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Admission B-Type Natriuretic Peptide Levels and In-Hospital Mortality in Acute Decompensated Heart Failure

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Objectives This study was designed to determine whether admission B-type natriuretic peptide (BNP) levels are predictive of in-hospital mortality in acute decompensated heart failure (HF).

Background Levels of BNP have been demonstrated to facilitate the diagnosis of HF and predict mortality in chronic systolic HF.

Methods B-type natriuretic peptide levels within 24 h of presentation were obtained in 48,629 (63%) of 77,467 hospitalization episodes entered in ADHERE (Acute Decompensated Heart Failure National Registry). In-hospital mortality was assessed by BNP quartiles in the entire cohort and in patients with reduced (n = 19,544) as well as preserved (n = 18,164) left ventricular systolic function using chi-square and logistic regression models.

Results Quartiles (Q) of BNP were Q1 (<430), Q2 (430 to 839), Q3 (840 to 1,729), and Q4 (≥1,730 pg/ml). The BNP levels were <100 pg/ml in 3.3% of the total cohort. Patients in Q1 versus Q4 were younger, more likely to be women, and had lower creatinine and higher left ventricular ejection fraction. There was a near-linear relationship between BNP quartiles and in-hospital mortality: Q1 (1.9%), Q2 (2.8%), Q3 (3.8%), and Q4 (6.0%), $p < 0.0001$. B-type natriuretic peptide quartile remained highly predictive of mortality even after adjustment for age, gender, systolic blood pressure, blood urea nitrogen, creatinine, sodium, pulse, and dyspnea at rest, Q4 versus Q1 (adjusted odds ratio 2.23 [95% confidence interval 1.91 to 2.62, $p < 0.0001$]). The BNP quartiles independently predicted mortality in patients with reduced and preserved systolic function.

Conclusions An elevated admission BNP level is a significant predictor of in-hospital mortality in acute decompensated HF with either reduced or preserved systolic function, independent of other clinical and laboratory variables. (Registry for Acute Decompensated Heart Failure Patients; http://www.clinicaltrials.gov/show/NCT00366639; NCT00366639). (J Am Coll Cardiol 2007;49:1943–50) © 2007 by the American College of Cardiology Foundation

The natriuretic peptides are counter-regulatory hormones involved in volume homeostasis and cardiovascular remodeling. B-type natriuretic peptide (BNP) is a 32-amino-acid neurohormone synthesized in ventricular myocardium and released into the circulation in response to ventricular dilatation and pressure overload (1,2). B-type natriuretic peptide is derived from an intracellular 108-amino-acid precursor that is cleaved predominately into 2 fragments, yielding a 76-amino-acid N-terminal fragment (NT-proBNP) and BNP (1). Levels of BNP and NT-proBNP have been shown to be elevated in patients with left ventricular (LV) dysfunction and correlate with the New York Heart Association functional class (3). Clinical investigations of natriuretic peptides have focused on the diagnostic usefulness for heart failure (HF) and LV dysfunction and their prognostic usefulness in chronic HF, acute coronary syndromes, stable coronary artery disease, other medical conditions, and community cohorts (3–11).

Whether plasma levels of BNP are predictive of in-hospital mortality risk in patients hospitalized with acute decompensated HF has not been well studied. The prior studies that have examined the relationship between presentation levels of BNP or NT-proBNP and short-term mortality risk have been relatively small and not adequately powered to assess in-hospital mortality independent of other variables (12–18). The primary aim of this study was to assess

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Abbreviations and Acronyms

BMI = body mass index
BNP = B-type natriuretic peptide
BUN = blood urea nitrogen
HF = heart failure
LV = left ventricular
LVEF = left ventricular ejection fraction
NT-proBNP = N-terminal pro-B-type natriuretic peptide
Q = quartile

the relationship of BNP to in-hospital mortality by using data from ADHERE (Acute Decompensated Heart Failure National Registry). This registry collects detailed hospitalization data from the initial presentation at the hospital or emergency department until discharge, transfer, or in-hospital death (19,20). Coming from a large observational database, these data reflect recent clinical characteristics and in-hospital outcomes for a broad cohort of patients hospitalized with acute decompensated HF (19–22).

