Lipoprotein (a) {Lp(a)} : It's Not the Cholesterol Content. It's the Apolipoprotein(a) {apo(a)} !

"High lipoprotein(a) and high-risk mortality" by Ann Langsted, Pia Kamstrupt and Borge Nordestgaard (1) concludes that the number of KIV-2 repeats in the apolipoprotein(a) were associated with high risk of mortality not the cholesterol content of Lp(a). This requires a change in the way we conceptualize, study and treat elevated Lipoprotein(a).

Yes, Lp(a) does have an apoB-100 LDL component that carries cholesterol, but the apo(a) component is clearly most significant. Lp(a) should be considered in terms of its apolipoprotein(a) component and called an apo(a) lipoprotein.

Apo(a) is the only apolipoprotein with an intrinsic atherogenic nature. Apo(a)'s plasminogen homology can promote the thrombosis leading to myocardial infarction. Apo(a) carries 85% of all the oxidized phospholipids which can damage the coronary intima of all individuals and facilitate the development and eventual rupture of plaques(2).

Lp(a)-Cholesterol is included with the "LDL-C" in the Friedewald Formula. Lp(a)-C can be calculated by Lp(a) total mass in mg/dL / 3 since approximately 33% of the Lp(a) is cholesterol. When Lp(a) total mass is high, the Lp(a)-C contribution to the "LDL-C" is significant. Statin therapy increases the relative contribution of the Lp(a)-C because statins lower actual LDL-C but not Lp(a)-C.

The apo(a) component results in diseases not associated with other lipoproteins. Its plasminogen homology promotes thrombosis of cerebral arteries in children with resultant strokes. Oxidized phospholipids of the apo(a) by delineated mechanisms can lead to CAVD(3). Separate measurement of Lp(a) is required.

Apo(a) interferes with cholesterol lowering agents. This mandates that Lp(a) be measured in all clinical trials and clinical practice. Statins do not lower Lp(a) nor Lp(a)-C levels. The JUPITER trial found that statins did not improve cardiovascular outcomes in patients with elevated Lp(a). Niacin in the AIM-HIGH trial despite lowering Lp(a) levels did **not improve clinical outcomes**.

An exception is that PCSK-9 inhibitors lower Lp(a) levels by 20-40% **and** in the ODYSSEY trial patients on the PCSK-9i with Lp(a) above 60 mg/dL had a further 18% reduction in **clinical events** over 4 years beyond the reduction from lowering LDL-C. Apheresis however can reduce MACE 90%.

This lead article for 2019 calls for Lp(a) to be considered an "apo(a) lipoprotein" and always separately measured universally. If HDL is the "good" and LDL is "bad", then Lp(a) because of it's apo(a) is truly the "**ugly**" lipoprotein.

1. Langsted A, Kamstrupt P, Nordestgaard B. High Lipoprotein(a) and high-risk mortality. Eur Heart J 2019;40:1-12.
2. Nordestgaard B, Langsted A. Lipoprotein(a) as a cause of cardiovascular disease Insights from epidemiology, genetic and biology. J of Lipid Res 2016;57:953-1975.
3. Rogers M. Aikawa E. Not-So-Little Role for Lipoprotein(a) in Development CAVD. Circulation 2015;132:621-623.

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