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Plasma sphingomyelin is not associated with microvascular changes in the retina

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To the Editor,

Plasma sphingomyelin has been proposed to be a novel biomarker for cardiovascular disease (Jiang et al., 2000). Evidence from experimental, animal, and human studies supports its potential pathogenic role in the development of large artery atherosclerotic disease (Tabas, 2004). However, whether it also exerts adverse effects on the microcirculation (e.g., arterioles) is unknown. To test this hypothesis, we examined, in the Multi-Ethnic Study of Atherosclerosis (MESA), the associations between plasma sphingomyelin and retinal microvascular changes that have been previously identified as independent predictors of future cardiovascular disease (Wong et al., 2004).

Of the 6,814 MESA participants at the first examination (2000–2), when plasma sphingomyelin levels were measured (Nelson et al., 2006), 6,147 participants returned at the second examination (2002–4) for fundus photography (Wong et al., 2006). Of these, we excluded those without gradable retinal photographs or sphingomyelin data, leaving 6,056 participants for our current analysis. Retinal vascular calibers were measured by a computer-based program using a previously validated protocol (Wong et al., 2006). For each photograph, all retinal arterioles and venules coursing through an area of half to one optic disc diameter from the optic disc margin were measured and summarized as the central retinal arteriolar and venular equivalents, which represented the averaged projected caliber for the central retinal vessels. We also graded retinopathy signs based on the Early Treatment of Diabetic Retinopathy Study severity scale.

As the Table shows, quartiles of plasma sphingomyelin levels were not associated with retinal vascular calibers or retinopathy. Using multiple linear regression analysis with adjustments for age, gender, race/ethnicity, study center, smoking, diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol and C-reactive protein, each standard deviation increase in plasma sphingomyelin (15.5 mg/dL) was not significantly associated with retinal vascular caliber (0.08 μ m increase in arteriolar caliber, $p=0.65$ and 0.43 μ m decrease in venular caliber, $p=0.15$) or presence of retinopathy.

Our data thus suggest that plasma sphingomyelin is not associated with retinal microvascular signs that have been previously shown to predict clinical cardiovascular diseases (Wong et al., 2004). The vascular effects of sphingomyelin are possibly confined to large vessels only (Nelson et al., 2006). Further research is needed to elucidate the exact pathophysiological

mechanisms underlying the associations between retinal microvascular changes and cardiovascular disease risk.

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Table
Relationship of Plasma Sphingomyelin and Retinal Vascular Changes, the MESA.

Sphingomyelin levels (in mg/dl)	Arteriolar Caliber N=5889*		Venular Caliber N=5888*		Retinopathy N=6056	
	n	Mean (SE)*	n	Mean (SE)*	N	n (%)
≤39	1938	143.9 (0.32)	1931	214.5 (0.51)	1989	328 (16.5)
40–49	1656	144.4 (0.36)	1658	214.3 (0.54)	1695	280 (16.5)
50–59	1147	144.0 (0.44)	1147	213.3 (0.65)	1182	212 (17.9)
≥60	1148	144.0 (0.42)	1152	213.2 (0.65)	1190	180 (15.1)
<i>p</i> for trend		0.89		0.07		0.63

n = number at risk in different sphingomyelin categories; n (%) = number with retinopathy (percentage);

* Arteriolar caliber represented by the central retinal arteriolar equivalent and venular caliber by the central retinal venular equivalent, both measured in μm .