

# Abstract

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## Lipoprotein(a) and ischemic heart disease--a causal association? A review.

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**OBJECTIVE:** The aim of this review is to summarize present evidence of a causal association of lipoprotein(a) with risk of ischemic heart disease (IHD).

**BACKGROUND:** Evidence for causality includes reproducible associations of a proposed risk factor with risk of disease in epidemiological studies, evidence from in vitro and animal studies in support of pathophysiological effects of the risk factor, and preferably evidence from randomized clinical trials documenting reduced morbidity in response to interventions targeting the risk factor.

**FINDINGS:** Elevated and in particular extreme lipoprotein(a) levels have in prospective studies repeatedly been associated with increased risk of IHD, although results from early studies are inconsistent. Data from in vitro and animal studies implicate lipoprotein(a), consisting of a low density lipoprotein particle covalently bound to the plasminogen-like glycoprotein apolipoprotein(a), in both atherosclerosis and thrombosis, including accumulation of lipoprotein(a) in atherosclerotic plaques and attenuation of t-PA mediated plasminogen activation. No randomized clinical trial of the effect of lowering lipoprotein(a) levels on IHD prevention has ever been conducted. Lacking evidence from randomized clinical trials, genetic studies, such as Mendelian randomization studies, can also support claims of causality. Levels of lipoprotein(a) are primarily determined by variation in the LPA gene coding for the apolipoprotein(a) moiety of lipoprotein(a), and genetic epidemiologic studies have documented association of LPA copy number variants, influencing levels of lipoprotein(a), with risk of IHD.

**CONCLUSION:** In conclusion, results from epidemiologic, in vitro, animal, and genetic epidemiologic studies support a causal association of lipoprotein(a) with risk of IHD, while results from randomized clinical trials are presently lacking.

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