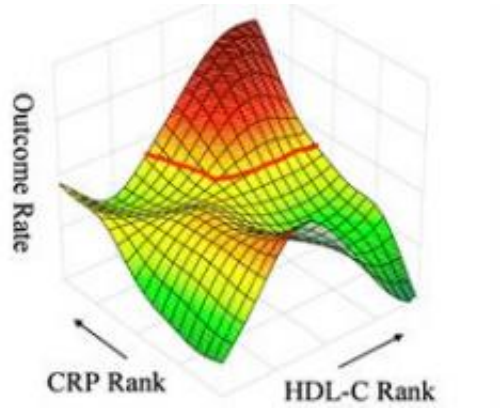
More 'good' cholesterol is not always good for your health

May 25 2010



(PhysOrg.com) -- We've all heard about the importance of raising HDL, or the so-called "good" cholesterol, and lowering LDL, or "bad" cholesterol, to improve heart health. While we've come to assume HDL cholesterol is an inherently good thing, a new study shows that for a certain group of patients, this is not always the case. The study is the first to find that a high level of the supposedly good cholesterol places a subgroup of patients at high risk for recurrent coronary events, such as chest pain, heart attack, and death.

The findings, published in *Arteriosclerosis, Thrombosis, and Vascular Biology*, a journal of the American Heart Association, could help explain disappointing results from a high-profile Pfizer clinical trial testing

torcetrapib, an experimental drug designed to increase levels of HDL cholesterol, that some predicted would become a blockbuster medicine. The trial was halted in 2006 due to a surprisingly excessive number of cardiovascular events and death. As in the current study, cardiovascular events in the torcetrapib trial were associated with higher levels of "good" HDL cholesterol, though the reasons were unclear.

"It seems counterintuitive that increasing good cholesterol, which we've always thought of as protective, leads to negative consequences in some people," said James Corsetti, M.D., Ph.D., professor of Pathology and Laboratory Medicine at the University of Rochester Medical Center and lead author of the study. "We've confirmed that high HDL cholesterol is in fact associated with risk in a certain group of patients."

Using a novel graphical data mapping tool - outcome event mapping - Corsetti and his team identified a group of patients in which elevated levels of HDL cholesterol place them in a high-risk category for coronary events.

"The ability to identify patients who will not benefit from efforts to increase HDL cholesterol is important because they can be excluded from trials testing medications that aim to raise HDL cholesterol," said Charles Sparks, M.D., professor of Pathology and Laboratory Medicine and co-author of the study. "With these patients excluded, researchers may find that raising HDL cholesterol in the remaining population is effective in reducing cardiovascular disease risk."

Despite the outcome of the Pfizer torcetrapib trial and findings in the existing literature, including the current study, that suggest high HDL cholesterol can be a bad thing, drug companies remain invested in identifying drugs to increase HDL cholesterol. Merck recently announced plans to launch a major clinical trial in 2011 to test whether anacetrapib - a molecular cousin to torcetrapib designed to raise good

cholesterol - reduces the risk of heart attack and death.

Patients in the high-risk subgroup were characterized as having high levels of C-reactive protein (CRP), a well-known marker of inflammation, in addition to high HDL cholesterol. Study authors believe genetics and environmental factors, particularly inflammation, influence whether high levels of HDL cholesterol are protective or if they increase cardiovascular risk in individual patients. Given an inflammatory environment, an individual's unique set of genes helps determine whether HDL cholesterol transforms from a good actor to a bad actor in the heart disease process.

In the high-risk subgroup of patients with elevated HDL cholesterol and CRP, researchers also identified two genetic factors associated with recurrent coronary events. The activity of cholesterol ester transfer protein (CETP), which moves cholesterol away from the vascular system and is associated with HDL cholesterol, and p22phox, which influences inflammation-related processes and is associated with CRP, are both risk predictors in this subgroup of patients.

"Our research is oriented around the ability to better identify patients at high risk," said Corsetti. "Identifying these patients and determining what puts them at high risk may be useful in choosing treatments tailored to the specific needs of particular patient subgroups. This gets us another step closer to achieving the goal of personalized medicine."

Corsetti's team identified individuals at high risk for recurrent coronary events among 767 non-diabetic patients who experienced at least one prior heart attack. Outcome event maps plot risk over an area defined by high and low levels of two biomarkers, in this case HDL cholesterol and CRP. Peaks and valleys in the maps correspond to high- and low-risk patient subgroups. Patients were followed for recurrent events for approximately two years and were part of the Thrombogenic Factors and

Recurrent Coronary Events (THROMBO) study led by cardiologist Arthur Moss, M.D., professor of Medicine at the University of Rochester Medical Center and study co-author.

The current results parallel findings from a study of a healthy population. The Prevention of Renal and Vascular End-Stage Disease (PREVEND) study also identified a high-risk subgroup of patients with elevated HDL cholesterol and CRP levels among individuals who had no prior coronary events.

Provided by University of Rochester Medical Center