Heart Failure Ups Risk For New-Onset Diabetes

ARTICLES BY
MITCHEL L. ZOLER

ORLANDO — Patients with heart failure had a greater than twofold increased risk of subsequently developing diabetes, compared with people without heart failure in a review of more than 4,600 individuals in the Framingham Offspring Study.

The analysis also showed a strong association between the severity of heart failure symptoms and the risk for new-onset diabetes: Patients with higher New York Heart Association–class heart failure faced a greater risk for developing diabetes than did patients with less severe heart failure symptoms, Dr. Ankit Rathod reported at the annual scientific sessions of the American Heart Association.

The implications are that patients with heart failure should undergo more intensive surveillance for development of insulin resistance and diabetes. The findings also present a new reason for optimized heart failure treatment to minimize symptom severity because this may cut the patient's risk for developing diabetes, Dr. Rathod said in an interview.

The hypothesized causal link between heart failure and diabetes is the neurohormonal, sympathetic activation that characterizes heart failure. This leads to norepinephrine release, which can trigger insulin resistance and hence increased susceptibility to developing diabetes, said Dr. Rathod, an internal medicine physician at Wayne State University in Detroit. In addition, patients with more severe heart failure symptoms have reduced activity, which might exacerbate insulin resistance and the risk for developing diabetes.

"I believe the connections between insulin resistance and neurohormonal activation are a real phenomenon," said Dr. Clyde W. Yancy, medical director of the Baylor Heart and Vascular Institute at Baylor University Medical Center in Dallas. He cited study results showing that treatment with drugs that block neurohormonal activation also cut development of diabetes, such as with ramipril in the HOPE study (N. Engl. J. Med 2000; 342:145-53) and treatment with carvedilol in the CAPRICORN study (Lancet 2001; 357:1385-90).

Dr. Rathod's study used data collected from the more than 4,900 people enrolled in the Framingham Offspring Study in 1971. He and his associates excluded people with a history of diabetes or heart failure at the time of enrollment, as well as those who had missing data on their subsequent rate of new-onset diabetes. The 4,614 people included in the study had an average age of 35 years, and about half were women.

Patients who first developed heart failure had a 2.5-fold increased risk for later developing diabetes.

DR. RATHOD

During an average follow-up of 24 years, 123 developed heart failure and 468 developed new-onset diabetes. Forty-one of the 123 patients (33%) who developed heart failure later developed diabetes, compared with 427 new cases of diabetes among the other 4,491 people (10%).

In a multivariate analysis that adjusted for baseline demographic and clinical differences, including drug treatments and baseline blood glucose levels, patients who first developed heart failure had a statistically significant 2.5-fold increased risk for later developing diabetes, compared with the people who did not have heart failure.

The link between heart failure and diabetes should be examined in other databases, Dr. Rathod said. ■

Disclosures: *Dr. Rathod and Dr. Yancy both reported having no financial disclosures.*

Gout Associated With Worse Heart Failure Outcomes

ORLANDO — Gout boosted the risk of death or hospitalization for heart failure in an observational, case-control study of more than 150,000 patients with heart failure.

The analysis also showed that patients with heart failure and gout who were on long-term allopurinol treatment had a significantly reduced risk for death or heart failure hospitalization, Dr. George Thanassoulis said at the annual scientific sessions of the American Heart Association.

These findings do not warrant the use of allopurinol in heart failure patients without gout, but the data suggest that if such patients are candidates for allopurinol because of coexisting gout, the new results "increase the reasons to treat them," said Dr. Thanassoulis, a cardiologist at Boston University and the Framingham Heart Study.

He hypothesized that allopurinol exerts its benefit for heart failure outcomes not by lowering blood levels of uric acid, but by inhibiting oxidative stress and the endothelial dysfunction that oxidative stress produces. Dr. Thanassoulis suggested that allopurinol inhibits xanthine oxidase, the same action that also blunts uric acid production.

