Heart Failure Boosts Risk For New-Onset Diabetes

BY MITCHEL L. ZOLER

Orlando — Patients with heart failure had a greater than twofold increased risk of 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 severity of heart failure symptoms and risk for new-onset diabetes.

The study’s lead author, Dr. Ankit Rathod, said at the annual scientific sessions of the American Heart Association that the hypothesis is that the usual 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 internist 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. Treatment with drugs that block neurohormonal activation also can develop 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), he said. Dr. Rathod collected data from the more than 4,900 people who enrolled into the Framingham Offspring Study in 1971. He analyzed the data to determine how many those who had a history of diabetes or heart failure with and without the development of diabetes.

Forty-one of the 123 patients (33%) who developed heart failure later developed diabetes. DR. RATHOD

The average age was 79 years among the patients who had acute gout, with a statistically significant 2.5-fold increase in the rate of death or new heart failure hospitalizations. 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.

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, said Dr. Thanassoulis, a cardiologist at Boston University and the Framingham (Mass.) Heart Study. He suggested that allopurinol inhibits xanthine oxidase, the same action that also blunts uric acid production.

The study used administrative health record data from Quebec residents aged older than 65 years. Control groups were 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. Cases and controls 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 demographics and clinical variables including age, gender, comorbidities, and medications.

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 2.4-fold 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. Dr. Thanassoulis and his associates had no conflicts of interest to disclose.