

Abstract

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Apolipoprotein E polymorphism and cardiovascular disease: a HuGE review.

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OBJECTIVE: This review examines the association between the apolipoprotein (apo) var epsilon gene polymorphism (or its protein product (apo E)), metabolic regulation of cholesterol, and cardiovascular disease.

BACKGROUND: The apo var epsilon gene is located at chromosome 19q13.2. Among the variants of this gene, alleles (*) epsilon2, (*) epsilon3, and (*) epsilon4 constitute the common polymorphism found in most populations. Of these variants, apo (*) epsilon3 is the most frequent (>60%) in all populations studied.

DISCUSSION: The polymorphism has functional effects on lipoprotein metabolism mediated through the hepatic binding, uptake, and catabolism of chylomicrons, chylomicron remnants, very low density lipoprotein (VLDL), and high density lipoprotein subspecies. Apo E is the primary ligand for two receptors, the low density lipoprotein (LDL) receptor (also known as the B/E receptor) found on the liver and other tissues and an apo E-specific receptor found on the liver. The coordinate interaction of these lipoprotein complexes with their receptors forms the basis for the metabolic regulation of cholesterol.

SUMMARY OF FINDINGS: Allelic variation in apo var epsilon is consistently associated with plasma concentrations of total cholesterol, LDL cholesterol, and apo B (the major protein of LDL, VLDL, and chylomicrons). Apo var epsilon has been studied in disorders associated with elevated cholesterol levels or lipid derangements (i.e., hyperlipoproteinemia type III, coronary heart disease, strokes, peripheral artery disease, and diabetes mellitus). The apo var epsilon genotype yields poor predictive values when screening for clinically defined atherosclerosis despite positive, but modest associations with plaque and coronary heart disease outcomes. In addition to genotype-phenotype associations with vascular disease, the alleles and isoforms of apo var epsilon have been related to dementias, most commonly Alzheimer's disease.

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