Methods

Data used to determine risk associated with BNP levels were taken from ADHERE. This registry collects detailed hospitalization data from initial presentation in the hospital or emergency department until discharge, transfer, or in-hospital death (19,20). The ADHERE registry contains data on patients hospitalized with acute decompensated HF in community, tertiary, and academic centers from all regions of the country (20). For the purpose of the registry, acute decompensated HF is defined as new-onset decompensated HF or decompensation of chronic, established HF with symptoms sufficient to warrant hospitalization. The design, methods, and patient characteristics in ADHERE have been described previously (19). Briefly, medical records are reviewed at participating study sites, and data from consecutive eligible male and female patients ≥18 years of age at the time of hospitalization are entered in the registry using an electronic case report form incorporating real-time validity checking (19,20). These data include demographic information, medical history, baseline clinical characteristics, initial evaluation, treatment received, procedures performed, hospital course, and patient disposition. Standardized definitions are used for all patient-related variables, clinical diagnoses, and hospital outcomes. Importantly, registry participation does not require any alteration of treatment or hospital care, and entry of data into the registry is not contingent on the use of any particular therapeutic agent or treatment. Institutional review board approval is required for all participating centers; however, informed consent of individuals was not required for registry entry. To preserve patient confidentiality, direct patient identifiers are not collected, and data are reported only in aggregate format. Therefore, registry entries reflect individual hospitalization episodes, not individual patients, and multiple hospitalizations of the same patient may be entered into the registry as separate records.

In the beginning of 2003, ADHERE hospitals began employing the expanded range BNP testing (range 0 to 5,000 pg/ml). This current study analyzed ADHERE data from April 2003 through December 2004 (February 2005 data transfer). During this time frame 191 of 229 ADHERE hospitals reported having the capability of assessing BNP levels (176 BNP only, 15 BNP and NT-proBNP, 14 NT-proBNP only, and 24 none). B-type natriuretic peptide levels on presentation (first level obtained within 24 h of presentation) were analyzed by the local hospital laboratory and recorded in the medical record. During the analysis time frame, 48,629 (63%) of 77,467 patients episodes had BNP assessment. For the primary analyses, patients were grouped by BNP quartiles. Data were analyzed for the overall cohort as well as for those patients with reduced (left ventricular ejection fraction [LVEF] <40%) and preserved (LVEF ≥40%) systolic function. Analysis of patients with LVEF ≥50% was also performed. Data were also assessed for each weight category by body mass index (BMI) (kg/m^2): underweight (BMI <18.5), healthy weight (BMI 18.5 to 24.9), overweight (BMI 25.0 to 29.9), and obese (BMI ≥30).

Statistical analyses. Data from ADHERE were used for analyses of clinical characteristics, treatments, and outcomes for patient episodes of HF grouped by quartiles of BNP. Analysis by BNP quartiles, continuous, and log-transformed BNP was performed. As log transformation produced similar findings, data are presented without log transformation for clarity. A relationship between mortality and BNP was examined using locally weighted smoother regression scatterplots (loess). Procedure PLSMO from Hmisc S-PLUS library (F.E. Harrell, Department of Biostatistics, Vanderbilt University, Nashville, Tennessee) was used to create the plot. The hypothesis of no differences in patients' characteristics and outcomes among 4 BNP quartiles was tested using chi-square, analysis of variance, and Kruskal-Wallis tests as appropriate. The Kruskal-Wallis test was used to analyze outcome variables with skewed distribution. Two-sided p values were reported. Because of anticipated differences among the 4 BNP quartile groups in medical history and clinical characteristics at presentation, it was important to adjust the mortality comparison for relevant prognostic factors. Of 80 demographic, medical history, and initial evaluation variables collected in ADHERE, classification and regression tree analysis and/or logistic regression models previously identified 8 variables as the most important risk factors for in-hospital mortality (20,21,23). Mortality rates in the BNP quartiles were compared using logistic regression adjusted for these 8 variables: age, blood urea nitrogen (BUN), systolic blood pressure (SBP), diastolic blood pressure, creatinine, sodium, heart rate, and dyspnea at rest, as well as gender. A total of 1.2% of records were excluded for 1 or more missing values. Multivariable analysis using 48 of 51 variables previously described (21) resulted in little incremental improvement in prognostic value. To adjust for multiple comparisons (e.g., 3), only p values <0.017 were considered statistically significant

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