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Short-Term Serial Sampling of Natriuretic Peptides in Patients Presenting With Chest Pain

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Objectives The purpose of this study was to characterize the diagnostic and prognostic utility of short-term dynamic changes in natriuretic peptides in patients presenting with chest pain.

Background Although single levels of natriuretic peptides in patients admitted for acute coronary syndromes (ACS) have important prognostic value, it is unclear whether serial sampling of natriuretic peptides might have both diagnostic and prognostic value in the setting of chest pain.

Methods We followed 276 patients for 90 days who presented to the emergency department with chest pain. We sampled brain natriuretic peptide (BNP) and amino-terminal (NT)-proBNP up to 5 times within 24 h of presentation and again at discharge. Follow-up data was collected at 30 and 90 days after admission. Adverse events included emergency department visits for chest pain, cardiac readmission, and death. We assessed the prognostic and diagnostic value of baseline natriuretic peptide measurements with receiver-operating characteristic analyses.

Results Natriuretic peptides were diagnostic for congestive heart failure (CHF) and new-onset CHF but less so for ACS. The prognostic utility of serial sampling was evaluated through testing the statistical contribution of each future time point (as well as variability over time) over and above the baseline values in logistic regression models.

Conclusions Baseline elevated BNP and NT-proBNP concentrations were predictive of adverse events at 30 and 90 days. Serial sampling did not improve the prognostic value of BNP or NT-proBNP. (J Am Coll Cardiol 2007;49: 1186–92) © 2007 by the American College of Cardiology Foundation

Twenty percent of patients arriving at the emergency department have symptoms suggestive of acute myocardial infarction (MI) (1). Diagnosis of acute MI is based on the rise and fall of troponin or creatine kinase-MB with at least 1 of the following: ischemic symptoms, electrocardiographic (ECG) changes, or coronary artery intervention (2). Although the tissue specificity of cardiac troponin T (cTnT) and cardiac troponin I have improved our ability to make an accurate diagnosis, there is a continued search for optimal markers for acute coronary syndromes (ACS).

Natriuretic peptides, which have primarily been devoted to the diagnosis of congestive heart failure (CHF) (3), have also been found to be elevated in the setting of ACS (1,3–5). Natriuretic peptides are vasoactive hormones secreted by the heart as part of a systemic response to cardiac stress and ventricular dysfunction. The precursor peptide of brain natriuretic peptide (BNP) is stored in granules of ventricular myocytes. There, it is cleaved into an amino-terminal product (NT-proBNP) and the physiologically active BNP (6). Release of BNP and NT-proBNP are regulated by wall stress and myocyte stretch (6–8). The BNP levels trend upward to a peak between 14 and 40 h after an ischemic event (5–6,9). Elevated BNP and NT-proBNP concentrations at admission in the setting of ACS are associated with poor prognosis, including increased mortality, development of CHF, and recurrent ischemic events (6,10–13).

The present study sought to characterize the diagnostic and prognostic utility of short-term dynamic changes in BNP and NT-proBNP in patients presenting to the emergency department with chest pain. Most previous studies involving the serial use of natriuretic peptides in the setting of ACS examined time points in the time frame of days, weeks, and months (5–8). Because BNP is synthesized on demand in response to an appropriate stimulus (8), we were interested in determining if serial measurements of natriuretic peptides during the first 24 h had diagnostic

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and/or prognostic value in addition to standard cTnT measurements.

Methods

Patient enrollment. From July 2003 through April 2005, 306 patients presenting with chest pain to the emergency department at the Veterans Affairs Medical Center, La Jolla, California, were enrolled. The inclusion criteria were age >18 years, symptoms suggestive of cardiac ischemia, and ability to provide informed consent. The study was approved by the institutional review board. A sample size of 300 was determined to yield a power of 0.8 for an odds ratio of 2.0. Of the 306 subjects who consented, patients with only 1 time point or with no baseline sample were excluded, leaving a total of 276 patients included in the data analysis.

Biomarker sampling. We sampled BNP and NT-proBNP at up to 5 time points within the first 24 h of presentation (baseline, 90 min to 3 h, 3 to 6 h, 6 to 12 h, and 12 to 24 h) and again at discharge. Troponin T (TnT) was sampled at 3 to 6 h after presentation.

