Winnaar VvE Publicatieprijs junior onderzoeker 2016

J. Besseling

Association between familial hypercholesterolemia and prevalence of type 2 diabetes mellitus

(JAMA. 2015 Mar 10;313(10):1029-36. doi: 10.1001/jama.2015.1206)

Abstract

IMPORTANCE:

Familial hypercholesterolemia is characterized by impaired uptake of cholesterol in peripheral tissues, including the liver and the pancreas. In contrast, statins increase the cellular cholesterol uptake and are associated with increased risk for type 2 diabetes mellitus. We hypothesize that transmembrane cholesterol transport is linked to the development of type 2 diabetes.

OBJECTIVE:

To assess the association between type 2 diabetes prevalence and familial hypercholesterolemia.

DESIGN, SETTING, AND PARTICIPANTS:

Cross-sectional study in all individuals (n = 63,320) who underwent DNA testing for familial hypercholesterolemia in the national Dutch screening program between 1994 and 2014.

EXPOSURES:

Deleteriousness and nondeleteriousness of familial hypercholesterolemia mutations were based on literature or laboratory function testing. Low-density lipoprotein (LDL) receptor mutations were considered more severe than apolipoprotein B gene (APOB) mutations, and receptor-negative LDL receptor mutations were considered more severe than receptor-deficient mutations.

MAIN OUTCOMES AND MEASURES:

Prevalence of type 2 diabetes.

RESULTS:

The prevalence of type 2 diabetes was 1.75% in familial hypercholesterolemia patients (n = 440/25,137) vs 2.93% in unaffected relatives (n = 1119/38,183) (P < .001; odds ratio [OR], 0.62 [95% CI, 0.55-0.69]). The adjusted prevalence of type 2 diabetes in familial hypercholesterolemia, determined using multivariable regression models, was 1.44% (difference, 1.49% [95% CI, 1.24%-1.71%]) (OR, 0.49 [95% CI, 0.41-0.58]; P < .001). The adjusted prevalence of type 2 diabetes by APOB vs LDL receptor gene was 1.91% vs 1.33% (OR, 0.65 [95% CI, 0.48-0.87] vs OR, 0.45 [95% CI, 0.38-0.54]), and the prevalence for receptor-deficient vs receptor-negative mutation carriers was 1.44% vs 1.12% (OR, 0.49 [95% CI, 0.40-0.60] vs OR, 0.38 [95% CI, 0.29-0.49]), respectively (P for trend <.001 in both comparisons).

CONCLUSIONS AND RELEVANCE:

In a cross-sectional analysis in the Netherlands, the prevalence of type 2 diabetes among patients with familial hypercholesterolemia was significantly lower than among unaffected relatives, with variability by mutation type. If this finding is confirmed in longitudinal analysis, it would raise the possibility of a causal relationship between LDL receptor-mediated transmembrane cholesterol transport and type 2 diabetes.