Abstract

Lancet. 2010 May 1;375(9725):1536-44.

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


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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.

FUNDING: UK Medical Research Council, GlaxoSmithKline, and British Heart Foundation.

PMID: 20435228

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