Impact of Increased Body Mass Index on Accuracy of B-Type Natriuretic Peptide (BNP) and N-Terminal proBNP for Diagnosis of Decompensated Heart Failure and Prediction of All-Cause Mortality

Robert H. Christenson,1* Hassan M.E. Azzazy,2 Show-Hong Duh,1 Susan Maynard,3 Stephen L. Seliger,4 and Christopher R. deFilippi5

BACKGROUND: BNP and N-terminal proBNP (NT-proBNP) concentrations may be depressed in patients with increased body mass index (BMI). Whether increased BMI affects accuracy of these biomarkers for diagnosing decompensated heart failure (HF) and predicting outcomes is unknown.

METHODS: We measured BNP and NT-proBNP in 685 patients with possible decompensated HF in a free-living community population subdivided by BMI as obese, overweight, and normal weight. HF diagnosis was adjudicated by a cardiologist blinded to BNP and NT-proBNP results. We tabulated all-cause mortality over a median follow-up of 401 days and assessed marker accuracy for HF diagnosis and mortality by ROC analysis.

RESULTS: Of the 685 patients, 40.9% were obese (n = 280), 28.2% were overweight (n = 193), and 30.9% had normal BMI (n = 212). Obese patients had lower BNP and NT-proBNP compared with overweight or normal-weight individuals (P < 0.001) and decreased mortality compared with normal-weight individuals (P < 0.001). Both biomarkers added significantly to a multivariate logistic regression model for diagnosis of decompensated HF across BMI categories. NT-proBNP outperformed BNP for predicting all-cause mortality in normal-weight individuals (χ² for BNP = 6.4, P = 0.09; χ² for NT-proBNP = 16.5, P < 0.001). Multivariate regression showed that both biomarkers remained significant predictors of decompensated HF diagnosis in each BMI subgroup.

CONCLUSIONS: In this study population, obese patients had significantly lower BNP and NT-proBNP that reflected lower mortality. BNP and NT-proBNP can be used in all BMI groups for decompensated HF diagnosis, although BMI-specific cutpoints may be necessary to optimize sensitivity.

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The WHO defines obesity according to body mass index (BMI),6 with BMI < 25 being normal, BMI between 25 and 30 overweight, and BMI > 30 obese. Although calculation of BMI is imperfect because it does not address fat mass, lean body mass, or fluid volume (1), obese people classified by the BMI calculation are at greater risk of developing heart failure (HF) than normal-weight individuals (2,3). BNP and N-terminal proBNP (NT-proBNP) are established biomarkers helpful for HF diagnosis and estimating prognosis (4–6). In obese patients, however, there may be variation in the diagnostic and prognostic performance of BNP and NT-proBNP due to differences in clearance mechanisms and other factors.

BNP is secreted by the heart and circulates as a hormone to induce diuresis, natriuresis, and vasodilation (2). Although the metabolism of the natriuretic peptides is not fully elucidated, according to conventional models BNP is produced in response to pressure overload as preproBNP, which is subsequently cleaved into the 108–amino acid protein proBNP108. According to the conventional model, proBNP108 is then enzymatically cleaved with release of the biologically active BNP (32 amino acids) and inactive amino-terminal metabolite termed NT-proBNP (76 amino acids). Clearance of BNP is through both renal excretion and its interaction with natriuretic peptide recep-

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6 Nonstandard abbreviations: BMI, body mass index; HF, heart failure; NT-proBNP, amino-terminal proBNP; NPR, natriuretic peptide receptor; AMR, analytical measurement range; LVEF, left ventricular ejection fraction; AUC, area under the curve; DEXA, dual-energy x-ray absorptiometry; MRI, magnetic resonance imaging.
tor (NPRs) type C, whereas clearance of NT-proBNP is mainly through renal mechanisms. BNP and NT-proBNP are released in response to pressure overload in the ventricles; however, many other factors also affect BNP blood concentrations, including sex, age, renal function, and comorbid diseases, as well as obesity (7).

In this study, we evaluated the accuracy of NT-proBNP and BNP across a range of BMIs for diagnosis of decompensated HF in a community-based dyspneic patient population. We also investigated whether the prognostic accuracies of NT-proBNP and BNP concentrations differed based on BMI for predicting 1-year all-cause mortality. This evidence will provide more insight for use of NT-proBNP and BNP in diverse, unselected community-dwelling populations and will be useful for more effective interpretation in obese populations.

