature covers a wide range of time, although most of it was published recently when attention toward adipokines and Lp(a) increased.

The exclusion criteria were as follows: small studies, conference abstracts without any full text, and studies examining adipokines or Lp(a) in contexts other from cardiovascular diseases. Studies on other fat-related molecules or lipids were added to the review only when the adiponectin/leptin or Lp(a) data were also included. Two reviewers searched the titles and abstracts of the selected studies to determine their relevance. Subsequently, the researchers examined all relevant papers. Due to the broad nature of the narrative, we did not assess the risk of bias; as in other narrative reviews, we only wanted to provide an overview of the findings. We combined all our findings by theme, grouping work into groups that relate to (1) the adiponectin/leptin ratio as a risk marker for CVD, (2) Lp(a) as a risk factor for CVD, and (3) how the results from the two groups may interact and give rise to different effects together. The purpose of our scoping review is to organize ideas and a lack of knowledge, and not to add effective information. Combining the mechanisms of the body with clinical observations is made easier using the narrative approach.

RESULTS

Adiponectin/leptin ratio as an Independent Cardiovascular Risk Factor

The adiponectin/leptin ratio is often used to assist in evaluating problems related to heart health and the chances of developing CVD.

Many researchers now relate the L/A ratio (leptin over adiponectin) to how healthy a person's adipose tissue is. In normal people, adiponectin is present at high levels and leptin is suitable to the amount of extra weight; in metabolic syndrome, both adiponectin and leptin are reduced, but leptin is still higher, which lowers the A/L ratio to indicate there is dysfunction in fat cells [2]. The ratio summarizes the balance between anti-atherogenic adiponectin and pro-atherogenic leptin. To illustrate, a 2013 study showed that in 428 men, those with a higher adiponectin/leptin ratio had fewer triglycerides, increased HDL cholesterol, and less insulin resistance than the men with a lower ratio [4]. It was also observed that the A/L ratio decreased with the growing number of risk factors for metabolic syndrome [4]. The ratio demonstrates that it shows the level of abnormal metabolic changes in the body related to adipose tissue. According to many studies, there is a connection between the A/L ratio and both hidden atherosclerosis and an increased risk of CVD. In their study of healthy men in Italy, Norata et al. [8] proved that the ratio of leptin to adiponectin was a more effective independent predictor of thickening in the arteries than each adipokine alone. When there is more leptin compared to adiponectin (higher L:A), the arterial walls thicken and these ratios were still connected to greater intima media thickness (IMT) even after considering other main risks [8]. Alone, leptin was connected to IMT, but adiponectin was not, and researchers found that the combined ratio best showed the chances of atherosclerosis [8]. As reported by Kappelle et al. [3] in a prospective nested case-control study, the plasma L/A ratio was able to predict the initial

cardiovascular events in men. While examining the men, scientists discovered that those who developed CVD had elevated leptin levels and larger L/A ratios than the controls, and adiponectin was not found to be any different either. Significantly, adjusting for various risk factors kept the L/A ratio strongly connected with an increased risk of developing CVD (hazard ratio of about 1.4), but leptin and adiponectin were no longer predictive. Based on their findings, the authors stated that the A/L ratio might show cardiovascular risk better than either of the hormones [3].

People have also looked at the A/L ratio in certain groups of patients. In another research project, Rahmani et al. [9] discovered by comparing 150 patients diagnosed with CAD to 150 healthy patients, that those with CAD had higher average leptin/adiponectin ratios. All three aspects examined in that study were linked to having CAD, but the ratio was the most reliable way to tell the two conditions apart. Besides, in individuals with CAD, people with wider coronary lesions (in more than one vessel) showed a noticeably higher L/A ratio, suggesting that this ratio may indicate greater disease severity. It is thanks to Lypez-Jaramillo et al. [2] that we know how the lack of adiponectin and the abundance of leptin in patients with abdominal obesity and coronary disease is linked to problems of endothelial function, including limited relaxation and boosted constriction caused by angiotensin II. As a result, high leptin counts raise the amount of TNF-α and IL-6, which leads to inflammation and insulin resistance, while poor adiponectin levels decrease protective and nitric oxide actions in the body [2]. Such inflammatory changes in the endothelial cells most likely cause atherosclerosis to develop more swiftly in those who have low A/L ratios.