Biomarker testing. All samples were collected in plastic EDTA tubes and frozen at −70°C until the time of analysis. The BNP testing was performed using both an Advia Centaur BNP assay (Bayer Healthcare, Tarrytown, New York) and Triage BNP assay (Biosite Diagnostics, San Diego, California). The NT-proBNP and TnT were measured with an Elecsys 2010 analyzer (Roche Diagnostics, Indianapolis, Indiana). Clinicians could order BNP (Biosite assay), cardiac troponin I, myoglobin, and creatine kinase-MB tests for clinical purposes to aid in ACS diagnosis. Cardiac biomarkers (research BNP, NT-proBNP, and cTnT) obtained solely for research purposes were not made available to clinicians.

Follow-up. Final diagnoses were assigned for all patients by the same cardiologist based on patient history, biochemical data, and diagnostic procedures. Acute coronary syndrome was defined as ST-segment elevation MI, non–ST-segment elevation MI, or unstable angina (UA), Unstable angina was a clinical diagnosis based on ischemic chest pain and absence or presence of ECG changes without elevations of cardiac markers. Unstable angina was confirmed by stress testing or coronary angiography. Patients were followed for 90 days, and outcome data were collected after both 30 and 90 days by chart review. A combined end point included repeat emergency department visits for chest pain, cardiac-related readmission, and death.

Statistical analyses. Patients with only 1 sample were removed from the data analysis. Means with standard deviations or percentages were used for description of the sample. Natriuretic peptide levels are presented as medians for various patient groupings and compared with Mann-Whitney *U* tests. Receiver-operating characteristic (ROC) curves were used to evaluate diagnostic and prognostic utility. To assess the prognostic contribution of serial natriuretic peptide measurements, logistic regression models were used. Log-transformed natriuretic peptide values were used throughout. Prognostic utility was evaluated in 2-step models in which the baseline value was entered first, followed by a test of the incremental contribution of either the 90-min value, the standard deviation of all values (to evaluate the variability over time), or the mean of all values. Odds ratios were not adjusted for other demographic or clinical indicators. Pearson correlation of log-transformed values was used to quantify the relationship of baseline levels to subsequent levels. All data analysis was performed using SPSS version 13.0 (SPSS Inc., Chicago, Illinois).

Abbreviations and Acronyms

ACS = acute coronary syndromes
BNP = brain natriuretic peptide
CI = confidence interval
MI = myocardial infarction
NT-proBNP = amino-terminal pro-brain natriuretic peptide
ROC = receiver-operating characteristic

Results

Patient characteristics are shown in Table 1. Table 2 shows the median natriuretic peptide concentrations at presentation for the various patient subgroups. Patients older than 65 years had significantly higher natriuretic peptide concentrations than younger patients. Reduced BNP and NT-proBNP levels were seen in obese patients (body mass index >30 kg/m^2). As would be expected, a history of CHF was associated with higher baseline natriuretic peptide concentrations. This was also true of patients with a prior MI and known coronary artery disease (CAD). These trends were not seen among those with diabetes, hypertension, hyperlipidemia, smoking history, or a family history of premature CAD. Stage 2 or worse chronic kidney disease (estimated glomerular filtration rate <90 ml/min) (14) was associated with elevated natriuretic peptides. Positive TnT levels (>0.2 ng/ml between 3 and 6 h) were not associated with high baseline peptide levels.

The diagnostic utility of these natriuretic peptides was first evaluated through ROC analysis. When using baseline natriuretic peptide levels, the ROCs for the diagnosis of CHF were highly significant. The area under the curve (AUC) (95% confidence interval [CI]) was 0.94 (95% CI 0.91 to 0.98) for BNP (Bayer), 0.93 (95% CI 0.89 to 0.97) for BNP (Biosite), and 0.92 (95% CI 0.87 to 0.96) for NT-proBNP. The ROC analysis also found baseline natriuretic peptides to be useful in detecting new-onset CHF in patients without a prior history of CHF: AUC 0.90 (95% CI 0.83 to 0.97) for BNP (Bayer), 0.85 (95% CI 0.77 to 0.96) for BNP (Biosite), and 0.84 (95% 0.75 to 0.93) for NT-proBNP. When the same ROC analysis was applied to ACS diagnosis, the results were much more equivocal. The AUC was 0.58 (95% CI 0.51 to 0.65) for BNP (Bayer), 0.57 (95% CI 0.50 to 0.65) for BNP (Biosite), and 0.56 (95% CI 0.49 to 0.63) for NT-proBNP. Similar results were obtained for differentiating cardiac chest pain from noncardiac chest

