

Abstract

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Lipoprotein-associated phospholipase A(2) and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies.

Lp-PLA(2) Studies Collaboration, Thompson A, Gao P, Orfei L, Watson S, Di Angelantonio E, Kaptoge S, Ballantyne C, Cannon CP, Criqui M, Cushman M, Hofman A, Packard C, Thompson SG, Collins R, Danesh J.

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BACKGROUND: Lipoprotein-associated phospholipase A(2) (Lp-PLA(2)), an inflammatory enzyme expressed in atherosclerotic plaques, is a therapeutic target being assessed in trials of vascular disease prevention. We investigated associations of circulating Lp-PLA(2) mass and activity with risk of coronary heart disease, stroke, and mortality under different circumstances.

METHODS: With use of individual records from 79 036 participants in 32 prospective studies (yielding 17 722 incident fatal or non-fatal outcomes during 474 976 person-years at risk), we did a meta-analysis of within-study regressions to calculate risk ratios (RRs) per 1 SD higher value of Lp-PLA(2) or other risk factor. The primary outcome was coronary heart disease.

FINDINGS: Lp-PLA(2) activity and mass were associated with each other ($r=0.51$, 95% CI 0.47-0.56) and proatherogenic lipids. We noted roughly log-linear associations of Lp-PLA(2) activity and mass with risk of coronary heart disease and vascular death. RRs, adjusted for conventional risk factors, were: 1.10 (95% CI 1.05-1.16) with Lp-PLA(2) activity and 1.11 (1.07-1.16) with Lp-PLA(2) mass for coronary heart disease; 1.08 (0.97-1.20) and 1.14 (1.02-1.27) for ischaemic stroke; 1.16 (1.09-1.24) and 1.13 (1.05-1.22) for vascular mortality; and 1.10 (1.04-1.17) and 1.10 (1.03-1.18) for non-vascular mortality, respectively. RRs with Lp-PLA(2) did not differ significantly in people with and without initial stable vascular disease, apart from for vascular death with Lp-PLA(2) mass. Adjusted RRs for coronary heart disease were 1.10 (1.02-1.18) with non-HDL cholesterol and 1.10 (1.00-1.21) with systolic blood pressure.

INTERPRETATION: Lp-PLA(2) activity and mass each show continuous associations with risk of coronary heart disease, similar in magnitude to that with non-HDL cholesterol or systolic blood pressure in this population. Associations of Lp-PLA(2) mass and activity are not exclusive to vascular outcomes, and the vascular associations depend at least partly on lipids.

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