Prediction with the A/L ratio does not end with middle-aged men and clear CAD; it works in other patient populations. Researchers noted that women facing gestational diabetes (GDM) had more leptin and more L/A ratio and less adiponectin, both shortly after their pregnancy and some time after [10]. Having a high A/L ratio in pregnancy, especially if a patient has GDM – was shown to increase the chances of developing poor heart-related health on follow-up. So, adiponectin-leptin imbalance may reveal how young women are at risk of cardiometabolic diseases ahead of any observable signs of CVD. Since the A/L ratio is considered a marker of adipose tissue inflammation, as noted by Frьhbeck et al. [11], it reflects both adipose disease activity and metabolic health. As a result, these studies prove that lower adiponectin and greater leptin are linked to metabolic syndrome, hidden atherosclerosis, and more chances of cardiovascular disease in a wide range of areas.

Lipoprotein(a) as an Independent Cardiovascular Risk Factor

People are now paying greater attention to lipoprotein(a) as a reason for increased cardiovascular risks. Lp(a) is formed by a covalent link between an LDL particle and apolipoprotein(a), a protein that brings some special traits. A person's Lp(a) levels usually depend more on genetics than on the choices they make in food and lifestyle. About 20% of individuals have levels of Lp(a) higher than 50 mg/dL, and higher Lp(a) levels are independently connected with increased chances of myocardial infarction, stroke, and peripheral artery disease (as stated by Poznyak et al. [12]). Both Mendelian randomization and using genetic approaches have shown that Lp(a) causes an increased risk of atherosclerotic CVD and calcific aortic valve stenosis [12]. Often, high levels of Lp(a) contribute to certain heart complications in people whose LDL levels are controlled. So, experts now recommend that people get their Lp(a) checked at least once in their life, especially when they have a history of early heart disease or risk coming from their family [6].

Experts sometimes explain that Lp(a) carries two risks to the heart, from the LDL portion as well as some extra pro-blood clotting and pro-inflammatory actions from apo(a) [5]. Like LDL, the core part of Lp(a) is able to deliver cholesterol to artery walls, thus contributing to plaque formation (hence leading to atherosclerosis). Besides, the long chain of apolipoprotein(a) consists of kringle domains that help attach it to oxidized phospholipid and connect it to cells inside the blood vessel wall and to white blood cells. Apo(a)'s structure is similar to plasminogen and is meant to function the same, but apo(a) does not display fibrinolytic activity. For this reason, Lp(a) prevents plasminogen from doing its job and helps to build clots [5]. According to those studies, Lp(a) has the ability to connect to endothelial cells and monocytes, which blocks the way for plasminogen [5]. Having an increased amount of Lp(a) in the system tends to cause blood clots to build on plaques instead of being removed. Besides, Lp(a) assists in bringing in oxidized phospholipids (OxPLs) into vessel walls; this leads to inflammation by recruiting many inflammatory cells and increasing adhesion molecules (ICAM-1, VCAM-1) in the area of blood vessels. For this reason, Lp(a) also brings about inflammation in the heart and artery tissues [7]. Experts have learned that apolipoprotein B particles in Lp(a) show high OxPL content, suggesting that this connection relates to the inflammation in plaques.

Medical research proves that Lp(a) carries many harmful effects. Various studies show that rising Lp(a) blood levels increase the chances of developing CVD. As an illustration, if Lp(a) is high (greater than 100 mg/dL or 250 nmol/L), it is linked to a greater than two-fold increased risk for heart attacks whether or not other factors, such as LDL, are taken into account. Even though adipokines heavily influence insulin resistance and metabolic syndrome, this is not the main impact of Lp(a). Among patients with familial hypercholesterolemia or improved LDL levels, having high Lp(a) tends to lead

to the risk of further complication. Because of this acknowledgment, new Lp(a)-directed therapies (like antisense oligonucleotides and siRNA agents against apo(a)) have been developed, and in studies they may decrease Lp(a) by more than 80%.

The information about the adiponectin/leptin ratio and Lp(a) in CVD is highlighted in Table I. Every type illustrates a unique part of risk, where the first is linked to metabolic inflammation and how fat metabolism functions, and the second is attached to genetic factors that influence lipoproteins, knowing about both forms of risk may present a clearer picture of a person's heart risk.

Potential interplay between adipokine imbalance and Lp(a)

A main concern and the topic of this review is if there is a connection between the adiponectin/leptin axis and Lp(a). As seen from the literature, studies that focus on the impact of the A/L ratio combined with Lp(a) on the risk of heart disease are very few because no study was composed mainly for this purpose. This may show that there is something missing in the research so far. It is possible to make sense of several areas in which these factors come together and could increase each other's effect.

