HDL Efflux Capacity May Correlate With CAD Risk

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

HDL cholesterol's efflux capacity, a measure of its ability to promote cholesterol efflux from lipid-laden macrophages, was strongly inversely correlated with atherosclerotic burden in a study of two independent groups of subjects.

In a study assessing HDL cholesterol efflux capacity in two independent populations, this key measure of HDL function was a stronger predictor of both subclinical atherosclerosis disease (as assessed by carotid intima-media thickness) and coronary artery disease than was HDL level itself.

"These results could be important in the assessment of new therapies targeting HDL metabolism and reverse cholesterol transport," and may even guide the development of new treatments, said Dr. Amit V. Khera of the cardiovascular institute at the University of Pennsylvania, Philadelphia, and his associates.

They first tested efflux capacity in serum samples from a cohort of 203 healthy white adults participating in a study of HDL-related biomarkers and atherosclerosis. These subjects underwent measurement of carotid artery intima-media thickness as part of that study.

There was no association between HDL level and subclinical CAD. In contrast, there was a significant inverse correlation between HDL cholesterol efflux capacity and subclinical CAD, which remained robust after the data were adjusted for HDL and apolipoprotein A-1 levels.

The investigators then assessed efflux capacity using serum samples from 793 white participants in a case-control cohort who underwent cardiac catheterization. The 442 patients found to have CAD showed significantly lower efflux capacity than did the 351 control subjects who were free of CAD.

In a further analysis, the proportion of patients with CAD decreased consistently with increasing efflux capacity. When the cohort was divided into quartiles of efflux capacity, the quartile with the highest efflux capacity showed a distinct decrease in CAD compared with the quartile with the lowest capacity.

All of these correlations remained robust after adjustment for subject age, sex, and traditional cardiovascular disease risk factors, Dr. Khera and his colleagues said (N. Engl. J. Med. 2010;364:127-35).

"Although cholesterol efflux from macrophages represents only a small fraction of overall flux through the reverse-cholesterol-transport pathway, it is probably the component that is most relevant to atheroprotection," they noted.

"These findings reinforce the concept that assessment of HDL function" – not just HDL levels – "may prove informative in refining our understanding of HDL-mediated atheroprotection," the researchers added.

This study was supported by the National Heart, Lung, and Blood Institute; the National Center for Research Resources; the Doris Duke Charitable Foundation; and the Howard Hughes Medical Institute. Dr. Khera's associates reported ties to Kinemed, Vascular Strategies, and GlaxoSmithKline, as well as involvement with a patent on cell culture systems for determining cholesterol efflux potential in serum. ■

VIEW ON THE NEWS

HDL Function Deserves Further Study

The central hypothesis of the study, which was based on findings from studies in animals and cell cultures, was that HDL promotes cholesterol efflux from macrophage foam cells in atheromatous vessels, thus decreasing both the cholesterol burden and macrophage-driven inflammation, said Dr. Jay Heinecke.

The results thus "provide important evidence that the ability of HDL to promote cholesterol efflux from macrophage foam cells is a key property that explains in part the inverse relationship between HDL and the risk of atherosclerotic coronary artery disease in humans."

Measuring efflux capacity thus may become a useful tool in further investigation of HDL function as well as in developing treatments for CAD, he said.

DR. HEINECKE is with the University of Washington, Seattle. He reported ties to several drug and biomedical technology companies. These comments are taken from his editorial accompanying Dr. Khera's report (N. Engl. J. Med. 2010;364:170-1).

High-Normal Hematocrit Linked to Heart Failure

BY BRUCE JANCIN

FROM THE ANNUAL SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION

CHICAGO – A high-normal hematocrit was associated with an increased risk of new-onset heart failure in a Framingham Heart Study analysis.

"To our knowledge, this is the only study to show such a relationship in men and women in middle age. … Our results should prompt consideration of a cautious and measured approach to the aggressive treatment of low hematocrit in a variety of disease states," Dr. Erin E. Coglianese said at the meeting.

