NT-proBNP Testing Cut Time to Heart Failure Dx

BY DEBRA L. BECK
Contributing Writer

CHICAGO —Measuring N-terminal-proB–type natriuretic peptide in the emergency department facilitated diagnosis of acute heart failure, shortened visits, and saved money, according to results of IMPROVE-CHF, a multicenter randomized-controlled trial of the use of NT-proBNP–guided strategy in the management of suspected acute heart failure.

"Our economic analysis found that adding this test to physician judgment reduced the duration of the emergency department visit from an average of 6.3 hours to an average of 5.6 hours," Dr. Gordon W. Moe reported at the annual scientific sessions of the American Heart Association.

"In addition, it reduced the number of patients rehospitalized within 60 days from 51 to 33 and reduced costs in 2005 U.S. dollars from $5,592 to $4,631 per patient overall, a savings of $961 per patient," Dr. Moe said.

The IMPROVE-CHF study included 501 patients who presented to seven Canadian emergency departments with dyspnea. NT-proBNP samples were taken in all patients, but in only about half were the treating physicians made aware of the results. In the other half of patients, physicians utilized standard clinical tools to determine a diagnosis.

Patients were followed for 60 days to determine whether knowledge of NT-proBNP values improved the management of patients with suspected acute heart failure in a publicly funded, universal-access health care setting.

Although the amount of time spent in the ED was significantly reduced, the number of ICU admissions, median duration of ICU stay, and the number of patients requiring hospitalization after their ED visit did not differ between the NT-proBNP group and the usual-care group. By 60 days, 23% of patients enrolled had died or were rehospitalized, with no difference between groups.

Discussant Dr. Margaret M. Redford of the Mayo Clinic in Rochester, Minn., noted that the researchers were not clear on whether the cost savings were caused by more efficient treatment of patients or to less use of other diagnostic testing. It was also unclear whether the test was most helpful in making a diagnosis of heart failure or in excluding heart failure.

She also noted that the setting for IMPROVE-CHF—in Canada, where there is a single-payer system and carefully controlled costs—is both a strength and a limitation of the trial. "In this system costs are already carefully controlled, making it a rigorous testing ground for cost-saving measure … but we cannot assume the savings observed in the Canadian system would necessarily be observed in other health care systems." ■

Treat Anemia to Improve Outcomes in Heart Failure Patients

BY MITCHEL L. ZOLER
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BARCELONA — Researchers moved a step closer toward proving that correcting the anemia that often occurs in patients with heart failure improves outcomes, with results from three phase II studies that tested two different ways to boost hemoglobin levels.

Reports from two controlled studies that compared darbepoetin alfa with placebo in 475 patients showed that the treatment was safe, that it produced improvements in patients' exercise capacity that were tied to boosts in hemoglobin levels, and that the drug could cut the rate of death or hospitalization for heart failure at a rate that approached statistical significance, Dr. William T. Abraham reported at a joint meeting of the European Society of Cardiology and the World Heart Federation.

And results from the first randomized, observer-blinded test of intravenous iron in 35 patients with heart failure and low iron levels supported the idea that iron repletion is safe and associated with improvement in exercise capacity and heart failure symptoms, Dr. Stefan D. Anker said in a separate report at the meeting.

Anemia is a common complication of heart failure, but just how common depends on how it's defined. In data collected from one recent, large heart failure treatment trial, 30% of women and 16% of men had anemia if it was defined as a serum hemoglobin level of less than 12.5 g/dL. With a more conservative definition of less than 11.5 g/dL, the prevalence was 10% among women and 8% among men, said Dr. Anker, a cardiologist and professor of medicine at Charité University in Berlin.

These hemoglobin levels would not be severe enough to warrant drug interventions if they occurred in otherwise healthy people, in whom the hemoglobin level would have to be less than 10 g/dL to make drug intervention reasonable, Dr. Anker said in an interview. But in the context of heart failure, experts have hypothesized that higher hemoglobin levels might lead to clinically important improvements in exercise capacity and quality of life, and to a significant drop in heart failure hospitalizations.

The two most obvious ways to correct anemia are treatment with an erythropoietin agent and treatment with iron supplementation. These approaches could also be used together.

Three phase II studies of darbepoetin alfa, a long-acting erythropoietin, were recently completed, and results from the two largest of these studies were reported at the meeting. All three studies were sponsored by Amgen, which markets darbepoetin (Aranesp). Dr. Abraham has received research support from Amgen.