The first thing to think about is the condition of the body's inflammatory environment. If there are low amounts of adiponectin and high levels of leptin, it results in a long-term inflammation called 'metabolic inflammation.' On the contrary, Lp(a) includes oxidized lipids that straightaway activate inflammation inside the arteries. A possibly occurrence is that because inflammation is usually high in individuals with a low A/L ratio, Lp(a) may enhance the risk of atherosclerosis more than in standard cases. Inflammation of the blood vessels increases the expression of some molecules, and these proteins 'stick' Lp(a) and immune cells to the blood vessel walls. Usually, adiponectin reduces vascular adhesion and stops the expression of some sticky proteins, but in cases of a low A/L state, reduced adiponectin fails to counteract these factors.

Also, adiponectin increases the body's production of nitric oxide in the endothelium, which promotes better circulation and blood flow, whereas extreme levels of leptin in the body may lead to endothelial dysfunction. Having a low A/L ratio usually goes with decreased NO availability in the endothelium [2]. If there is not enough NO, Lp(a) may trigger platelet clumping more and contribute to thickening blood on endothelium that is not working properly. Basically, Lp(a) could make matters

Table I: Comparison of the adiponectin/leptin ratio and lipoprotein(a) in the context of cardiovascular disease.

Aspect	Adiponectin/Leptin (A/L) Ratio	Lipoprotein(a) [Lp(a)]
Primary source	Adipose tissue hormones (adiponectin from fat, leptin from fat; A/L ratio reflects their balance) (2).	Liver-synthesized apolipoprotein(a) attached to an LDL particle (5).
Variation with obesity	Worsens with obesity: adiponectin decreases and leptin increases, lowering the A/L ratio (2, 4). A high ratio is seen in lean, insulin-sensitive states.	Largely genetic; only modestly affected by obesity or diet. Even lean individuals can have high Lp(a); weight loss has minimal effect on Lp(a) levels.
Association with metabolic syndrome	Strongly linked: Low A/L ratio correlates with insulin resistance, high triglycerides, low HDL, and hypertension (4). Proposed as an index of adipose tissue dysfunction in metabolic syndrome.	Not directly part of metabolic syndrome criteria. High Lp(a) does not cause insulin resistance; one can have metabolic syndrome with normal Lp(a) or vice versa.
Cardiovascular effects	Low ratio (high leptin, low adiponectin) creates a pro-inflammatory, pro-atherogenic state: leptin excess promotes TNF-α, IL-6 and oxidative stress, while adiponectin deficiency means loss of nitric oxide promotion and anti-inflammatory action (2). Endothelial dysfunction and arterial inflammation ensue.	Elevates CVD risk via arterial deposition and coagulation: Lp(a) delivers cholesterol and *oxidized phospholipids* into plaques (increasing foam cells, inflammation) (13). Apo(a) impairs fibrinolysis by competing with plasminogen, fostering a thrombogenic environment (5).
CVD risk association	Low A/L ratio is associated with greater atherosclerosis (e.g. carotid IMT) (8) and higher risk of coronary events (3). Predicts incident CVD in some studies even after adjusting for standard risk factors.	High Lp(a) is an *independent* risk factor for CVD (14). Individuals with Lp(a) in the top quintile have significantly higher rates of MI, stroke, and aortic stenosis. Risk is independent of LDL, and cumulative over a lifetime of exposure.
Intervention potential	No direct drug to alter the ratio, but it improves with lifestyle: weight loss, exercise, and certain insulin-sensitizing therapies raise adiponectin and/or lower leptin, thereby increasing the ratio. Acts as a *marker* of improved metabolic health rather than a target itself.	Dedicated therapies in development: antisense oligonucleotides and siRNA targeting apo(a) have shown >80% Lp(a) reduction. Currently, Niacin and PCSK9 inhibitors can mildly lower Lp(a), but lifestyle has minimal impact. Screening is important to identify those who might benefit from upcoming Lp(a)-lowering therapies.

The A/L ratio reflects adipose tissue-driven, metabolic and inflammatory risk, whereas Lp(a) represents inherited, lipoprotein-mediated risk. Both can contribute to atherosclerosis through different pathways.

worse in a vessel that has been affected by adipokine problems. In the case of too much adiponectin (where A/L is high), it could ease the damage caused by Lp(a), since it helps the endothelium.

There could also be connections in cells or organs that affect not only adipokines but also Lp(a). Administration of inflammatory signals might increase or decrease the apolipoprotein(a) production by the liver in some people, but little is known since studies on the topic are conflicting (by some accounts, inflammation does not always change Lp(a) levels). Anti-inflammatory treatment taken in a small group of patients with psoriasis (a chronic condition) worked to lower both leptin and Lp(a) at the same time, hinting that inflammation may play a part in their connection [13]. On the other hand, the levels of Lp(a) are usually not reduced by shedding extra weight or taking anti-inflammatory drugs as much as they can be for leptin. It means that any link is probably only useful on the artery walls (tied to the process of atherosclerosis formation) and not directly involved in controlling levels.

