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Lipoprotein-A vs. B: The Better Predictive Marker of Cardiovascular Disease Muhammed Talha Tahir PGY-3 Parkview Medical Center IM Residency

Doug Duffee*

Internal Medicine Residency Program Director, ADJ Associate Professor of Medicine Rocky Vista University, USA

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***Corresponding author:** Doug Duffee, Internal Medicine Residency Program Director, ADJ Associate Professor of Medicine Rocky Vista University, USA

Background

Cardiovascular disease (CVD) is one of the leading causes of death worldwide and its prevalence is expected to continue to rise in the coming years [1]. The American Heart Association (AHA) estimates that one in three people will experience CVD at some point in their lifetime [2]. Coronary artery disease (CAD) and ischemic stroke are the most common clinical manifestations of CVD [3]. Despite the efforts to decrease the disease's incidence and prevalence through primary and secondary prevention strategies, the risk continues to be substantial. This highlights the need to identify accurate and reliable predictors of future cardiovascular events for risk stratification and personalized preventive strategies. Lipoproteins have gained attention as potential predictive values due to their involvement in atherogenesis and plaque formation.

What are Lipoproteins A and B?

Lipoproteins are complex particles having a central hydrophobic lipid core surrounded by the hydrophilic outer layer of phospholipids, free cholesterol, and apolipoproteins [4]. Their main function is to transport lipids to tissues, as lipids (like cholesterol) are insoluble in plasma. Lipoproteins are grouped into seven categories based on the size of the particle, the composition of the lipids, and apolipoproteins [4]. Each class of lipoprotein particles has a unique apolipoprotein that helps in stabilizing its structure.

Lipoprotein A (Lp (a)) is a low-density lipoprotein (LDL) particle and has an apolipoprotein (a) which is attached to Apolipoprotein B-100 (ApoB-100) by a disulfide bond. It is a pro-atherogenic particle [4,5] and its function is unknown.

Lipoprotein B (Lp (b)) on the other hand is an umbrella term that comprises different lipoprotein particles, including very-low-density-lipoprotein (VLDL), intermediate-density-lipoprotein (IDL), and LDL. These particles all contain apolipoprotein B (ApoB) as their primary protein component [4]. Therefore, li poprotein B is synonymous with apolipoprotein B, as they both pertain to the protein component present in these lipoprotein particles.

Role of Lipoproteins in Cardiovascular Disease -

Lipoprotein A promotes the proliferation of vascular smooth muscle cells and their migration to endothelial cells by inhibiting the activation of the transforming growth factor (TGF); this enables the growth of arterial atherosclerotic plaques [6]. It also acts as a pro-inflammatory mediator in the plaques through its role as a carrier of oxidized phospholipids (OxPLs) and speeds up lesion formation. Furthermore, by decreasing the activity of tissue plasminogen activator and inhibiting the binding of plasminogen to endothelial cell surfaces, LpA creates a pro-thrombotic state favorable for plaque formation [7].

All the Lipoprotein B particles, on the other hand, act as key structural components of atherosclerotic plaque. They also have ApoB, which plays a role in the transport of lipids and regulation of their metabolism and is usually considered to be a measure of the number of atherogenic particles [1].

Can Lipoprotein A and Lipoprotein B be used as predictive markers for CVD?

Many studies concluded that lipoprotein A and lipoprotein B individually, can be considered as predictive markers for CVD.

The study done by Francesca et al. [8] concluded that there is a significant relationship between Lpa and CVD in older men and also emphasized the need to develop Lpa-lowering drugs and regular monitoring of Lpa levels to reduce the burden of disease. In addition, there are several other studies [9-11] that also evaluated the connection between Lpa and CVD in both sexes and came to the same conclusion: there is a strong association between Lpa and CVD.

The research done [12,13] to find the relationship between lipoproteinB (ApoB) proved that lpb can be used as a predictive marker for CVD and is more accurate than conventional values like LDL-C, and HDL-C.

Lipoprotein A vs. Lipoprotein B - The Better Predictive Marker?

There aren't many studies done that compared the efficacy between Lpa and Lpb. One study [14] evaluated polygenic risk scores (PRSs) for Lp(a) and ApoB in 15,050 people of European ancestry and 419,364 white British people in the EPIC-Norfolk cohort, respectively. While the ApoB PRS was generally less predictive of atherosclerotic cardiovascular disease risk than measured ApoB, the Lp(a) PRS and measured Lp(a) showed comparable association with atherosclerotic cardiovascular disease incidence.

Why is there a need to find "the better" Predictive Marker?

The leading cause of death globally is CVD. According to estimates, 32% of all deaths are due to CVD [15]. In the same year, 38% of all premature deaths i.e. below 70 years caused by non-communicable diseases are due to CVD [15]. Low and middle-income nations have a high percentage of CVD fatalities [15]. These statistics point out the dire need for preventive measures to lower the mortality rate. Lp a and Lp b individually, have already been proven as predictive markers for CVD. By establishing a better marker through thorough research, the testing process can be made less cumbersome and cost-effective for all facets of the population. Furthermore, this facilitates regular check-ups and enables the people and the policymakers to devise appropriate strategies to reduce the disease burden.

Conclusion

A new need for precise predictive markers to lessen the burden of the disease arises with cardiovascular disease-related deaths still on the rise. Due to their role in the pathogenesis of the disease, lipoproteins have become potential predictive markers. The two main particles that have been studied are lipoproteins A and B. Lpa is an LDL with apolipoprotein A, a marker unique to it. It plays a role in the pathogenesis of atherosclerotic plaque formation, Whereas LpB is a general term that refers to various particles like LDL, IDL, and VLDL, which function as structural components of the plaque. Apolipoprotein B serves as a distinctive marker for each of these particles and aids in controlling lipid metabolism. Numerous studies concluded that lipoproteins A and B independently can function as CVD predictive markers. According to one study, lipoprotein A is more accurate at predicting outcomes than lipoprotein B. By finding a better predictive marker, the preventative testing processes get simpler, more cost-effective, and acceptable to the masses.

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