Materials and Methods

PATIENT POPULATION

We included 904 consecutive patients with dyspnea presenting to the Carolinas Medical Center from June 2003 to June 2004 in whom a natriuretic peptide concentration was measured at presentation for clinical indication of dyspnea. Weight and height information necessary to calculate BMI (kg/m²) was available for 675 (74.7%) of these patients. The protocol for this study was approved by the Institutional Review Boards of the University of Maryland School of Medicine and the Carolinas Medical Center.

NATRIURETIC PEPTIDE MEASUREMENT

Blood samples were collected in EDTA tubes and sent immediately to the clinical laboratory; all measurements were performed within 4 h of specimen collection. For BNP measurements (Triage, Biosite), whole blood was used. For NT-proBNP measurements (Elecsys 2010, Roche Diagnostics), plasma was used. Total imprecision values for BNP were 10%–15% at 115 ng/L, and for NT-proBNP, 2%–5% at 175 and 4550 ng/L. The analytical measurement range (AMR) for NT-proBNP was 5–35 000 ng/L. We maintained a BNP assay reportable range of 5–1150 ng/L throughout the study, although we extended the manufacturer’s AMR above 1150 ng/L. No sample dilutions were performed—we reported NT-proBNP values exceeding AMR as >35 000 ng/L, and all BNP values >1150 ng/L as >1150 ng/L. Thirty-five (3.9%) of the patients had an NT-proBNP value above the AMR, and 165 (18.3%) had a BNP value above the AMR.

DATA COLLECTION AND HF ADJUDICATION

As reported previously for this cohort of patients (8), all patient charts were reviewed by staff, and demographics, serum creatinine, cardiovascular risk factors, cardiovascular history, cardiovascular test results, medications, and discharge codes [International Classification of Diseases, Ninth Revision (ICD-9); http://www.cdc.gov/nchs/icd/icd9.htm] were abstracted into a case report form. We defined prior coronary artery disease as a history of myocardial infarction or revascularization or an ischemic cardiomyopathy; history of HF as a prior diagnosis, or if uncertain, by the use of loop diuretics in the setting of a known left ventricular ejection fraction (LVEF) ≤40%. A cardiologist blinded to the natriuretic peptide results reviewed case report forms for a final diagnosis. To determine whether interobserver agreement would be comparable to prior studies that used 2 adjudicators, a second cardiologist reviewed 50 randomly selected cases. Agreement between the reviewers was 84%, comparable to the agreement between reviewers in a multicenter study (9). Factors influencing the adjudicated diagnosis of the cardiologist included the clinicians’ diagnosis, presenting symptoms, presenting laboratory results other than natriuretic peptides, hospital course, diagnostic test results during hospitalization, prior history of HF or cardiomyopathy, and absence of alternative explanations for dyspnea. The adjudicator confirmed the diagnosis of decompensated HF when it was a primary discharge diagnosis, when other causes of dyspnea were absent, and when the treatment plan was consistent with decompensated HF. In the absence of a clinical diagnosis of decompensated HF, the adjudicator would contradict the clinician diagnosis only in the presence of documented treatment and test results consistent with decompensated HF.

FOLLOW-UP

We reviewed the Social Security Death Index database through April 2005 for all-cause mortality with a median follow-up of 401 days (interquartile range 330–480 days). Mortality status could be determined in 816 (98%) of all patients and 662 (98%) of those with calculated BMI.

STATISTICAL ANALYSIS

We compared patient characteristics across the 3 BMI categories (normal weight, overweight, obese) with 1-way ANOVA tests for continuous variables and χ² tests for categorical variables. The cohort was categorized into quartiles based on variables and χ² tests for categorical variables. The cohort was categorized into quartiles based on variables and χ² tests for categorical variables. We generated ROC curves and calculated areas under the curve (AUCs) to compare the diagnostic performance of BNP and NT-proBNP for decompensated HF in normal-weight, overweight, and obese patients. We used multiple logistic regression to estimate the
association of each biomarker with the diagnosis of HF, adjusting for other factors within each category of BMI, and Cox proportional hazard models to estimate the association of biomarkers with 1-year all-cause mortality after adjusting for age, sex, race, and serum creatinine. We assessed effect modification by BMI on the association of BNP and NT-proBNP with HF diagnosis and 1-year mortality by testing multiplicative interaction terms.