JACC Vol. 49, No. 11, 2007
March 20, 2007:1186–92

Table 1 Patient Characteristics (n = 276)

Demographics (%)	
Age >65 yrs	38.0
Gender (% male)	96.7
Race	
White	79.0
Black	9.8
Hispanic	9.1
Asian	2.2
BMI >30 kg/m^2	43.4
History (%)	
CHF	27.5
CAD	59.3
MI	49.6
PTCA	37.1
CABG	26.4
DM	44.7
HTN	74.6
Family history of CAD	60.5
Hyperlipidemia	66.9
Cigarette smoking	79.7
Lab values*	
eGFR <90 ml/min (%)	75.7
BNP (Bayer) pg/ml	57 (20–142)
BNP (Biosite) pg/ml	62 (18–163)
NT-proBNP pg/ml	249 (6–1,015)
cTnT >0.20 ng/ml (%)	44.9
Number of patients at each time point	
Admission	276
90 min to 3 h	215
3 h to 6 h	189
6 h to 12 h	187
12 h to 24 h	163
Discharge	132

*Natriuretic peptide data are reported as median (25% percentile to 75% percentile).

BMI = body mass index; BNP = brain natriuretic peptide; CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; cTnT = cardiac troponin T; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HTN = hypertension; MI = myocardial infarction; NT-proBNP = amino-terminal pro-brain natriuretic peptide; PTCA = percutaneous transluminal coronary angiography.

pain, yielding 0.66 (95% CI 0.59 to 0.72) for BNP (Bayer), 0.65 (95% CI 0.58 to 0.72) for BNP (Biosite), and 0.64 (95% CI 0.57 to 0.71) for NT-proBNP.

Baseline natriuretic peptide concentrations were consistently associated with 30- and 90-day adverse events (Table 3). This composite outcome includes mortality, presentation to the emergency department with a complaint of chest pain, and cardiac-related readmission. The median natriuretic peptide concentrations were significantly different between those with and those without adverse events at 30 days (122 vs. 50 pg/ml [$p = 0.001$] for Bayer BNP, 141 vs. 57 pg/ml [$p = 0.001$] for Biosite BNP, and 882 vs. 212 pg/ml [$p < 0.001$] for NT-proBNP). This held true at 90 days as well (120 vs. 46 pg/ml [$p < 0.001$] for Bayer BNP, 129 vs. 49 pg/ml [$p < 0.001$] for Biosite BNP, and 819 vs. 190 pg/ml [$p < 0.001$] for NT-proBNP). Table 4 shows that natriuretic peptides were able to predict the separate end points of readmission for cardiac-related reasons and death but not emergency department visits.

Receiver-operating characteristics showed that baseline BNP and NT-proBNP measurements are predictive of 30- and 90-day adverse events (Fig. 1). For baseline natriuretic peptides, the AUC for 30-day adverse events was 0.685 (95% CI 0.587 to 0.783) for Bayer BNP, 0.678 (95% CI 0.587 to 0.782) for Biosite BNP, and 0.707 (95% CI 0.617 to 0.798) for NT-proBNP. The results were similar for 90-day adverse events: 0.663 (95% CI 0.584 to 0.742) for Bayer BNP, 0.678 (95% CI 0.598 to 0.758) for Biosite BNP, and 0.694 (95% CI 0.621 to 0.767) for NT-proBNP. These curves were used to determine cut points for the 2 peptides to evaluate the likelihood of adverse events. Decision limits yielding 70% sensitivity for the Bayer BNP assay are 52 pg/ml (50.4% specificity) for 30-day events and 46 pg/ml (50.0% specificity) for 90-day events. Cut points for 70% sensitivity for the other 2 assays are 59 pg/ml for Biosite BNP (specificity of 51.4% and 53.6% at 30 and 90 days, respectively) and 222 pg/ml for NT-proBNP (specificity of 51.5% and 54.1% at 30 and 90 days, respectively).