The study used administrative health-record data from residents of the province of Quebec who were aged older than 65 years. Cases were 14,327 people hospitalized for heart failure but without another heart failure hospitalization during the 3 years before the index episode, a restriction that helped ensure a uniform level of heart failure severity among the patients. Controls were 143,255 people in the Quebec database matched to the cases by follow-up duration and by calendar year.

The average age was 79 years among the cases and 77 years among the controls. Both groups were evenly split among men and women. Identification of gout relied on hospitalization, a physician visit, or a diagnostic code in the medical record.

During an average follow-up of 2 years, the rate of death or new heart failure hospitalization was 63% higher in the patients with gout than in those without gout, a statistically significant difference in an analysis that controlled for several demographic and clinical variables including age, gender, comorbidities, and medications.

The risk for death or heart failure hospitalization was even higher in patients who had acute gout, with a twofold higher risk in the adjusted analysis. The researchers defined acute gout as hospitalization or a physician visit for gout within 60 days of the index heart failure event.

Another pair of analyses looked at the impact of allopurinol treatment. Among patients with an index heart failure event who also had gout treatment with allopurinol, there was a significant 31% reduction in the subsequent rate of death or heart failure hospitalization in the adjusted analysis. This benefit was limited to the patients on chronic allopurinol treatment for more than 30 days. Patients on allopurinol for 30 days or less showed no significant reduction in mortality or new heart failure hospitalizations.

The allopurinol analysis also showed no link between the drug and outcomes for the entire heart failure population studied, suggesting that benefit from allopurinol is not general for all heart failure patients, only those with gout.

The next step is to assess the relationship between heart failure, gout, and allopurinol treatment in a prospective, controlled study, Dr. Thanassoulis said. ■

Disclosures: *Dr. Thanassoulis and his associates have no conflicts of interest.*

Higher HDL Cholesterol Tied to Lower Cancer Incidence

ORLANDO — Higher serum levels of high-density lipoprotein cholesterol were linked with lower risk for incident cancer in a meta-analysis of 21 randomized, controlled trials involving nearly 140,000 people.

An unadjusted analysis of cancer incidence rates in the 21 studies relative to baseline levels of high-density lipoprotein (HDL) cholesterol showed that every 10-mg/dL increment in HDL was linked with a 24% relative reduction in new-onset cancers.

The association was statistically stronger in a multivariate analysis that adjusted for baseline levels of low-density lipoprotein (LDL) cholesterol, age, body mass index, and smoking status. In this model, every 10-mg/dL increment in baseline HDL cholesterol correlated with a 21% drop in incident cancers, Dr. Haseeb Jafri and his associates reported in a poster at the annual scientific sessions of the American Heart Association.

This is the first report of a strong and significant inverse relationship between serum level of HDL cholesterol at baseline and subsequent development of cancer, according to Dr. Jafri, an internal medicine physician at Tufts Medical Center in Boston, and his coauthors.

The antioxidant and anti-inflammatory effects of HDL cholesterol particles is one hypothesized mechanism for the link between HDL cholesterol levels and cancer susceptibility, said Dr. Richard H. Karas, director of preventive cardiology and vice chairman of the department of medicine at Tufts and senior investigator on the report.

For example, HDL cholesterol particles carry the antioxidant enzyme paraoxonase, Dr. Karas said in an interview.

The 21 lipid-intervention trials included in the meta-analysis appeared in journal articles published during 1987-2009, and included more than 73,000 people allocated to lipid interventions and more than 66,000 in the control arms.

For inclusion in the analysis, published reports had to contain data on both baseline HDL cholesterol levels and incident cancer rates. The median duration of follow-up was 5 years, and the cumulative exposure studied totaled 586,000 person-years.

The median serum level of HDL cholesterol at baseline was about 45 mg/dL. During follow-up, the study participants developed 7,928 new-onset cancers.

In the multivariate model, baseline levels of LDL cholesterol and age also were significantly related to the rate of incident cancers.

Future studies should look at the relationship between HDL cholesterol and cancer incidence in other databases, Dr. Karas said. ■

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