BNP Predicts In-Hospital Mortality in Heart Failure

BY BRUCE JANCIN
Denver Bureau

DALLAS — An elevated B-type natriuretic peptide level upon admission for acute decompensated heart failure is an independent predictor of in-hospital mortality, Dr. Gregg C. Fonarow reported at the annual scientific sessions of the American Heart Association.

Also, B-type natriuretic peptide (BNP) is an equally robust predictor of in-hospital mortality regardless of whether the patient has preserved or reduced left ventricular systolic function, added Dr. Fonarow, professor of cardiovascular medicine at the University of California, Los Angeles, and director of the Ahmanson-UCLA Cardiomyopathy Center.

"These data suggest that the BNP assay should be part of the standard admission assessment of the acute decompensated heart failure patient," he said.

Dr. Fonarow analyzed the relationship between admission BNP level and in-hospital mortality in 48,629 hospitalizations for acute decompensated heart failure during 2003-2004 at more than 275 U.S. hospitals participating in the Acute Decompensated Heart Failure National Registry (ADHERE).

He found a near-linear relationship between BNP quartile and in-hospital mortality (see chart at right.) The relationship was similar in the 52% of patients with a left ventricular ejection fraction of less than 40% and in those with preserved systolic function.

The median hospital length of stay rose from 4.0 days in patients in the lowest quartile of BNP to 4.9 days in those in the top quartile, a difference that was highly significant because of the huge number of patients involved in the study. ICU admission was required for 12.8% of patients in BNP quartile 1, compared with 19.6% in quartile 4.

The BNP assay should be part of the standard admission assessment of the heart patient.

DR. FONAROW

In an earlier study from ADHERE, Dr. Fonarow and his coworkers developed and validated a practical bedside tool for mortality risk stratification in patients with acute decompensated heart failure (JAMA 2005;293:572-80).

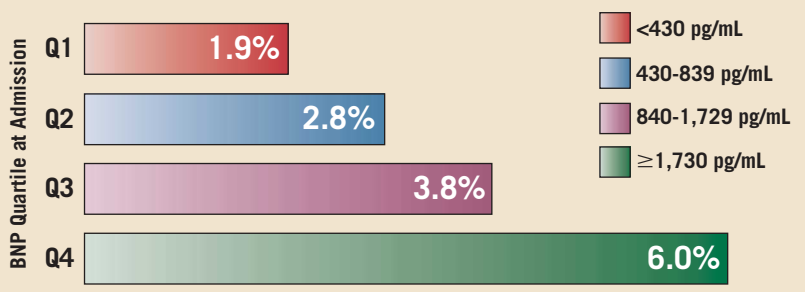
The strongest in-hospital mortality predictors in this risk stratification method were admission blood urea nitrogen level, systolic blood pressure, and serum creatinine. Other significant predictors included in the bedside assessment tool were age, gender, serum sodium, pulse, and the presence of dyspnea at rest.

After adjustment for all of these other predictive factors, admission BNP quartile remained a highly significant independent predictor of in-hospital mortality. In fact, patients in the highest BNP quartile were 2.2-fold more likely to die during that hospitalization than were those in the lowest quartile, even after adjusting for the other eight predictors.

BNP has previously been shown to facilitate diagnosis of heart failure and to predict long-term mortality risk in patients with chronic heart failure. However, the lab assay's prognostic utility in acute decompensated heart failure hadn't previously been studied.

The next step will be to see whether acutely decompensated patients with higher admission BNP levels benefit from a more aggressive monitoring and treatment strategy. If this hypothesis is shown to be sound, then it's possible that treatment regimens will be stratified based on a patient's admission BNP, according to Dr. Fonarow. The ADHERE Registry is funded by Scios Inc. ■

In-Hospital Mortality Increases With Admission BNP Level In Acute Decompensated Heart Failure Patients



Note: Based on 48,629 hospitalizations for acute decompensated heart failure during 2003-2004 at more than 275 U.S. hospitals.
Source: Dr. Fonarow

Two Extra Deaths in Nesiritide Study Deemed Accidental

BY MITCHEL L. ZOLER
Philadelphia Bureau

Safety concerns rose again for the heart failure drug nesiritide when the manufacturer, Scios, announced in early January that two additional patients had died in the nesiritide arm of a placebo-controlled trial with 237 patients.

