Lipid-related markers addition linked with slight improvement in cardiovascular disease prediction

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Among individuals without known cardiovascular disease (CVD), the addition of certain apolipoproteins and lipoproteins to risk scores containing total cholesterol and high-density lipoprotein cholesterol (HDL-C) was associated with slight improvement in CVD prediction, according to a study in the June 20 issue of *JAMA*.

"Routinely used risk prediction scores for CVD contain information on total cholesterol and HDL-C and several other conventional risk factors. There is considerable interest in whether CVD prediction can be improved by assessment of various additional lipid-related markers either to replace, or supplement, traditional cholesterol measurements in these scores," according to background information in the article.

Emanuele Di Angelantonio, M.D., of the University of Cambridge, England, and colleagues with the Emerging Risk Factors Collaboration writing group conducted a study to determine whether adding information on apolipoprotein B and apolipoprotein A-I, lipoprotein (a), or lipoprotein-associated phospholipase A2 to total cholesterol and HDL-C improves CVD risk prediction. For this study, individual records were available for 165,544 participants without CVD at the beginning of the study (calendar years of recruitment: 1968-2007) with up to 15,126 incident fatal or nonfatal CVD outcomes (10,132 coronary heart disease [CHD] and 4,994 stroke outcomes) during a median (midpoint) follow-up of 10.4 years.

The researchers found that replacement of information on total cholesterol and HDL-C with various lipid parameters did not improve CVD prediction. "For example, none of the following measures were superior to total cholesterol and HDL-C when they replaced traditional cholesterol measurements in risk prediction scores: the total cholesterol:HDL-C ratio; non-HDL-C; the linear combination of apolipoprotein B and A-I; or the apolipoprotein B:A-I ratio. Furthermore, replacement of total cholesterol and HDL-C with apolipoprotein B and A-I actually significantly worsened risk discrimination."

The authors did find that the addition of information on various lipid-related markers to total cholesterol, HDL-C, and other conventional risk factors yielded improvement in the model's discrimination. "We estimated that for 100,000 adults aged 40 years or older, 15,436 would be initially classified at intermediate risk using conventional risk factors alone. Additional testing with a combination of apolipoprotein B and A-I would reclassify 1.1 percent; lipoprotein (a), 4.1 percent; and lipoprotein-associated phospholipase A2 mass, 2.7 percent of people to a 20 percent or higher predicted CVD risk category and, therefore, in need of statin treatment under Adult Treatment Panel III guidelines."

However, the authors note that "The clinical benefits of using any of these biomarkers remains to be established."

Scott M. Grundy, M.D., Ph.D., of the University of Texas Southwestern Medical Center, Dallas, writes in an accompanying editorial that the need for reevaluation of statin treatment recommendations for primary prevention is made clear by a recent report from the Cholesterol Treatment Trialists' Collaborators.

"This report argues that a sizable portion of patients previously identified as low-risk by multiple-risk-factor algorithms could now be considered

candidates for cost-effective statin therapy. These algorithms probably are of less value in selection of patients for drug therapy than in the past. More promising approaches for the future risk assessment may be either testing for early, subclinical atherosclerosis by imaging methods or by simple, qualitative risk projection based on age, sex, low-density lipoprotein levels, and perhaps another major risk factor."

More information: *JAMA*. 2012;307[23]:2499-2506.
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