To assess the prognostic contribution of subsequent natriuretic peptide measurements in addition to baseline levels, logistic regression models were used (Table 5) with log-transformed concentrations used throughout. The baseline levels of natriuretic peptides were significant predictors of 30- and 90-day events ($p \leq 0.001$ in all cases). The 90-min observations did not add significant additional prognostic utility to the baseline model ($p = 0.329$ to 0.855). To explore whether or not individual variability (nondirectional) was prognostic beyond baseline values the standard deviation of values was used. The variability of natriuretic peptides did not add significant additional prognostic utility to the baseline model ($p = 0.251$ to 0.962). Finally, the average of all time points did not add additional prognostic utility ($p = 0.152$ to 0.908). Cardiac TnT elevation of >0.2 pg/ml at 3 to 6 h was also unable to add to the prognostic utility of baseline natriuretic peptides (data not shown). We also examined lower concentrations of cTnT, and they did not add prognostic value.

Correlations of natriuretic peptide levels at baseline with subsequent time points are presented in Table 6. The baseline levels correlated highly with subsequent samples taken up to 12 h after presentation (all correlations >0.91). This indicates that measurements taken at baseline were very predictive of subsequent concentrations.

Discussion

The roles of BNP and NT-proBNP are well established for heart failure. However, their utility in ACS is still evolving. Although diagnostic, prognostic and treatment strategies for ST-segment elevation MI have become routine, given the universal use of thrombolysis and early-invasive reperfusion, the same is not true of non–ST-segment elevation acute coronary syndrome (NSTEACS). Patients with

Table 2 Concentration of Natriuretic Peptides at Presentation (Medians in pg/ml) for Various Patient Groups

	BNP (Bayer)			BNP (Biosite)			NT-proBNP (Roche)		
Characteristic	Yes	No	p Value	Yes	No	p Value	Yes	No	p Value
Demographics									
Age >65 yrs	114	33	<0.001	150	35	<0.001	733	156	<0.001
Gender (male)	57	61	0.912	62	61	0.994	247	293	0.890
BMI >30 kg/m^2	46	65	0.046	54	66	0.035	215	341	0.043
History									
CHF	156	39	<0.001	195	41	<0.001	1,121	163	<0.001
CAD	69	33	0.005	75	39	0.023	374	184	0.035
MI	78	42	0.001	84	44	0.002	433	174	0.002
PTCA	69	52	0.091	66	61	0.177	342	220	0.246
CABG	73	46	0.027	85	54	0.026	462	213	0.050
DM	72	47	0.188	79	57	0.302	310	212	0.265
HTN	68	37	0.055	65	47	0.086	289	213	0.064
Family history of CAD	67	48	0.258	62	56	0.199	247	222	0.293
Hyperlipidemia	56	63	0.621	59	80	0.528	215	367	0.178
Smoker	59	45	0.835	62	59	0.699	244	283	0.604
Lab values									
eGFR <90 ml/min	65	38	0.020	65	44	0.067	320	174	0.006
CTnT >0.20 ng/ml*	67	61	0.672	71	62	0.800	284	293	0.942

*cTnT as measured between 3 and 6 h after presentation.
Abbreviations as in Table 1.

NSTEACS represent a diverse population, making risk stratification increasingly important. The present study focused on the assessment of neurohormonal activation to aid in diagnosis and prognosis of these groups.

Brain natriuretic peptide has been found to increase in the setting of MI. Peak levels occur 14 to 40 h after the ischemic event (5–6). The degree of natriuretic peptide elevation is related to the size of the ischemic injury (15–16). The amount of compensatory force generated by the remaining functional myocardium must increase for the heart to generate adequate forward flow. This increased force could result in increased natriuretic peptide expression and secretion.