Talking about independent genes, adiposity and insulin sensitivity influence adiponectin and leptin levels, whereas Lp(a)'s levels are almost entirely dependent on genes. So, it is possible for an individual to have an unfavorable adipokines and low Lp(a), a favorable adipokines and high Lp(a), or simply to live with low risk factors on both sides. When both the L/A ratio and Lp(a) are high, the risk of cardiovascular disease might increase further or become greater than expected. It may happen mostly in people whose risk is caused by both family history and becoming overweight or developing metabolic syndrome. The weakness in research can cause doctors to overlook Lp(a) while handling metabolic syndrome, or to neglect the metabolic syndrome when working on Lp(a) treatment, among other things.
As of now, published studies have not pointed out that leptin or adiponectin correlate with Lp(a) in people in the general population. When both topics are studied, the few reports so far suggest little connection between the two, a review showed that studies either do not connect adiponectin and Lp(a) or might reveal a very weak trend on the contrary [14]. Even though there is no link between the levels of these biomarkers, it stresses that they still have certain impacts on the blood vessels. There have been no studies that evaluated cardiovascular events by considering patients with both low A/L and high Lp(a).

DISCUSSION

For this scoping review, we intended to join the research on adipokines and molecules such as adiponectin, leptin, and lipoprotein(a), both of which are usually discussed separately as cardiovascular risk aspects. The results show once more that both are essential, since an imbalanced adiponectin/leptin ratio may promote insulin resistance and inflammation, possibly leading to arterial plaques, and similarly, high values of Lp(a) represent a genetic trait that harbors risks for cholesterol and coagulation.

At least one significant gap is found in the literature, as A/L ratio is mainly not linked directly to Lp(a). Even though there is a lot of information about adiponectin, leptin, and Lp(a) independently, we found no research that mostly investigated how these three interact. It is clear that the huge benefits from diverse industries have not yet been noticed. A likely explanation is that adipokine researchers work mostly on their own and Lp(a) experts concentrate on their area. Sometimes, it's about practicality: many of these types of studies never gathered enough data together, and Lp(a) and the adiponectin/leptin pair were badly understudied in the past. Thus, not much data exists to be used for collaborative analysis. The review points out that it would be helpful to combine research efforts by, for instance, checking cohort data for interactions of adipokines and Lp(a), or by carrying out studies that evaluate them together to predict cardiometabolic issues.

How would the connection between the mutations and the diseases be useful to patients? There is no standard practice to include adipokines or Lp(a) in today's risk scores. Still, if someone is almost at risk (borderline), having checked that A/L ratio and Lp(a), we might decide to treat them more intensely and move them to a higher level of risk concern. In actual fact, clinicians have proposed single markers for better comparison of risks. Lp(a) testing is now used to discover risks not noticed by other markers [6], and in overweight or obese patients, a change in adiponectin/leptin ratio might show residual risk that was left out by other guidelines [3]. One more consideration is treatment monitoring: losing weight leads to higher adiponectin and lower leptin and thus improves the ratio, but it is ineffective for Lp(a). Nevertheless, upcoming Lp(a) antisense therapy will help with lipoproteins but not with metabolic conditions. Treatment may consist of changing the patient's diet and using a medication to manage their Lp(a).

We examined that adiponectin, leptin, and Lp(a) have an impact on the body's inflammatory, endothelial, and clotting systems. As an example, adiponectin is involved in cholesterol outflow from macrophages and lessens the number of foam cells; less adiponectin might result in more foam cells from cholesterol carried by Lp(a). Leptin may lead to division of muscle cells in blood vessels and may also aid the growth of new blood vessels, both of which may make plaques unstable if they contain large amounts of lipids [15]. The connections between these theories have to be checked using evidence. The idea of "biomarker synergy" should be investigated through research studies. This issue might be studied by considering an interaction term that relates Lp(a) to leptin (or adiponectin) levels when trying to foresee

health results from epidemiological data.

Emerging omics approaches could help interrogate cross-talk between A/L and Lp(a) pathways. Proteomics may quantify adipokine-related signaling proteins (e.g., inflammatory mediators, adhesion molecules) alongside apo(a)-associated peptides, while metabolomics can profile NO-bioavailability, oxidative stress, and lipid oxidation products (e.g., OxPL surrogates). Integrating multi-omics with clinical biomarker data could identify endotypes in whom low A/L and high Lp(a) co-localize, generating testable hypotheses for targeted prevention.

