

Abstract

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Measurement issues related to lipoprotein heterogeneity.

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BACKGROUND: In clinical practice, the coronary artery disease (CAD) risk associated with high levels of low-density lipoprotein (LDL) or low levels of high-density lipoprotein (HDL) is assessed not by measuring LDL and HDL particles directly, but by measuring the amount of cholesterol carried by these lipoproteins. It is not generally appreciated how much the amount of cholesterol per particle varies from person to person, especially for LDL, because of differences in the relative amounts of cholesterol ester and triglycerides in the particle core as well as differences in particle diameter.

DISCUSSION: As a consequence of the magnitude and prevalence of this lipid compositional variability, even the most accurate lipoprotein cholesterol measurements will, for many individuals, provide an inaccurate measure of the number of circulating lipoprotein particles and the CAD risk they confer. Nuclear magnetic resonance (NMR) spectroscopy offers an efficient new means of measuring lipoprotein levels in plasma, with quantification based not on cholesterol content, but on the amplitudes of spectral signals emitted by lipoprotein subclasses of different size. Because the subclass signal amplitudes are not influenced by cholesterol compositional variability, they provide a direct measure of lipoprotein particle concentrations. NMR data from the Framingham Offspring Study demonstrate a significant "disconnect" between LDL cholesterol and LDL particle concentrations in patients with low levels of HDL cholesterol.

CONCLUSIONS: The results imply that a substantial portion of the excess CAD risk of patients with low HDL stems from an unrecognized excess of LDL particles containing less cholesterol than normal. Patients with this abnormality would benefit from LDL-lowering therapy but are not identified as candidates for such treatment on the basis of traditional LDL cholesterol tests.

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