Unlike BNP, the kinetics of NT-proBNP is governed primarily by renal excretion (17). In addition to renal excretion, BNP is actively degraded by circulating endopeptidases as well as cleared by cellular binding receptors (18). This results in a longer half-life for NT-proBNP (70 to 120 min) than BNP (20 min) (17–19). The longer half-life may allow for greater accumulation of NT-proBNP and potentially greater sensitivity in detecting more subtle structural and functional changes. A greater incremental rise in NT-proBNP has been noted in patients with cardiac decompensation (17). However, the greater half-life of NT-proBNP may result in a masking of subtle acute changes in cardiac function. Also, in patients with renal insufficiency, NT-proBNP may accumulate relative to BNP and potentially overshadow clinically significant changes.

In this study, several trends were observed relating to the behavior of natriuretic peptide concentrations in the presence of comorbid conditions. Higher natriuretic peptide concentrations levels were associated with low estimated glomerular filtration rates. Impaired renal function often leads to elevated natriuretic peptide levels because of decreased clearance rates (20). Obese patients were found to have lower natriuretic peptide concentrations levels than nonobese patients. This is in part a result of increased natriuretic peptide receptor-containing adipose cells leading to more rapid degradation of BNP (21,22). A recent study suggests that obese patients also tend to have suppressed natriuretic peptide secretion (23). This finding would explain lower NT-proBNP concentrations in obese patients.

In another study, elevated BNP of >100 pg/ml was found to be 70% sensitive for acute MI in patients with NSTEACS, and an elevated troponin I was 51% sensitive (24). In the present population, we found that baseline

Table 3 Concentration of Natriuretic Peptides (Medians in pg/ml) at Presentation for End Point Groups

	BNP (Bayer)			BNP (Biosite)			NT-proBNP (Roche)		
Prognosis	Yes	No	p Value	Yes	No	p Value	Yes	No	p Value
30-day adverse event	122	50	0.001	141	57	0.001	882	212	<0.001
90-day adverse event	120	46	<0.001	129	49	<0.001	819	190	<0.001

Abbreviations as in Table 1.

JACC Vol. 49, No. 11, 2007
March 20, 2007:1186–92

Table 4 Odds Ratios (95% Confidence Interval) of Log Transformed Baseline Natriuretic Peptide Values for Prognosis of Individual End Points at 90 Days

Assay	Visit to ED (n = 32)	Readmission (n = 22)	Death (n = 9)
BNP (Bayer)	1.6 (0.9–3.0)	2.3 (1.1–4.9)	7.9 (2.1–30)
BNP (Biosite)	1.4 (0.8–2.4)	2.7 (1.3–5.6)	11.7 (3.1–44)
NT-proBNP	1.5 (0.9–2.3)	2.3 (1.3–4.2)	6.8 (2.4–20)

Visits to the emergency department (ED) were for complaints of chest pain. Readmissions were for cardiac-related reasons.
Abbreviations as in Table 1.

natriuretic peptide assessment was not a helpful clinical test when assessing for ACS diagnosis. Diagnostic power was not added to this test through short-term serial sampling. However, the natriuretic peptides clearly showed value in detecting previously undiagnosed CHF in patients presenting with symptoms of ACS.

Natriuretic peptides assessed at baseline contribute to the multimarker approach to risk stratification in patients with NSTEACS (25). Although the prognostic utility of baseline BNP and NT-proBNP has been established, questions regarding the frequency of sampling have been only partially answered. A purpose of the present study was to evaluate the relationship between short-term dynamic changes in natriuretic peptide concentrations and prognosis. We show that baseline assessment of natriuretic peptides is sufficient for diagnosis of CHF, even in patients with no history of symptomatic ventricular dysfunction, and that these peptides can be used to prognosticate poor outcomes. The present results show that serial sampling did not add prognostic power to these biomarkers in the setting of ACS, a result that is similar to findings for CHF diagnosis (26). These results are consistent with an earlier report where NT-proBNP was sampled at baseline and 6 hours in ACS patients, which concluded that the "incremental value of serial measurements is limited" (27). Because we had a limited number of samples after the 12-h time point, our study does not rule out the value of serial sampling beyond 12 h. Our short-term serial sampling results are clearly different than those reported for longer-term follow-up of ACS patients in the outpatient setting. Morrow et al. (13) demonstrated that serial sampling of BNP 4 and 12 months after presenting with symptoms of ACS predicted risk of death or new-onset CHF.

