A better way to measure heart disease risk for an overweight society

Low density lipoprotein (LDL) cholesterol or the “bad cholesterol” is an established measure of cardiovascular risk. LDL particles interact with the lining of the blood vessel and contribute to cholesterol loading in the arterial wall. Continued buildup of cholesterol in the arterial wall results in narrowing of the artery. Lowering LDL cholesterol levels is achieved with dietary reductions in total calories and saturated fat, weight loss and several classes of medications. In controlled trials, LDL cholesterol lowering, particularly with statins, reduce the risk for heart attack, stroke, death from cardiovascular disease and the death rate.

LDL cholesterol concentration is estimated by the Freidewald formula:

LDL cholesterol = Total cholesterol (TG) minus very low density lipoprotein (VLDL) cholesterol (20% of the triglyceride level) minus HDL cholesterol.

As people become more overweight and develop diabetes, triglyceride levels increase in the bloodstream. Triglycerides are transported by a different lipoprotein, very low density lipoprotein. The triglycerides carried by VLDL and other triglyceride-transporting lipoproteins are exchanged for the cholesterol in the LDL particles. This exchange results in a LDL particle that contains more triglyceride and less cholesterol. Thus, LDL cholesterol, which is calculated with Freidewald equation, underestimates the actual number of LDL particles.

Another measure of atherogenic risk is non-HDL cholesterol.

Non-HDL cholesterol = total cholesterol minus HDL cholesterol.

Many physicians use the non-HDL cholesterol to evaluate risk because it does not require the patient to fast, and it is more strongly associated with future risk of cardiovascular events in women, patients with type 2 diabetes, chronic kidney disease and human immunodeficiency virus infection.

Why has there been an emphasis on measuring Apolipoprotein B?

Apolipoprotein B (apoB) is the major structural protein on the surface of all plaque-causing cholesterol or atherogenic lipoproteins and its role is to carry these particles to the blood. There is only one apoB protein per atherogenic particle. Thus, in contrast with LDL cholesterol measurement, the concentration does not vary by triglyceride level. Apolipoprotein B has been shown to be more strongly associated with cardiovascular events (heart attack and strokes) than LDL cholesterol, particularly in certain patients, such as those with obesity and type 2 diabetes. In a study that included 2,155 men that were followed for 5 years, apoB was strongly associated with

higher risk for the build up of calcium, a measure of atherosclerosis, in the heart arteries. In mathematical models that control for differences in triglycerides, HDL cholesterol, and total cholesterol/HDL cholesterol ratio, the association between apoB and coronary artery risk remained statistically significant.

In addition to the increase in accuracy of coronary artery disease risk, measuring apoB has several other benefits: (1) apoB is directly measured and not calculated; (2) it can be measured without fasting; and (3) the measurement is standardized and widely available. The use of apoB as a biomarker for estimating cardiovascular disease risk will allow for strategies to improve treatment for the modern patient, who more often suffers from overweightness and its consequences.

Yashira Henriquez, *MSc and* ***Robert S. Rosenson****, MD*
Icahn School of Medicine at Mount Sinai, New York, USA

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