

Low cholesterol transfer protein activity associated with heart disease risk

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Although seen as a potential heart disease therapy, raising high-density lipoprotein (HDL) cholesterol levels by inhibiting activity of a transfer protein may not be effective, a new study suggests. Scientists at the Jean Mayer USDA Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts University and Boston University School of Medicine found an association between low plasma cholesterol ester transfer protein (CETP) activity and increased risk of heart disease in the Framingham Heart Study population.

CETP is a protein that shuttles cholesterol throughout the body, thus controlling the levels of HDL, [low-density lipoprotein](#) (LDL), and very-low-density lipoprotein (VLDL) in the blood. "Our findings differ from studies suggesting that inhibiting CETP activity would bring a cardiovascular benefit by raising HDL, the so-called good cholesterol credited with lowering the risk of heart disease," says senior author Jose Ordovas, PhD, director of the Nutritional Genomics Laboratory at the USDA HNRCA. "In a clinical trial testing that hypothesis, heart disease unexpectedly advanced in a surprising number of participants."

Based on those results, Ordovas and colleagues examined CETP activity in 1,978 Caucasian men and women with a mean age of 51 years and no history of heart disease. They analyzed 15 to 18 years of study visits looking for first cardiac events including heart failure, heart attack, angina, stroke and [peripheral vascular disease](#).

"By the end of the follow-up period, 320 men and women had

experienced their first cardiac event," says Ordovas who is also a professor at the Friedman School of Nutrition Science and Policy at Tufts University. "Participants with low CETP activity were 18 percent more likely to develop cardiovascular disease than people with CETP activity above the median."

A more in-depth investigation of models eliminated the possibility that age, sex and common risk factors such as smoking, weight, diabetes, and cholesterol levels interfered with the findings. The results are published in the December 15 issue of *Circulation*.

The authors stress the preliminary nature of their data. "The relationship between CETP activity and HDL levels carries many unknowns, including the influence of genetics," Ordovas says, pointing to studies of some Japanese families. "Despite very low levels of CETP activities, they still have high heart disease risk. Other genetic studies question the inhibition of CETP, but there is not enough research to discount the possibility that raising HDL levels through CETP inhibitors may reduce the risk of [heart disease](#)," he adds.

More information: Ramachandran S. Vachon, Michael J. Pencina, Sander J. Robins, Justin P. Zachariah, Guneet Kaur, Ralph B. D'Agostino, and Jose M. Ordovas . "Association of Circulating Cholesteryl Ester Transfer Protein Activity With Incidence of Cardiovascular Disease in the Community" *Circulation*. 2009;120:2414-2420; published online before print November 30 2009.

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