One trial involved 319 patients with New York Heart Association class II-IV heart failure and a serum hemoglobin level of 9.0-12.5 g/dL; their average baseline hemoglobin level was 11.35 g/dL. Of the 319 patients, 157 were randomized to receive placebo and 162 received darbepoetin alfa at a starting dosage of 0.75 mcg/kg administered subcutaneously every 2 weeks. The dosage was titrated to produce a rise in hemoglobin of 0.5-1.5 g/dL every 3 weeks and then to maintain a hemoglobin level of 13.0-15.0 g/dL. All patients also received supplemental iron, given as an oral dosage of 200 mg/day.

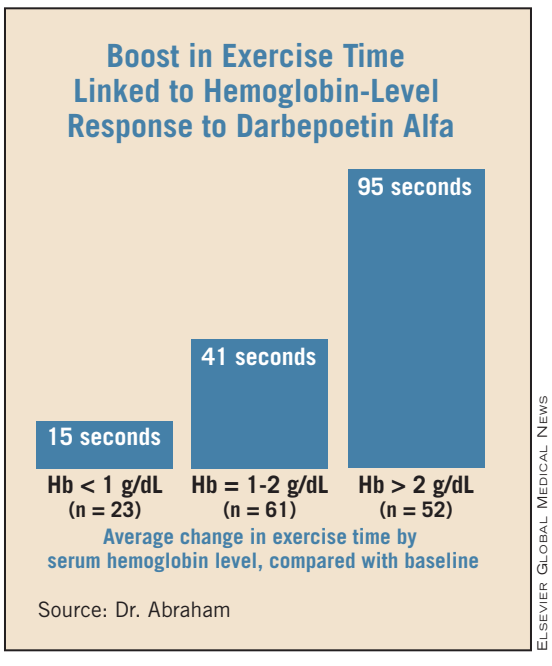
The primary end point for this study was the change in exercise capacity from baseline after 6 months of treatment, measured as time spent walking on a treadmill.

The regimen produced an average hemoglobin level of 13.5 g/dL in patients who were treated with darbepoetin alfa and no change in the patients treated with placebo.

The change in treadmill-exercise time was an average of 46.5 seconds in placebo patients and 57.3 seconds in the darbepoetin alfa–treated patients, a nonsignificant difference, reported Dr. Abraham, professor of medicine and director of the division of cardiovascular medicine at Ohio State University, Columbus.

However, a post hoc analysis of these data showed a promising and statistically significant link between the rise in serum hemoglobin level and improvements in exercise time (see graph). More than 80% of patients treated with darbepoetin alfa had a "robust response to treatment," with a hemoglobin rise of more than 1 g/dL, and these patients had substantial improvements in their exercise time, Dr. Abraham noted.

A prespecified end point for the two largest of the trials was a combined analysis to assess safety and efficacy measured by the incidence of all-cause death or first hospitalization for heart failure after 1 year of treatment. This combined the results from the 319-patient study described above and the results from a study with 165 patients. The second study randomized 55 patients to placebo, 56 to a weight-based dosage of darbepoetin that was the same as was used in the larger study, and 54 patients to a fixed-dosage regimen of the drug that used 50 mcg every 2 weeks. The results showed no difference between the effects of the weight-based and fixed dosages.



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Data for the combined analysis were available for 209 patients who received placebo and 266 who received darbepoetin alfa.

The 1-year incidence of death or hospitalization for heart failure was reduced by 33% in the patients treated with darbepoetin, compared with those who received placebo, a difference that neared statistical significance ($P = .064$).

Darbepoetin alfa treatment was also associated with trends in improved quality of life and in the patients' global self-assessment.

The incidence of serious adverse events was similar in the placebo and drug-treated arms, and treatment with darbepoetin alfa showed no evidence of any increases in the events that are of particular concern in patients who receive erythropoietin-type drugs, such as hypertension or thrombotic events.

Supplementation with oral iron in patients with anemia is often ineffective in routine practice, because the supplements taste bad and patients stop taking them, which makes an intravenous supplement an attractive alternative, Dr. Anker said.

The results that he reported were collected from 18 heart failure patients with anemia (hemoglobin less than 12.5 g/dL) and 17 patients with no anemia (hemoglobin 12.5-14.5 g/dL) but with iron deficiency as measured by their serum ferritin or transferrin saturation levels. Twelve patients from each of these two subgroups were randomized to treatment with weekly infusions of iron sucrose (Venofer), and the remaining 11 were treated with placebo. Patients were treated for 3 months. The study's primary end point was the change from baseline to the end of the study in peak oxygen consumption.

In the anemic patients, iron supplementation was associated with a significant 204 mL/min greater increase in oxygen consumption over baseline, compared with the placebo group. In the nonanemic patients, iron supplementation did not lead to a notable change in oxygen consumption, compared with the placebo group, Dr. Anker reported.

By other measures, iron supplementation was also linked to improvements in exercise duration and heart failure class. The treatment was also safe, with no difference in adverse event rates between the intervention and control groups. ■