Lipoprotein (a): A Forgotten Cardiovascular Risk Factor

Lipoproteína (a): Um Factor de Risco Cardiovascular Esquecido

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It is known since the 1960s, that lipoprotein (a) -Lp (a) - has an atherogenic potential, contributing to increase vascular risk. This concept enables the possibility to reclassify individual cardiovascular risk levels. Patients with high Lp(a) levels that have intermediate risk or are on the threshold between two risk categories can be reclassified to a higher level. We know that the atherogenic and pro-inflammatory properties of Lp(a) are due to the core of apoprotein B tin Lp(a) (similar as an LDL particle). However, Lp(a) contains another attached lipoprotein, apolipoprotein (a), which, in addition to its atherogenic and inflammatory potential, may also have a thrombogenic effect, given its structural similarity to plasminogen.[1,2] Inter-individual heterogeneity in Lp(a) levels are 90% genetically determined. Variation throughout life is discreet. However, hypothyroidism and chronic kidney disease (and nephrotic syndrome in particular) can increase Lp(a) levels. There are also gender differences, with Lp(a) concentration generally 5%–10% higher in women than men. In men, Lp(a) remains relatively constant, whereas in women levels tend to increase at menopause. [1,2] There is still a problem in determining values of Lp(a), which go through different laboratory evaluation methods. Some labs continue to report results in mg/dL, corresponding to the relative weight of Lp(a). However, determination in mmol/L is preferable. The measurement of mmol/L reflects the concentration of Lp(a), or the number of molecules, in one liter of blood.[3] It is known that there is a relationship between Lp(a) levels and vascular risk, starting at 30 mg/dL. Very high Lp(a) levels (>180 mg/dL or >430 nmol/L) identify individuals with a lifetime cardiovascular risk equivalent to untreated heterozygous familial hypercholesterolemia. Currently it is well established a linear relationship between Lp(a) levels with aortic valve stenosis, ischemic heart disease, ischemic stroke, and peripheral artery disease. Lp(a) levels above the (75th percentile) increased the risk for stroke and myocardial infarction, levels above 90th percentile are associated with increased risk for heart failure. Risk for cardiovascular mortality and ischemic stroke are increased at very high levels (>95th percentile).

In contrary there is no relation between Lp(a) with venous thromboembolism.[1]Given its scarce variability throughout life and the slight reduction that the available lipid lowering therapy have on Lp(a) levels, it is recommended to assess Lp(a) levels only once in lifetime. Lipid-lowering drugs such as nicotinic acid have a slight effect (less than 30%) on Lp(a) levels and its use in clinical trials did not prove benefit in reducing vascular events. PCSK9 inhibitors also reduce Lp(a) between 25%--30%. They have proven to reduce cardiovascular events, but the effect on LDL reduction, can explain this beneficial effect.

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Nevertheless, in the Fourier trial, patients with higher baseline Lp(a) levels experienced greater coronary benefit from PCSK9 inhibition.[1,2,4] In contrast, statins slightly increase Lp(a) levels and reduce vascular risk.[2]There are ongoing studies with new drugs that interfere with the synthesis of Lp(a), inhibiting the production of messenger RNA. These drugs lead to Lp(a) reductions greater than 80%, which brings new perspectives to reduce the residual cardiovascular risk in high-risk patients. It is expected that in secondary prevention, a reduction of Lp(a) by 50 mg/dL (105 nmol/L) for 5 years may be needed to reduce cardiovascular events by 20%.[1,2,5] Meanwhile, in the presence of high levels of Lp(a) we must intensify risk factors control (particularly LDL) with lifestyle and available therapies with proven cardiovascular events reduction. Lipoprotein (a) apheresis remains an option to severe and particular cases.[2]

Responsabilidades Éticas

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References

1. Kronenberg F, Mora S, Stroes ESG, Ference BA, Arsenault BJ, Berglund L, et al Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement. Eur Heart J. 2022;43:3925-46. doi: 10.1093/eurheartj/ehac361.
2. Reyes-Soffer G, Ginsberg HN, Berglund L, Duell PB, Heffron SP, Kamstrup PR, et al. Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association. Arterioscler Thromb Vasc Biol. 2022;42:e48-e60. doi: 10.1161/ATV.0000000000000147.
3. Virani SS, Koschinsky ML, Maher L, Mehta A, Orringer CE, Santos RD, et al. Global think tank on the clinical considerations and management of lipoprotein(a): The top questions and answers regarding what clinicians need to know. Prog Cardiovasc Dis. 2022;73:32-40. doi: 10.1016/j.pcad.2022.01.002.
4. O'Donoghue ML, Fazio S, Giugliano RP, Stroes ESG, Kanevsky E, Gouni-Berthold I, et al. Lipoprotein(a), PCSK9 Inhibition, and Cardiovascular Risk. Circulation. 2019;139:1483-92. doi: 10.1161/CIRCULATIONAHA.118.037184.
5. Madsen CM, Kamstrup PR, Langsted A, Varbo A, Nordestgaard BG. Lipoprotein(a)-Lowering by 50 mg/dL (105 nmol/L) May Be Needed to Reduce Cardiovascular Disease 20% in Secondary Prevention: A Population-Based Study. Arterioscler Thromb Vasc Biol. 2020;40:255-66. doi: 10.1161/ATVBAHA.119.312951.