The previously missed deaths, which were deemed to be accidental and unrelated to nesiritide treatment, were found by Scios researchers who were working on a request from the Food and Drug Administration for an "expanded analysis" of the trial's results using an extended, 180-day follow-up of patients in the study.

Questions about the drug's safety first surfaced last March, when the published results of a metaanalysis suggested that patients with acute decompensated heart failure who were treated with nesiritide had an increased rate of worsening renal function. A second metaanalysis published last April further suggested increased mortality associated with nesiritide treatment.

And last June, an expert panel of cardiologists assembled by Scios and led by Dr. Eugene Braunwald, Distinguished Hersey Professor of Medicine at Harvard Medical School, Boston, urged the company to run a new study to better define the safety and efficacy of nesiritide (Natrecor), compared with standard therapy. The panel also recommended that nesiritide use be limited to only its labeled indications and that Scios start an educational program to inform physicians about nesiritide's proper use.

The two previously missed deaths in nesiritide-treated patients were found in a study sponsored by Scios that was designed to assess the impact of nesiritide treatment on patients with acute decompensated heart failure who were treated in a hospital emergency department or observation unit. Efficacy measures included the need for hospital admission, the length of hospitalization, and the rate of rehospitalization during 30 days of follow-up.

The study, done at 38 hospitals in the United States, was led by Dr. W. Franklin Peacock IV, an emergency medicine physician at the Cleveland Clinic. When the results were published last October, the report said that 5 patients of the 120 who had received nesiritide had died within 30 days of treatment, compared with 1 patient out of 117 in the placebo group, a difference that was not statistically significant (J. Emerg. Med. 2005;29:243-52).

Both Dr. Peacock and Scios downplayed the significance of the two additional deaths, which also occurred during the first 30 days after treatment. Both deaths were accidental and not linked to nesiritide treatment. One patient died from carbon monoxide poisoning, and the second was in a traffic accident, said a Cleveland Clinic spokeswoman on behalf of Dr. Peacock. The two extra deaths would not have changed the study's conclusions about nesiritide's safety, the spokeswoman added. ■

Carvedilol Shortage Temporary, Emergency Shipments Available

A temporary shortfall in the supply of carvedilol may cause some patients to have difficulty filling their prescriptions, the drug's maker, GlaxoSmithKline, announced in a "Dear Healthcare Professional" letter.

The company is working diligently to resolve the situation, the letter states.

Coreg (carvedilol) is indicated for mild and moderate heart failure and for essential hypertension, as well as for severe heart failure and post–myocardial infarction left ventricular dysfunction. It is the only β-blocking drug approved by the U.S. Food and Drug Administration for treatment of the latter two indications.

Because of the life-threatening nature of these two indications, GlaxoSmithKline (GSK) is working to provide emergency overnight shipments to local pharmacies of such patients who cannot get prescriptions filled.

To conserve available drug for those with the greatest need, the company asked that new patients with mild or moderate heart failure or essential hypertension not be started on Coreg and that a switch to Toprol-XL (metoprolol) be considered for those with mild to moderate heart failure who are already being treated with carvedilol; metoprolol is the only other β-blocker approved for use in this population.

Patients who are switched or who stop carvedilol treatment should be monitored carefully, the letter states.

Newly introduced documentation procedures are the cause of the delays in the release of the drug, according to GSK. The procedures were implemented as part of a consent decree with the FDA that was signed last year by GSK after the company was cited for manufacturing deficiencies associated with Paxil CR (paroxetine) and Avandamet (rosiglitazone and metformin), which are produced at the same Cidra, Puerto Rico, manufacturing facility that makes Coreg.

The consent decree requires third-party review documentation prior to any product release from the facility, and this process has delayed release of the drug and caused the "spot shortages," according to a company spokesperson, who predicted the problem will be resolved in a matter of weeks rather than months.

The delays are also affecting Paxil CR and Avandamet supplies, but a "Dear Healthcare Professional" letter was not issued in regard to these drugs, because unlike severe heart failure patients and patients with post–myocardial infarction left ventricular dysfunction, patients on these drugs have alternative treatment options and are not generally considered to have life-threatening illness, she explained.

For information regarding the Coreg supply or to work with GSK to get emergency shipments of Coreg to local pharmacies for patients in need of the drug, call 888-825-5249.

—Sharon Worcester