Results

Baseline characteristics for patients with calculated BMI are shown in Table 1. Higher BMI was associated with younger age, female sex, African-American race, less hypertension, and more diabetes. There was no difference in the prevalence of HF ($P = 0.2$), median NT-proBNP ($P = 0.25$), or median BNP ($P = 0.3$) in patients with ($n = 675$) and without ($n = 229$) data available to calculate BMI. The incidence of the diagnosis of decompensated HF was similar across BMI groups (Table 1). The concentrations of the natriuretic peptides, however, were inversely related to BMI in patients with decompensated HF (Fig. 1). The ROC AUC for the diagnosis of decompensated HF in the overall population for BNP was 0.73 (95% CI 0.69–0.76), and for NT-proBNP, 0.72 (0.68–0.75), $P = 0.12$ comparing AUC between biomarkers. The accuracy of NT-proBNP and BNP concentrations for identifying decompensated HF was similar between the 2 tests within normal-weight, overweight, and obese BMI categories. For patients with BMI $\geq 25$ kg/m$^2$ ($n = 212$), the AUC for BNP was 0.78 (0.71–0.84) vs an AUC for NT-proBNP of 0.77 (0.70–0.84), $P = 0.6$ comparing AUC between biomarkers. For overweight patients ($n = 193$) with BMI between 25 and 30 kg/m$^2$, the AUC for BNP was 0.62 (0.54–0.70) vs an AUC for NT-proBNP of 0.64 (0.56–0.72), $P = 0.5$ comparing AUC between biomarkers. For obese patients ($n = 270$) with BMI $>30$ kg/m$^2$, the AUC for BNP was 0.72 (0.66–0.79) vs an AUC for NT-proBNP of 0.71 (0.65–0.77), $P = 0.4$ comparing AUC between biomarkers.

### Table 1. Baseline characteristics of study population, by BMI category.

<table>
<thead>
<tr>
<th>BMI category</th>
<th>n</th>
<th>Age (mean (SD))</th>
<th>Male sex (%</th>
<th>African-American (%)</th>
<th>Hypertension (%)</th>
<th>Diabetes (%)</th>
<th>Prior HF diagnosis (%)</th>
<th>Coronal artery disease (%)</th>
<th>LVEF, %</th>
<th>Serum creatinine (mg/dL)</th>
<th>BNP, ng/L (median (IQR))</th>
<th>NT-proBNP, ng/L (median (IQR))</th>
<th>Disposition</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight (&lt;25 kg/m$^2$)</td>
<td>212</td>
<td>69.8 (15.5)</td>
<td>111 (52.4)</td>
<td>64 (30.2)</td>
<td>87 (41.0)</td>
<td>62 (29.3)</td>
<td>77 (36.3)</td>
<td>52 (24.5)</td>
<td>63.9 (31.8)</td>
<td>1.1 (0.9–1.6)</td>
<td>512 (108–1150)</td>
<td>3005 (883–9353)</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Overweight (25–30 kg/m$^2$)</td>
<td>193</td>
<td>66.6 (13.8)</td>
<td>111 (57.5)</td>
<td>54 (28.0)</td>
<td>56 (29.0)</td>
<td>62 (32.1)</td>
<td>72 (37.3)</td>
<td>45 (23.3)</td>
<td>62.9 (37.9)</td>
<td>1.2 (0.9–1.8)</td>
<td>365 (91–964)</td>
<td>1767 (427–7005)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese (&gt;30 kg/m$^2$)</td>
<td>280</td>
<td>62.5 (14.6)</td>
<td>102 (37.8)</td>
<td>128 (47.2)</td>
<td>66 (24.4)</td>
<td>121 (44.8)</td>
<td>87 (32.2)</td>
<td>50 (18.5)</td>
<td>94 (34.8)</td>
<td>1.1 (0.9–1.8)</td>
<td>210 (59–576)</td>
<td>1100 (300–4080)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data are n (%), mean (SD), or median (interquartile range), unless noted otherwise.

b The normal-weight group included 24 underweight individuals (BMI $<18.5$ kg/m$^2$).

Information on LVEF was available in 516 (77%) subjects.
We calculated sensitivity and specificity of natriuretic peptides at accepted cutoffs for the specific tests used [BNP = 100 pg/mL; NT-proBNP cutoffs (International Collaborative of NT-proBNP Study (10)) = 450 pg/mL for age <50 years, 900 pg/mL for 50–75 years, and 1800 pg/mL for >75 years] across the various BMI groups. Cutoffs based on estimated glomerular filtration rate were not used in this study. Sensitivity and specificity of BNP were 89% and 38% for normal-weight patients, 85% and 38% for overweight patients, and 81% and 49% for obese patients, respectively. Sensitivity and specificity of NT-proBNP were 88% and 50% for normal-weight patients, 68% and 51% for overweight patients, and 69% and 64% for obese patients, respectively.

