Association of small low-density lipoprotein particles with the incidence of coronary artery disease in men and women.

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OBJECTIVE: To investigate the prospective association of low-density lipoprotein (LDL) particle diameter with the incidence of fatal and nonfatal coronary artery disease (CAD).

DESIGN: A nested case-control study.

SETTING: Cases and controls were identified from a population-based sample of men and women combining all of the 5 cross-sectional surveys conducted from 1979 to 1990 of the Stanford Five-City Project (FCP).

PARTICIPANTS: Incident CAD cases were identified through FCP surveillance between 1979 and 1992. Controls were matched by sex, 5-year age groups, survey time point, ethnicity, and FCP treatment condition. The sample included 124 matched pairs: 90 pairs of men and 34 pairs of women.

MAIN OUTCOME MEASURES: LDL peak particle diameter (LDL size) was determined by gradient gel electrophoresis on plasma samples collected during the cross-sectional surveys (stored at 70 degrees C for 5-15 years). Established CAD risk-factor data were available from FCP baseline measurements.

RESULTS: LDL size was smaller among CAD cases than controls (mean +/- SD) (26.17 +/- 1.00 nm vs 26.68 +/- 0.90 nm; P<.001). The association was graded across control quintiles of LDL size. The significant case-control difference in LDL size was independent of levels of high-density lipoprotein cholesterol (HDL-C), non-HDL cholesterol (non-HDL-C), triglyceride, smoking, systolic blood pressure, and body mass index, but was not significant after adjusting for the ratio of total cholesterol (TC) to HDL-C (TC:HDL-C). Among all the physiological risk factors, LDL size was the best differentiator of CAD status in conditional logistic regression. However, when added to the physiological parameters above, the TC:HDL-C ratio was found to be a stronger independent predictor of CAD status.

CONCLUSION: LDL size was significantly smaller in CAD cases than in controls in a prospective, population-based study. These findings support other evidence of a role for small, dense LDL particles in the etiology of atherosclerosis.

PMID: 8782636