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Is Nuclear Magnetic Resonance Lipoprotein Subclass related to Diabetic Retinopathy? The Multi-Ethnic Study of Atherosclerosis

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Abstract

Objective—To examine associations between nuclear magnetic resonance (NMR) defined lipoproteins and diabetic retinopathy (DR) in a population-based sample of adults with type 2 diabetes.

Research Design and Methods—921 persons with diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA) were included. DR was assessed from retinal photographs. Lipoproteins were measured by NMR spectroscopy.

Results—After controlling for age, race/ethnicity, study center and diabetes and vascular risk factors, no consistent patterns of associations between NMR defined lipoprotein particle concentrations and subclass with DR were evident.

Conclusion—The lack of association between NMR defined lipoproteins and DR does not support clinical use of NMR spectroscopy for management of patients with DR.

Keywords

lipoprotein; NMR-lipids; diabetic retinopathy; retinal photography

The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Study reported that fenofibrate reduced the incidence of laser therapy for diabetic retinopathy (DR) in patients with type 2 diabetes¹. However, in the FIELD study, the mechanism of this effect does not seem to be related to plasma lipid concentrations. Thus, further exploring whether specific characteristics of plasma lipids, such as subtype or size, are risk factors for DR and other complications is important².

Nuclear magnetic resonance (NMR) spectroscopy can provide detailed lipoprotein analysis^{3–5}. We examined associations between NMR-measured lipoproteins and DR in type 2 diabetes participants in the Multi-Ethnic Study of Atherosclerosis (MESA), a population-based study in four racial/ethnic groups (whites, blacks, Hispanics and Chinese) from six US communities without prior cardiovascular disease at baseline⁶. Retinal photography immediately followed baseline examination. Of the 6,814 baseline participants, 6,147 had photographs gradable for DR⁷, defined as level 14 or higher following the modification of Airlie House Classification System⁸. Diabetes, defined as fasting glucose ≥ 7.0 mmol/L (≥ 126 mg/dl), use of insulin or oral hypoglycemic agents, was present in 921 participants. Ethics approval was granted, and written informed consent obtained from each participant.

Standardized enzymatic methods were used to measure total cholesterol, high-density lipoprotein (HDL), very-low-density lipoprotein (VLDL) and triglycerides in fasting plasma. The Friedewald equation was used to estimate low-density lipoprotein (LDL)-cholesterol. Lipoprotein subclasses were measured on previously frozen plasma (-70°C) using NMR spectroscopy^{9, 10}. The subclasses included: large HDL (8.8–13 nm), medium HDL (8.2–8.8 nm), small HDL (7.3–8.2 nm); large LDL (21.2–23 nm), medium LDL (19.8–21.2 nm), small LDL (18.3–19.7 nm), intermediate density lipoprotein (IDL) (23–27 nm), large VLDL (>60 nm), medium VLDL (35–60 nm), and small VLDL (27–35 nm)⁷. NMR-determined lipoprotein measures correlate with standard lipid measures¹⁰.

Logistic regression models were used to assess associations of lipoprotein subclass with DR, while adjusting for age, race/ethnicity, study center, systolic blood pressure, use of anti-hypertensive and lipid-lowering medications, body mass index, smoking, diabetes duration, and HbA_{1C} levels. Statistical significance was taken at $p < 0.0025$ (Bonferroni correction).

Of participants with diabetes, 30.2% had DR, 52.0% were male and 25.6% were on lipid-lowering medications. Participants with DR were more likely to be black or Hispanic, on diabetic medications, have longer diabetic duration, higher plasma glucose and systolic blood pressure levels than those without DR (data not shown).

Presence of DR was not associated with any of the NMR-measured lipoproteins, either in all persons with diabetes, or in gender (Table) or by racial/ethnicity subgroups (data not shown). Supplement analyses conducted in users and non-users of lipid-lowering medications showed no associations (data not shown).

NMR spectroscopy has recently been used to assess lipoprotein subclasses. Compared with traditional measures of serum lipoproteins, NMR analysis provides more detail patterns of specific subtypes of lipid profiles associated with vascular damage.^{3–5} There has been no previous study on whether NMR measured lipoproteins is associated with DR in persons with type 2 diabetes. Our finding of lack of association of in the MESA cohort does not support current clinical use of this test in diabetes management.

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	Women, N=442			Men, N=479		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	OR (95% CI) per SD increase	OR (95% CI) per SD increase	OR (95% CI) per SD increase	OR (95% CI) per SD increase	OR (95% CI) per SD increase	OR (95% CI) per SD increase
VLDL	0.99 (0.81,1.22)	1.03 (0.83, 1.26)	1.00 (0.79,1.26)	0.89 (0.73,1.07)	0.85 (0.70, 1.04)	0.83 (0.67,1.03)

* Odds Ratio [OR] (95% CI) adjusted for Model 1: unadjusted, Model 2: age, race/ethnicity, study center, systolic blood pressure, body mass index, lipid lowering medication and cigarette smoking; Model 3: Model 2 plus hemoglobin A1c and duration of diabetes. None of estimates were statistically significant after Bonferroni correction for multiple comparisons using a significant level of p<0.0025.