The mechanism by which a hematocrit (HCT) within normal range is linked to heart failure is unclear. However, animal studies suggest one possibility – that a high-normal HCT could impair vasodilation as a result of scavenging of nitric oxide by hemoglobin, according to Dr. Coglianese of Massachusetts General Hospital, Boston.

To explore the relationship between HCT and the risk of heart failure, she and her coinvestigators turned to the Framingham Heart Study. They documented a strong, graded relationship between HCT level and the risk of developing heart failure in 3,523 Framingham participants aged 50-65 who were free of a history of heart failure at baseline and were followed prospectively for up to 20 years.

Indeed, individuals with a high-normal baseline HCT had almost double the risk of new-onset heart failure during follow-up, compared with those with a low HCT, even after adjustment for conventional risk factors for heart failure.

A low HCT was defined as 39% to less than 44% in men and 36% to less than 40% in women. Men with an HCT of 44% to less than 46% and women with a level of 40% to less than 42% were deemed as having a low-normal level. A normal HCT was defined as 46% to less than 50% in men and 42% to less than 46% in women. And a high-normal HCT was one greater than 50% in men or 46% in women.

When these definitions were used, the incidence of new-onset heart failure was 25/10,000 person-years in individuals with a low HCT level, 31/10,000 with a low-normal HCT, 38/10,000 with a normal HCT, and 48/10,000 in Framingham participants with high-normal HCT.

In a multivariate logistic regression analysis, the risk of new-onset heart failure, compared with the risk in those with a low HCT, was 27% greater in those with a low-normal HCT, 47% greater in those with a normal HCT, and 78% greater in those with a high-normal level. The analysis was adjusted for age, sex, total cholesterol, hypertension, body mass index, left ventricular hypertrophy, pack-years of smoking, and physical activity.

The big limitation of this study is that the original Framingham cohort, included in this analysis, looks quite different from contemporary patient populations. Specifically, roughly half of the men in the original cohort were smokers, Dr. Coglianese noted.

In contrast to these new findings regarding HCT and risk of new-onset heart failure, numerous studies have shown that in patients who already have heart failure, a low HCT is associated with an increased risk of heart failure hospitalization as well as all-cause mortality. It remains unclear, however, whether this increased risk of poor outcomes is due to pathophysiologic changes induced by low HCT, or if a low HCT is merely a marker of greater disease severity, she said.

Dr. Coglianese said she had no relevant financial disclosures. ■

Keep Home Warm in Winter for Better Blood Pressure Control

FROM THE ANNUAL SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION

CHICAGO – Keeping the bedroom warm at night during the cold winter months curbs the morning surge in blood pressure, according to a randomized Japanese trial.

This finding may help explain the well-established increased mortality due to heart disease and stroke during the winter months.

The data from this study indicate that if the ambient bedroom temperature is lower, morning blood pressure will be higher, the morning blood pressure surge will be greater, and there will be increased blood pressure variability during the 24-hour day, increasing the risk of a cardiac or cerebrovascular event, Dr. Keigo Saeki asserted at the meeting.

The investigators randomized 140 healthy 18- to 65-year-old participants to spend a night in either an inadequately heated room at 12° C (54° F) or a room maintained at 22° C (72° F). Participants were required to remain in the room between 9 p.m. and 6 a.m., stay awake until 11 p.m., and rise by 6 a.m. Blood pressure was measured every 30 minutes through the night. The subjects had access to all the clothing and blankets they needed to stay comfortable, said Dr. Saeki of Nara (Japan) Medical University.

Mean systolic blood pressure during the first 2 hours after awakening in the morning was 121.1 mm Hg in subjects who slept in the cold room, significantly higher than the 114.0 mm Hg for those in the warm room. The morning systolic blood pressure surge also was significantly higher in subjects after a night in the inadequately heated room: 21.9 mm Hg, compared with 14.3 mm Hg after a night in the warm room. However, there was no difference between the two study groups in terms of lowest sleeping systolic blood pressure, which averaged 99 mm Hg across three readings.

Dr. Saeki declared having no relevant disclosures.

–Bruce Jancin