

Abstract

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Why Cholesterol Measurements May be Misleading about Lipoprotein Levels and Cardiovascular Disease Risk – Clinical Implications of Lipoprotein Quantification Using NMR Spectroscopy

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BACKGROUND: In clinical practice, the cardiovascular disease risk (CVD) associated with high levels of LDL or low levels of HDL is assessed not by measuring LDL and HDL particles but by measuring the amounts of cholesterol carried by these lipoproteins. It is generally unappreciated how much the cholesterol content per particle varies from person to person, especially for LDL, due to differences in the relative amounts of cholesterol ester and triglycerides in the particle core as well as differences in particle diameter. As a consequence of the magnitude and prevalence of the lipid compositional variability of LDL, even the most accurate LDL cholesterol measurements will, for many individuals, provide an inaccurate assessment of the number of circulating LDL particles and the CVD risk they confer. An alternative means of measuring LDL and other lipoprotein levels in plasma is provided by nuclear magnetic resonance (NMR) spectroscopy, which bases quantification not on cholesterol content but the amplitudes of spectral signals emitted by lipoprotein subclasses of different size. Since these signal amplitudes are not influenced by cholesterol compositional variability, they provide a direct measure of lipoprotein particle concentrations.

SUMMARY: A significant “disconnect” between LDL cholesterol and NMR-measured LDL particle concentration is observed in subjects with low HDL in the Framingham Offspring Study, implying that a substantial portion of the excess CVD risk of such individuals stems not from low HDL per se, but from an unrecognized excess of LDL particles containing less cholesterol than normal. People from this abnormality would benefit from LDL lowering therapy, but traditional LDL cholesterol tests do not identify them as candidates for such treatment.