We assessed the independent association of each marker with decompensated HF across the BMI groups using multivariate logistic regression models. Both NT-proBNP and BNP added significantly and to a similar extent to a multivariate logistic regression model for predicting a diagnosis of decompensated HF in each category of BMI (Table 2). However, a significant interaction between BMI and natriuretic peptide concentrations was noted. For BNP, the interaction was significant with BMI group when comparing normal-weight to overweight groups (coefficient −0.59, P =

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**Fig. 1.** Natriuretic peptide concentrations in patients with or without decompensated HF: concentrations of BNP in patients with (A) and without (B) decompensated heart failure; concentrations of NT-proBNP in patients with (C) and without (D) decompensated heart failure.

BMI categories are obese (BMI >30 kg/m²), overweight (BMI 25–30 kg/m²), and normal (BMI <25 kg/m²). Each box in the figures represents the interquartile range (25th and 75th percentiles); the line inside each box is the median value. The whiskers represent the range of data up to a limit of 1.5-fold above or below the interquartile range; individual points are displayed for data exceeding the 1.5-fold limit.
Diagnostic and Prognostic Utility of BNP and NT-proBNP in Obesity

Table 2. Association of natriuretic peptides and decompensated HF, by BMI category. 

<table>
<thead>
<tr>
<th></th>
<th>Normal weight (&lt;25 kg/m²)</th>
<th>Overweight (25–30 kg/m²)</th>
<th>Obese (&gt;30 kg/m²)</th>
<th>P, test of biomarker–BMI interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>211</td>
<td>190</td>
<td>268</td>
<td>.01</td>
</tr>
<tr>
<td>BNP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>1.4 (0.5–3.9)</td>
<td>2.2 (0.9–5.3)</td>
<td>2.8 (1.4–5.5)</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>6.0 (2.3–15.7)</td>
<td>4.7 (1.8–12.2)</td>
<td>4.9 (2.3–10.1)</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>12.8 (4.8–33.7)</td>
<td>2.9 (1.1–7.2)</td>
<td>5.6 (2.4–13.3)</td>
<td></td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>43.6, P &lt; 0.001</td>
<td>11.5, P = 0.01</td>
<td>25.3, P &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
<td></td>
<td>.0007</td>
</tr>
<tr>
<td>Q1</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>4.5 (1.3–15.2)</td>
<td>3.2 (1.3–8.2)</td>
<td>2.4 (1.2–4.6)</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>10.4 (3.1–35.7)</td>
<td>7.5 (2.8–19.8)</td>
<td>4.2 (2.1–8.5)</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>28.2 (8.1–98.7)</td>
<td>3.2 (1.3–8.2)</td>
<td>5.1 (2.1–12.4)</td>
<td></td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>43.6, P &lt; 0.001</td>
<td>18.8, P &lt; 0.001</td>
<td>21.7, P &lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

* Data are odds ratios (95% CI) adjusted for age, sex, race, and serum creatinine. \( \chi^2 \) Values are for the biomarker in the model only.

0.004) but not when comparing normal-weight to obese (coefficient −0.30, P = 0.13), indicating that the diagnostic accuracy of BNP differed between the normal-weight and overweight groups. Similar findings were noted for NT-proBNP when comparing normal-weight to overweight groups (coefficient −0.65, P = 0.002) and comparing normal-weight to obese (coefficient −0.38, P = 0.06). NT-proBNP and BNP were the most powerful predictors of decompensated HF in normal-weight patients (Table 2).

All-cause mortality was inversely related to BMI; the respective number of death events (1-year mortality rate) were 91 (43%) for normal-weight patients, 52 (27%) for overweight patients, and 56 (20%) for obese patients (Table 1). However, no significant inverse trend was observed for natriuretic peptide concentrations across progressive BMI groups in patients who died (Fig. 2). In normal-weight individuals, NT-proBNP outperformed BNP (\( \chi^2 \) for BNP = 6.4, P = 0.09; \( \chi^2 \) for NT-proBNP = 16.5, P < 0.001) for predicting all-cause mortality. In overweight patients, NT-proBNP slightly outperformed BNP (\( \chi^2 \) for BNP = 7.6, P = 0.05; \( \chi^2 \) for NT-proBNP = 9.7, P = 0.02). The 2 peptides performed similarly in predicting all-cause mortality in obese patients. No significant interaction was found between BMI and natriuretic peptides across different BMI groups (Table 3).

