Worsening Depression Linked to HF Outcome

BY MICHELE G. SULLIVAN

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Worsening depression is associated with a doubling in the risk of cardiac-related hospitalization or death.

The significant increase in poor cardiovascular outcomes was seen regardless of any changes in the status of heart failure, suggesting that depression exerted the biggest influence on the increased risk, Andrew Sherwood, Ph.D., and his colleagues wrote (J. Am. Coll. Cardiol. 2011;57:418-23).

"Our findings support the recent American Heart Association position encouraging depression screening, and further suggest that it may be prudent for clinicians to reassess symptoms of depression routinely in heart failure patients who are at increased risk for adverse clinical outcomes and impaired quality of life," wrote Dr. Sherwood of Duke University Medical Center, Durham, N.C., and his coauthors.

The prospective study examined a cohort of 204 outpatients with confirmed heart failure; 27 died during the first year and 30 were unavailable for follow-up. Therefore, 147 were followed for a mean of 5 years. At baseline, patients' mean age was 57 years; 70% were men. Most had a New York Heart Association functional class of II (69%) or III (37%). The most common baseline medications were beta-blockers (88%) and ACE inhibitors (86%). Antidepressant use occurred in 20% of patients at baseline.

The study was unique among similar investigations because it assessed several clinical aspects of heart failure and depression at baseline and in each of the follow-up years. Heart failure assessments included plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP; mean baseline measure 1,159 pg/mL) and left ventricular ejection fraction (LVEF, baseline mean 32%).

At baseline, the average score on the Beck Depression Inventory (BDI) was 10, a level considered clinically significant for depressive symptoms.

Patients who died during the first year had significantly higher resting heart rates, lower LVEFs, and higher NT-proBNP levels, and were less likely to be taking nitrates. Analysis showed that only NT-proBNP and LVEF were significantly associated with early death.

Among the group of 147 followed through 5 years, 127 (86%) either died or were hospitalized (53). Of the deaths, 40 were from cardiac conditions and 15 occurred before any hospitalization.

Significant risks for cardiac hospitalization or death included cardiac ischemia (hazard ratio 1.84), NT-proBNP increase of 1,000 pg/mL (HR 1.17), and hospitalization within the first year (HR 2.4).

Over the follow-up period, 65 patients (44%) showed a 2-point change or less in either direction from their baseline BDI score; 43 (29%) showed an increase of 3 or more points in the BDI and 39 (27%) showed a decrease of 3 or more points.

Compared with those whose BDI changed 2 or fewer points, those with a 3-point or greater increase were twice as likely to experience cardiac hospitalization or death (HR 2.12), a significant difference. Those whose BDI was 3 points lower than baseline (indicating improvement in depression) showed a proportional risk reduction, compared with those with a change of 2 points or less (HR 0.87), but this was not a significant association.

The extent of depression at baseline was significantly related to the risk of cardiovascular hospitalization or death, with a 6% increase in risk for every 1-point increase in BDI. The 5-year change in BDI was also significantly related to the poor cardiovascular outcomes, with a 7% increased risk for every 1-point increase in the scale.

The extent of depression at baseline also significantly increased the risk of all-cause hospitalization or mortality, with a 9% increase in risk for every 1-point increase in BDI. The 5-year change in BDI increased the risk of all-cause hospitalization or mortality by 6% for every 1-point increase in BDI.

The relationship between increasing depression and adverse outcome remained significant, even after controlling for the severity of heart failure.

The study was sponsored by the National Institutes of Health. Dr. Sherwood had no financial declarations, but a coauthor, Dr. Christopher O'Connor, also of Duke University, declared relationships with Merck, Medtronic, Forest, GE Healthcare, Amgen, Medpace, Roche, Actelion, Johnson & Johnson, Novella, and Trevena. ■

THE NEWS VIEW ON

Screen Heart Failure Patients for Depression

"The findings [of Dr. Sherwood and colleagues] raise additional questions," about the relationship between depression and heart failure," Ingrid Connerney, Ph.D., and Dr. Peter A. Shapiro wrote in an accompanying editorial (J. Am. Coll. Cardiol. 2011;57:424-6).

While this study noted that antidepressant use at baseline was not associated with an improvement in clinical outcomes, others have shown conflicting results. "Importantly, however, treatment of depression in patients with cardiac disease has been linked to at least modest reduction in depressive symptoms, improved quality of life, and improved adherence."

The findings beg another question: Should cardiologists be screening heart failure patients for depression, or doing anything if they uncover it? The availability of a quick and easy-to-administer depression test points to yes, the authors said. "It is feasible for the cardiologist to assess patients regularly for depression. There are validated and brief screening instruments that can facilitate rapid identification of patients with depressive symptoms."

One is as simple as asking two questions. "Over the past 2 weeks, have you been bothered by any of the following problems: 1) Feeling little interest or pleasure in doing things? 2) Feeling down, depressed or hopeless?"

If a patient answers yes to either one, the cardiologist might wish to further investigate, or refer the patient for treatment.

Finally, noted Dr. Connerney and Dr. Shapiro, there really is no way the study can answer the question of reverse causality. "Multiple physiological and behavioral mechanisms may underlie the association between depression and mortality," they wrote. Further studies are needed of the relationship between the course of depression and mortality in heart failure patients, the mechanisms linking depression to adverse outcomes, and the effects of depression intervention."

DR. CONNERNEY *is the senior director of Quality, Safety, and Clinical Effectiveness at the University of Maryland Medical Center in Baltimore.* DR. SHAPIRO *is professor of clinical psychiatry at the New York Presbyterian Hospital–Columbia University Medical Center. Both reported that they had no relationships to disclose.*

High-Normal Hematocrit Predicts Increased 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 owing to scavenging of nitric oxide by hemoglobin, said Dr. Coglianese of Massachusetts General Hospital, Boston.

To explore the relationship between HCT and risk of heart failure, she and her colleagues 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 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 people 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.

Analysis showed that 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 in some ways 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, many studies have shown that in patients who already have heart failure, a low HCT is associated with an increased risk of heart failure hospitalization and all-cause mortality. It is unclear whether this increased risk is due to changes induced by low HCT, or if low HCT is a marker of disease severity, she said.

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