

Abstract

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Lipoprotein(a), measured with an assay independent of apolipoprotein(a) isoform size, and risk of future cardiovascular events among initially healthy women.

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CONTEXT: Controversy exists as to whether lipoprotein(a), a lipoprotein with homology to plasminogen, is a clinically meaningful cardiovascular risk marker in women. There is also poor agreement among lipoprotein(a) levels obtained by different assays.

OBJECTIVE: To determine the association of lipoprotein(a) levels, measured with an assay independent of apolipoprotein(a) isoform size, with the incidence of future cardiovascular events.

DESIGN, SETTING, AND PARTICIPANTS: Prospective study of 27,791 initially healthy women in the Women's Health Study, enrolled between November 1992 and July 1995 and followed up for 10 years. Lipoprotein(a) level was measured in blood samples obtained at baseline with an assay independent of apolipoprotein(a) isoform size.

MAIN OUTCOME MEASURE: Hazard ratios (HRs) for first-ever major cardiovascular events (nonfatal myocardial infarction, nonfatal cerebrovascular event, coronary revascularization, or cardiovascular deaths).

RESULTS: During follow-up, there were 899 incident cardiovascular events. After adjusting for age, smoking, blood pressure, body mass index, total cholesterol, high-density lipoprotein cholesterol, diabetes, hormone use, C-reactive protein, and randomization treatment groups, women in the highest quintile of lipoprotein(a) (≥ 44.0 mg/dL) were 1.47 times more likely (95% CI, 1.21-1.79; P for trend $<.001$) to develop cardiovascular events than women in the lowest quintile (≤ 3.4 mg/dL). This association, however, was due almost entirely to a threshold effect among those with the highest lipoprotein(a) levels. After adjusting for all of the variables listed above, the HR associated with lipoprotein(a) levels exceeding the 90th percentile (≥ 65.5 mg/dL) was 1.66 (95% CI, 1.38-1.99); 95th percentile (≥ 83 mg/dL), 1.87 (95% CI, 1.50-2.34); and 99th percentile (≥ 130.7 mg/dL), 1.99 (95% CI, 1.32-3.00), with almost no risk gradient at lower levels. Associations were strongest among women with low-density lipoprotein cholesterol (LDL-C) above the median level. In this subgroup, the adjusted HR associated with lipoprotein(a) levels exceeding the 90th percentile was 1.81 (95% CI, 1.48-2.23); 95th percentile, 1.93 (95% CI, 1.51-2.48); and 99th percentile, 1.93 (95% CI, 1.21-3.05) (P value for interaction with LDL-C = .001).

CONCLUSIONS: In this cohort of initially healthy women, extremely high levels of lipoprotein(a) (≥ 90 th percentile), measured with an assay independent of apolipoprotein(a) isoform size, were associated with increased cardiovascular risk, particularly in women with high levels of LDL-C. However, the threshold and interaction effects observed do not support routine measurement of lipoprotein(a) for cardiovascular stratification in women.

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