Discussion

In this prospective study of an observational cohort of patients, we evaluated the diagnostic accuracy of NT-proBNP and BNP for the diagnosis of decompensated HF and prognosis of 1-year all-cause mortality in an unselected patient population with a spectrum of BMI presenting with dyspnea and undergoing evaluation for decompensated HF. We demonstrated that obese patients have lower NT-proBNP and BNP concentrations than normal-weight patients. NT-proBNP and BNP had similar accuracy for diagnosing decompensated HF within each BMI category and remained independent predictors of all-cause mortality across a broad range of body mass categories. It is unclear why there were weaker associations of natriuretic peptides with HF among the overweight patients but not in the obese group. The only variable markedly different in the overweight group that could influence the diagnosis of HF compared to those with lower or higher BMIs was the lower LVEF. The presence of a low LVEF could lead clinicians to diagnose HF even in the absence of other more compelling findings. This larger proportion of patients diagnosed with HF with only moderately increased natriuretic peptide concentrations could reflect chronic depressed LVEF dysfunction and not acute decompensated HF. This may also explain the lower accuracy of the natriuretic peptides for HF diagnosis in this BMI group. Interestingly, in contrast to diagnosis, the prognostic accuracy of the natriuretic peptides remained comparable with the other BMI groups, as mortality was not influenced by a clinician assessment.

The ROC AUC values for diagnosis of decompensated HF in this overall population are lower than previously reported (4, 5); however, this is not surprising given the more narrow spectrum of patients included.
in the earlier studies and that clinical trials provide optimistic performance estimates (11). Although AUC values for BNP and NT-proBNP were not different within each BMI group, use of previously established NT-proBNP (10) and BNP (4) cutpoints yielded diagnostic sensitivity values in the range of 68% and 83%, respectively, for the obese and overweight groups. These results suggest that different decision points may be appropriate for higher BMI values to optimize the rule-out performance of these tests.

To our knowledge, 14 studies have investigated the effect of obesity on BNP and NT-proBNP concentrations. Six studies investigated the relationship between BNP and BMI (12–17), 2 studies correlated obesity with NT-proBNP (18–20), and 6 others included both BNP and NT-proBNP (7, 18, 21–24). Of the 12 studies that assessed BNP concentrations, 11 found reduced concentrations in obese and overweight patients; a single study showed that BNP concentrations were unaffected by BMI (21). Of the 8 studies that studied NT-proBNP, 7 found an inverse relationship between plasma concentrations and BMI, with only 1 study (21) finding increased NT-proBNP in obese patients compared with controls. Our work adds to existing knowledge by providing evidence in a large, unselected cohort of decompensated HF patients having both BNP and NT-proBNP measurements and adjudicated diagnostic and prognostic endpoints.

Fig. 2. Natriuretic peptide concentrations in patients who died or survived: concentrations of BNP in patients who died (A) and who survived (B); concentrations of NT-proBNP in patients who died (C) and who survived (D). BMI categories are obese (BMI >30 kg/m²), overweight (BMI 25–30 kg/m²), and normal (BMI <25 kg/m²). Each box in the figures represents the interquartile range (25th and 75th percentiles); the line inside each box is the median value. The whiskers represent the range of data up to a limit of 1.5-fold above or below the interquartile range; individual points are displayed for data exceeding the 1.5-fold limit.
A recent review notes that several factors may play a role in regulating the production and clearance of BNP and NT-proBNP, including the ratio between female and male steroid hormone concentrations in obese patients (25). Reported results suggest that circulating free testosterone may mediate sex differences in the natriuretic peptides. In agreement with this notion, a separate group also found that BMI and natriuretic peptide concentrations may be mediated by testosterone (26). Another popular hypothesis indicates that adipose tissues have increased expression of natriuretic peptide clearance receptor NPR-C, leading to increased BNP clearance in obesity (14–17, 20, 22, 23). A problem with this hypothesis, however, is that NT-proBNP concentrations are also reduced in obesity, although this inactive cometabolite is not cleared by the NPR-C mechanism (12, 18, 20, 22, 23). Further, van Kimmenade et al. (24) showed in an interventional study of 22 patients who had undergone surgical treatment for obesity that a decrease in BMI is accompanied by increased concentrations of both BNP and NT-proBNP. These data suggest a relationship between adipose tissue and the production of both peptides. Another explanation for the inverse relationship between natriuretic peptide concentrations and BMI may be because lean mass [derived from dual-energy x-ray absorptiometry (DEXA) assessment] has a stronger influence on synthesis/release of natriuretic peptides from cardiomyocytes than fat mass (22, 23).

