

Abstract

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Association of apolipoprotein E genotypes with lipid levels and coronary risk.

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CONTEXT: Previous reviews of associations of apolipoprotein E (apoE) genotype and coronary disease have been dominated by smaller studies that are liable to biases.

OBJECTIVE: To reassess associations of apoE genotypes with circulating lipid levels and with coronary risk.

DATA SOURCES: We conducted an updated meta-analysis including both published and previously unreported studies, using MEDLINE, EMBASE, BIOSIS, Science Citation Index, and the Chinese National Knowledge Infrastructure Database published between January 1970 and January 2007, reference lists of articles retrieved, and a registry of relevant studies.

STUDY SELECTION: Eighty-two studies of lipid levels (86,067 healthy participants) and 121 studies of coronary outcomes (37,850 cases and 82,727 controls) were identified, with prespecified principal focus on studies with at least 1000 healthy participants for lipids and those with at least 500 coronary outcomes.

DATA EXTRACTION: Information on genotype frequencies, lipid levels, coronary outcomes, and laboratory and population characteristics were recorded independently by 2 investigators and/or supplied by study investigators.

RESULTS: In the most extreme comparison, people with the epsilon2/epsilon2 genotype had 1.14 mmol/L (95% confidence interval [CI], 0.87-1.40 mmol/L [44.0 mg/dL; 95% CI; 33.6-51.1 mg/dL]) or about 31% (95% CI, 23%-38%) lower mean low-density lipoprotein cholesterol (LDL-C) values than those with the epsilon4/epsilon4 genotype. There were approximately linear relationships of apoE genotypes (when ordered epsilon2/epsilon2, epsilon2/epsilon3, epsilon2/epsilon4, epsilon3/epsilon3, epsilon3/epsilon4, epsilon4/epsilon4) with LDL-C and with coronary risk. The relationship with high-density lipoprotein cholesterol was inverse and shallow and that with triglycerides was nonlinear and largely confined to the epsilon2/epsilon2 genotype. Compared with epsilon3/epsilon3, the odds ratio for coronary disease was 0.80 (95% CI, 0.70-0.90) in epsilon2 carriers and was 1.06 (95% CI, 0.99-1.13) in epsilon4 carriers.

CONCLUSIONS: There are approximately linear relationships of apoE genotypes with both LDL-C levels and coronary risk. Compared with individuals with the epsilon3/epsilon3 genotype, epsilon2 carriers have a 20% lower risk of coronary heart disease and epsilon4 carriers have a slightly higher risk.

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