Analysis of the sensitivity and specificity of using natriuretic peptides to predict future events was accomplished by evaluating ROCs. The admission BNP and NT-proBNP were found to be useful for assessing prognosis characterized as adverse events at 30 and 90 days. Whereas there were slight differences in the AUC for the different BNP assays, the 95% CIs overlapped, indicating that they are equally useful. In this population, consisting of patients presenting to the emergency department with symptoms of chest pain, a BNP concentration between 46 and 59 pg/ml was 70% sensitive for predicting adverse events. For NT-proBNP, a concentration of 222 pg/ml was 70% sensitive for predicting adverse events. It is to be expected that a natriuretic peptide levels in the diagnostic range for cardiac pathology would be associated with increased adverse events. However, it was surprising to find that such low decision thresholds for BNP would have such prognostic value.

Correlation analysis showed that the levels at baseline were providing essentially the same information as subse-

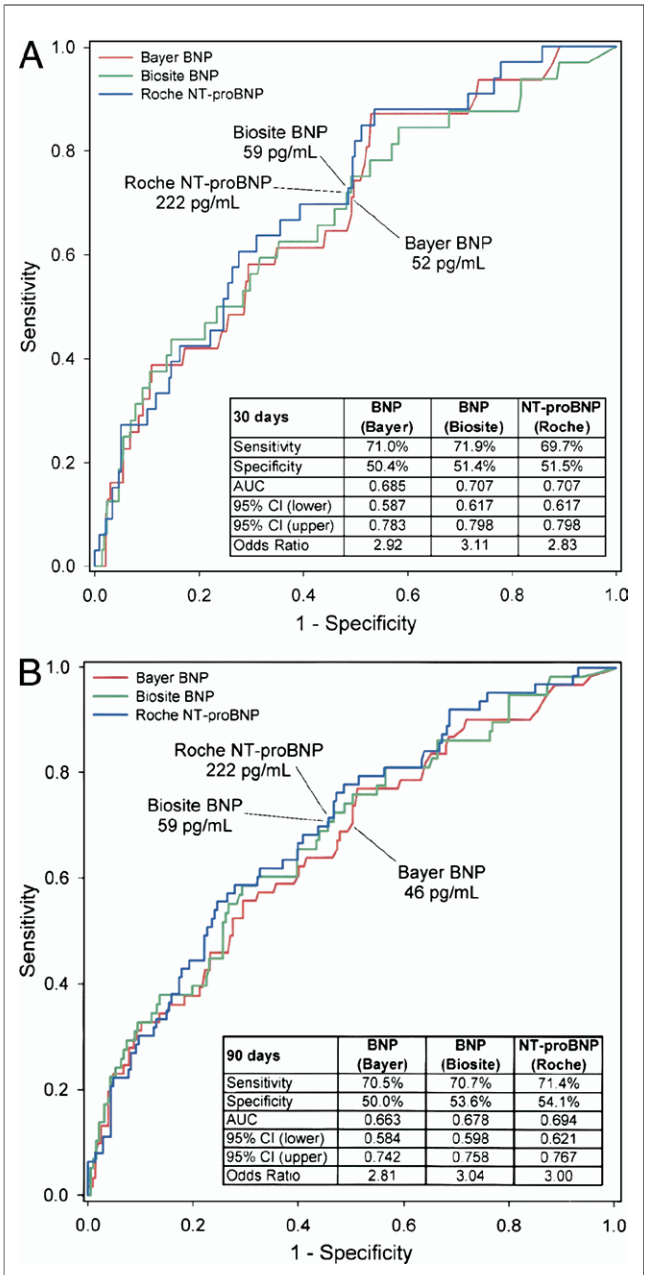

Figure 1 ROC Curves for Predicting Outcome in ACS Patients From Baseline Natriuretic Peptide Levels

Combined outcomes tested at 30 **(A)** and 90 days **(B)**. ACS = acute coronary syndromes; AUC = area under the curve; BNP = brain natriuretic peptide; CI = confidence interval; NT-proBNP = amino-terminal pro-brain natriuretic peptide; ROC = receiver-operating characteristic.