Several limitations of our study need to be addressed. Compared to calculated BMI used here, more accurate methods for assessment of body fat include abdominal scan by magnetic resonance imaging (MRI), logarithmic mean-based time-averaged concentrations of creatinine, or DEXA-derived measurement of body composition or assessment of free water by means of isotopes (1). This lack should not impact results substantially, however, because obese patients classified by the BMI calculation are at greater risk of developing HF than normal-weight individuals (2, 3). Another potential issue is that we were unable to adjust for the effects of admission medications on natriuretic peptide concentrations. Medications commonly used for the management of chronic heart failure such as ACE inhibitors and β-blockers can decrease natriuretic peptide concentrations (27, 28), perhaps because patients receiving appropriate doses of these medications are at less risk. It is unknown in this population if there was a different distribution of these medications based on BMI. It is unlikely that these medications had a large impact, however, since there was no difference in the prevalence of prior heart failure diagnosis across all 3 BMI groups. Also, as indicated in “Materials and Methods” and “Results,” roughly 4% of results for NT-proBNP results and 18% of the BNP results were above the upper measurable range for these assays. These above-range results precluded comparison of BNP and NT-proBNP as continuous variables, as the comparison would not be valid due to the truncated distribution of BNP. Finally, the adjudication of heart failure independent of natriuretic peptide results can be a challenge in an era where their use is ubiquitous. Despite adjudica-

### Table 3. Association of natriuretic peptides and all-cause mortality, by BMI category.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Normal weight (&lt;25 kg/m²)</th>
<th>Overweight (25–30 kg/m²)</th>
<th>Obese (&gt;30 kg/m²)</th>
<th>(P), test of biomarker-BMI interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP</td>
<td></td>
<td></td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Q1</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>2.4 (1.0–5.9)</td>
<td>1.9 (0.7–5.5)</td>
<td>2.1 (0.8–5.6)</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>1.9 (0.8–4.6)</td>
<td>2.3 (0.8–6.6)</td>
<td>3.3 (1.3–8.3)</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>2.5 (1.1–5.8)</td>
<td>3.7 (1.3–10.4)</td>
<td>4.1 (1.5–10.8)</td>
<td></td>
</tr>
<tr>
<td>(χ^2)</td>
<td>6.4, (P = 0.09)</td>
<td>7.6, (P = 0.05)</td>
<td>11.0, (P = 0.01)</td>
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<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Q1</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>3.0 (0.9–10.7)</td>
<td>1.5 (0.5–4.1)</td>
<td>4.1 (1.3–12.6)</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>4.7 (1.4–16.1)</td>
<td>3.1 (1.2–8.1)</td>
<td>5.2 (1.7–15.3)</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>6.5 (2.0–21.4)</td>
<td>3.4 (1.3–9.1)</td>
<td>8.7 (2.8–26.9)</td>
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<tr>
<td>(χ^2)</td>
<td>16.5, (P &lt; 0.001)</td>
<td>9.7, (P = 0.02)</td>
<td>20.05, (P &lt; 0.001)</td>
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</tbody>
</table>

\(^a\) Data are hazard ratios (95% CI) adjusted for age, sex, race, and serum creatinine. \(χ^2\) Values are for the biomarker in the model only.
tion that was blinded to the natriuretic peptide results and requiring findings other than just a primary final discharge diagnosis of HF, it is possible that the clinician’s treatment at least in part could have been based on the BNP or NT-proBNP concentrations, resulting in findings on review that appear consistent with HF even if the diagnosis by the clinician was incorrect. Using such a basis for diagnosis could falsely inflate the overall accuracy of the test; however, our clinician-referred population actually resulted in a lower accuracy by ROC analysis than prior “all-comers” studies (4, 5). Therefore, it unlikely that the accuracies of the natriuretic peptide tests were overly inflated by a self-fulfilling adjudication process.

In agreement with most previous studies, we have demonstrated that obese patients have lower NT-proBNP and BNP concentrations compared with normal-BMI patients. To the best of our knowledge, this is the first report in an unselected community-dwelling population to show that NT-proBNP and BNP have similar accuracy for diagnosing decompensated HF within each category of BMI. NT-proBNP performed better than BNP as an independent predictor of all-cause mortality in normal-weight and overweight individuals. Both peptides, however, were independent predictors of all-cause mortality in obese patients.

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