According to physiology, there is an interaction between blood vessels: adipokines can move inside the vessel wall (leptin acts on endothelial and immune cells there, while adiponectin acts too), and Lp(a) settles within the inside lining. Macrophages have been found to contain leptin in plaques, which could cause the macrophages to behave more actively in inflammation, whereas adiponectin has been discovered to lessen inflammation coming from plaques [16]. With elevated leptin and Lp(a), the surroundings of plaque can contain increased macrophages and lots of fats, which speed up its growth. Also, leptin can cause platelets to form blood clots, making Lp(a)'s harmful performance on fibrinolysis even worse [15]. In addition, deficiency of adiponectin removes a damaging function because it helps to block blood clot formation. Even though these substances do not directly change each other's levels, they still both contribute to the advancement of atherothrombosis.

Since this review is a narrative scoping study, we did not do any analyses to sum up possible results or examine how solid the available studies are. Studies in this review are not all the same: some looked at large groups of people over time, some examined a small sample at a given date, and a few studied how the disease develops in patients. There was no meta-analysis because the studies' techniques differed too much. Since studies showing that A/L ratio or Lp(a) is significant are more often published, our impressions might not be accurate. Moreover, several studies factored in many possible confounders, so their results were not easy to compare.

To fix the identified problem, one could focus on including both measurements of adipokines and Lp(a) in future studies. An ideal research project may put participants into groups according to A/L and Lp(a) levels and find out which group has the highest CVD risk. It would be possible to spot any interaction during this period. Researchers might also pay attention to tests such as interventional studies. As an example, when testing an Lp(a)-lowering drug, scientists could monitor adiponectin and leptin to identify if people with a bad adipokine pattern respond the same, differently, or even better. Alternatively, when people are involved in weight loss or anti-inflammatory drug tests, monitoring Lp(a) could show if lower body fat levels support better outcomes for Lp(a)-related problems without any direct changes.

LIMITATIONS

There are certain shortcomings in this review that are due to its method and the scope it covers. Initially, because we conducted a scoping (narrative) review, we did not do a systematic assessment of how strong the studies' designs are or combine their results. We aimed to gather all the facts available in the topic, so we did not exclude studies for being biased. Accordingly, our findings are qualitative and hypothesis-generating. Second, very little research has been done on how A/L ratio relates to Lp(a) because the subject is not well understood yet. Thirdly, the field of adiponectin and leptin is large and usually influenced by the fact that people differ in age, sex, obesity, and how the samples are analyzed. Some researchers consider the A/L ratio as leptin:adiponectin, others as adiponectin:leptin, and for some studies this ratio is based on diabetes, but for others on general groups of people. Fourth, there are difficulties when it comes to standardizing Lp(a). Scientists used different approaches for measuring Lp(a) (with and without isoforms, taken by mass or molar concentration), which changes the risk estimates. We did not standardize these technical variations.

Further, our research did not fully investigate other things that impact diabetes, because we mainly looked at adiponectin, leptin, and Lp(a). For instance, insulin resistance, extra fat around the internal organs, levels of C-reactive protein, or amount of LDL in the blood may all affect the mentioned connections. We focused on two important biomarkers, which automatically made the study of the metabolic-cardiovascular network simpler. In addition, studies that reveal important relationships between A/L ratio or Lp(a) and CVD might be present in higher numbers than those showing no such relationships. Therefore, while we wanted to cover the topic fully, the findings ought to inspire further investigations, as this kind of review is far from complete.

CONCLUSION

This study of narrative scoping reveals that adiponectin/leptin ratio and lipoprotein(a) point to various factors involved in the risk of cardiovascular disease. When there are more anti-atherogenic adipokines, the ratio of adiponectin to leptin shows healthy adipose tissue and low inflammation. A low ratio (less of adiponectin, more of leptin) usually means that metabolic syndrome, hurt endothelial cells, and atherosclerosis are risk factors. At the same time, lipoprotein(a) is a genetic risk factor that leads to extra cholesterol buildup in the arteries and makes the blood more likely to clot, apart from other types of lipid.

We believe that a combination of an unhealthy type

of adipokines and increased Lp(a) might speed up the formation of plaque in the arteries and clinical heart issues. This idea should be examined in more studies. Looking at these interactions from a healthcare point of view, it is suggested that more attention should be given to patients who have both metabolic-inflammatory and lipoprotein(a) risk because these patients should receive earlier or more aggressive medical treatment.

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