

Abstract

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Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality.

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CONTEXT: Circulating concentration of lipoprotein(a) (Lp[a]), a large glycoprotein attached to a low-density lipoprotein-like particle, may be associated with risk of coronary heart disease (CHD) and stroke.

OBJECTIVE: To assess the relationship of Lp(a) concentration with risk of major vascular and nonvascular outcomes.

STUDY SELECTION: Long-term prospective studies that recorded Lp(a) concentration and subsequent major vascular morbidity and/or cause-specific mortality published between January 1970 and March 2009 were identified through electronic searches of MEDLINE and other databases, manual searches of reference lists, and discussion with collaborators.

DATA EXTRACTION: Individual records were provided for each of 126,634 participants in 36 prospective studies. During 1.3 million person-years of follow-up, 22,076 first-ever fatal or nonfatal vascular disease outcomes or nonvascular deaths were recorded, including 9336 CHD outcomes, 1903 ischemic strokes, 338 hemorrhagic strokes, 751 unclassified strokes, 1091 other vascular deaths, 8114 nonvascular deaths, and 242 deaths of unknown cause. Within-study regression analyses were adjusted for within-person variation and combined using meta-analysis. Analyses excluded participants with known preexisting CHD or stroke at baseline.

DATA SYNTHESIS: Lipoprotein(a) concentration was weakly correlated with several conventional vascular risk factors and it was highly consistent within individuals over several years. Associations of Lp(a) with CHD risk were broadly continuous in shape. In the 24 cohort studies, the rates of CHD in the top and bottom thirds of baseline Lp(a) distributions, respectively, were 5.6 (95% confidence interval [CI], 5.4-5.9) per 1000 person-years and 4.4 (95% CI, 4.2-4.6) per 1000 person-years. The risk ratio for CHD, adjusted for age and sex only, was 1.16 (95% CI, 1.11-1.22) per 3.5-fold higher usual Lp(a) concentration (ie, per 1 SD), and it was 1.13 (95% CI, 1.09-1.18) following further adjustment for lipids and other conventional risk factors. The corresponding adjusted risk ratios were 1.10 (95% CI, 1.02-1.18) for ischemic stroke, 1.01 (95% CI, 0.98-1.05) for the aggregate of nonvascular mortality, 1.00 (95% CI, 0.97-1.04) for cancer deaths, and 1.00 (95% CI, 0.95-1.06) for nonvascular deaths other than cancer.

CONCLUSION: Under a wide range of circumstances, there are continuous, independent, and modest associations of Lp(a) concentration with risk of CHD and stroke that appear exclusive to vascular outcomes.

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