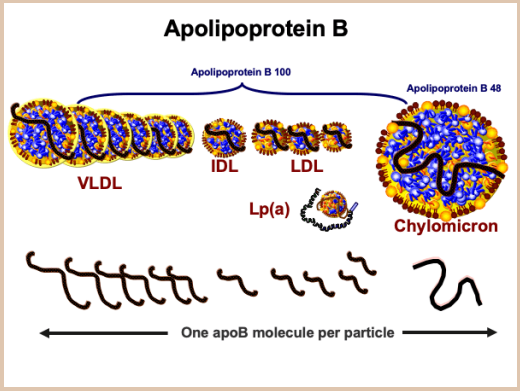
The Key to Heart Attack Risk?

Apo B is a better predictor of risk than LDL-C



The reason we check lipid panels is to try to get an idea of cardiovascular risk. Over the years, the LDL level has been deemed to be the one number we should focus on. Millions of people have been placed on cholesterol-lowering medications based on a calculated LDL level. However, is this the best tool to determine our risk? What if there is a better test to determine our risk more accurately for heart disease and heart attacks?

Abstract

Importance: Lipid management typically focuses on levels of low-density lipoprotein cholesterol (LDL-C) and, to a lesser extent, triglycerides (TG). However, animal models and genetic studies suggest that the atherogenic particle subpopulations (LDL and very-low-density lipoprotein [VLDL]) are both important and that the number of particles is more predictive of cardiac events than their lipid content.

Objective: To determine whether common measures of cholesterol concentration, TG concentration, or their ratio are associated with cardiovascular risk beyond the number of apolipoprotein B (apoB)–containing lipoproteins.

Design, Setting, and Participants: This prospective cohort analysis included individuals from the population-based UK Biobank and from 2 large international clinical trials, FOURIER and IMPROVE-IT. The median (IQR) follow-up was 11.1 (10.4-11.8) years in UK Biobank and 2.5 (2.0-4.7) years in the clinical trials. Two populations were studied in this analysis: 389 529 individuals in the primary prevention group who were not taking lipid-lowering therapy and 40 430 patients with established atherosclerosis who were receiving statin treatment.

Exposures: ApoB, non–high-density lipoprotein cholesterol (HDL-C), LDL-C, and TG.

Main Outcome and Measures: The primary study outcome was incident myocardial infarction (MI).

Results: Of the 389 529 individuals in the primary prevention group, 224 097 (58%) were female, and the median (IQR) age was 56.0 (49.5-62.5) years. Of the 40 430 patients with established atherosclerosis, 9647 (24%) were female, and the median (IQR) age was 63 (56.2-69.0) years. In the primary prevention cohort, apoB, non–HDL-C, and TG each individually were associated with incident MI. However, when assessed together, only apoB was associated (adjusted hazard ratio [aHR] per 1 SD, 1.27; 95% CI, 1.15-1.40; $P < .001$). Similarly, only apoB was associated with MI in the secondary prevention cohort. Adjusting for apoB, there was no association between the ratio of TG to LDL-C (a surrogate for the ratio of TG-rich lipoproteins to LDL) and risk of MI, implying that for a given concentration of apoB-containing lipoproteins, the relative proportions of particle subpopulations may no longer be a predictor of risk.

Conclusions and Relevance: In this cohort study, risk of MI was best captured by the number of apoB-containing lipoproteins, independent from lipid content (cholesterol or TG) or type of lipoprotein (LDL or TG-rich). This suggests that apoB may be the primary driver of atherosclerosis and that lowering the concentration of all apoB-containing lipoproteins should be the focus of therapeutic strategies.

This prospective cohort study of two patient populations, a primary prevention group without lipid-lowering therapy and a secondary prevention group on lipid-lowering therapy investigated whether common measures of cholesterol (LDL-C and HDL) or triglycerides (TG) were associated with cardiovascular risk beyond the number of apolipoprotein B (apoB)–containing lipoproteins. For the primary prevention group, apoB, HDL, and TG were individually associated with incident myocardial infarction (MI); however, when assessed together, only apoB was associated with a risk of MI. In the secondary prevention group, apoB was the only measure associated with incident MI. These findings suggest that the number of apoB-containing lipoproteins may be the primary predictor of MI risk.

In the typical lipid panel we have all had done, we get measures of total cholesterol, LDL (calculated), HDL, and triglycerides. It is important to know that the LDL level is not directly measured, it is calculated using either the Friedewald formula which is total cholesterol (TC) minus high-density lipoprotein (HDL)-cholesterol minus triglycerides (TGs)/5 in mg/dl or the newer Martin/Hopkins formula (LDL-C = TC – HDL-C – TG/ an adjustable factor based on a patient's Non-HDL-C and TG levels derived from a 174-cell 2D table). These formulas have been shown to often underestimate our actual LDL particle number. Low-density lipoprotein (LDL) cholesterol is the "bad" cholesterol that can build up in artery walls contributing to the formation of plaque which results in the hardening and narrowing of arteries. This can eventually lead to heart attacks and strokes. Cholesterol doesn't float freely in the bloodstream; it must be carried by lipoproteins which are particles formed by the liver made of fat and protein.

I have had discussions with some of you regarding ordering an apolipoprotein B (apoB) test. ApoB can now be measured accurately and inexpensively and gives more accurate information regarding possible cardiovascular risk. Cholesterol can only enter the arterial wall within apoB particles. Apolipoprotein B (apoB) particles are the basic unit of injury to the arterial wall. The mass of cholesterol that will be deposited within the arterial wall is determined by the number of apoB particles trapped in the wall and thus the greater the injury to the arterial wall. Each atherogenic particle contains one molecule of apoB. Therefore, apoB more accurately measures atherogenic risk than LDL or non–HDL cholesterol alone. The more apoB particles are reduced by therapy, the lesser the injury to the arterial wall and the greater the opportunity for healing.

So again, similar to the CT heart scan discussed in the previous article, this is another tool that can be used to determine individual risk of coronary artery disease and give us actionable information.

Association of Apolipoprotein B-Containing Lipoproteins and Risk of Myocardial Infarction in Individuals With and Without Atherosclerosis: Distinguishing Between Particle Concentration, Type, and Content
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