Table 5 Summary of Logistic Regression Tests for Baseline Concentrations and the Incremental Contribution of 90-Min Values, Standard Deviation of All Values, or the Average of All Values

End Point	Assay	Baseline				90 Min		Standard Deviation		Overall Average	
		Chi-Square	p Value	Exp(B)	95% CI	Chi-Square Increment	p Value	Chi-Square Increment	p Value	Chi-Square Increment	p Value
30-day adverse events	BNP (Bayer)	12.20	0.001	3.04	1.60–5.79	0.19	0.664	0.00	0.962	0.29	0.590
	BNP (Biosite)	11.60	0.001	2.69	1.50–4.84	0.95	0.329	1.13	0.287	2.05	0.152
	NT-proBNP (Roche)	15.68	<0.001	2.66	1.61–4.40	0.03	0.855	0.02	0.891	1.11	0.292
90-day adverse events	BNP (Bayer)	16.84	<0.001	2.74	1.66–4.52	0.26	0.612	0.93	0.334	0.13	0.719
	BNP (Biosite)	19.97	<0.001	2.88	1.77–4.69	0.23	0.631	1.32	0.251	0.27	0.602
	NT-proBNP (Roche)	23.13	<0.001	2.57	1.72–3.85	0.742	0.389	0.01	0.908	0.01	0.908

Abbreviations as in Table 1.

Table 6 Correlations of Baseline Natriuretic Peptide Levels With Subsequent Time Points

Time Point	BNP (Bayer)	BNP (Biosite)	NT-proBNP (Roche)
90 min to 3 h	0.971*	0.978*	0.986*
3 to 6 h	0.963*	0.968*	0.968*
6 to 12 h	0.913*	0.930*	0.935*
12 to 24 h	0.848*	0.881*	0.896*
Discharge	0.660*	0.695*	0.741*

*$p < 0.01$.
Abbreviations as in Table 1.

quent time points. With correlation coefficients between baseline and 90-min data as high as 0.986, there is no opportunity for the second observation to add prognostic utility. The analytic precision of these assays in our laboratory is in the range of 2% to 12% (data not shown). The obtained correlation coefficients are so high as to suggest that the observed changes in levels could be explained by normal laboratory variation. The correlation between baseline and discharge values was the lowest observed. However, logistic regression for these discharge time points failed to add to the prediction of outcome, and therefore serial monitoring within 24 h was not useful.

Study limitations. Collecting a full set of serial data was difficult. Our protocol called for sampling of 6 time points over the course of hospitalization. Five samples were required within the first 24 h after admission. Because of this difficulty, a substantial number of patients were without complete data sets. All patients without baseline data or with only one data point were excluded from statistical analysis. Only 62 patients had complete sets of data with 6 blood samples. When presenting with chest pain and an acute coronary syndrome is suspected, patients are immediately risk stratified in the emergency room. If a patient's clinical history and electrocardiograms are not worrisome, and biomarkers sampled twice in the first 90 min are negative, cardiac ischemia is generally ruled out. This resulted in 36 patients with only 2 data points (admission and 90 min). Because the number of samples varied across patients, we elected not to use peak or nadir natriuretic peptide measures as predictors, because these indicators can be confounded with the number of samples obtained.

Clinicians were allowed to order BNP for clinical uses. This was done mostly on presentation but occasionally afterward as well. This could lead to a bias in diagnosis favoring CHF (and away from ACS) in those with elevated BNP. Although this is a valid criticism of the present study, it is not ethical to restrict measurement of BNP in patients presenting with symptoms of ACS. Patients who had elevated concentrations of BNP would result in more intensive therapy, presumably manifesting as improved outcomes.

A final limitation of the study was that it was performed in a Veterans Affairs Medical Center and therefore did not

include a significant amount of women and may not be representative of other patient populations.

Conclusions

The natriuretic peptides BNP and NT-proBNP provide a measurement of ventricular dysfunction. Concentrations of these peptides rise in the setting of ischemia. Acute elevations detected on presentation with symptoms of ACS are diagnostic for the development of CHF, even in patients without a prior history of CHF. In this relatively small single-site study, the prognostic value of natriuretic peptides was in the assessment of baseline concentrations, and not in short-term monitoring for changing levels.

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