The Use of Brain Natriuretic Peptide as a Decision-supporting Tool in Hospitalized Patients

Regev Landau MD[1], Ana Belkin MD[1], Sapir Kon-Kfir MD[1], Nira Koren-Morag PhD[5], Avishay Grupper MD[2,5], David Shimunov MD[2], Ben-Ami Sela PhD[3], Ehud Grossman MD[1,5], Gadi Shlomai MD[1,5], and Avshalom Leibowitz MD[1,5]

[1]Department of Internal Medicine D, [2]Leviev Heart Center, [3]Institute of Chemical Pathology, Sheba Medical Center, Tel Hashomer, Israel
[4]Department of Epidemiology and Preventive Medicine, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[5]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** Most dyspneic patients in internal medicine departments have co-morbidities that interfere with the clinical diagnosis. The role of brain natriuretic peptide (BNP) levels is well-established in the acute setting but not in hospitalized patients.

Objectives: To evaluate the additive value of BNP tests in patients with dyspnea admitted to medical wards who did not respond to initial treatment.

Methods: We searched the records of patients who were hospitalized in the department of internal medicine D at Sheba Medical Center during 2012 and were tested for BNP in the ward. Data collected included co-morbidity, medical treatments, diagnosis at presentation and discharge, lab results including BNP, re-hospitalization, and mortality at one year following hospitalization.

Results: BNP results were found for 169 patients. BNP was taken 1.7 ± 2.7 days after hospitalization. According to BNP levels, dividing the patients into tertiles revealed three equally distributed groups with a distinctive character. The higher tertile was associated with higher rates of cardiac co-morbidities, including heart failure, but not chronic obstructive pulmonary disease. Higher BNP levels were related to one-year re-hospitalization and mortality. In addition, higher BNP levels were associated with higher rates of in-admission diagnosis change.

Conclusions: BNP levels during hospitalization in internal medicine wards are significantly related to cardiac illness, the existence of heart failure, and patient prognosis. Thus, BNP can be a useful tool in managing dyspneic patients in this setting.

IMAJ 2022; 24: 713–718

KEY WORDS: brain natriuretic peptide (BNP), diastolic dysfunction, dyspnea, heart failure, internal medicine

Dyspnea is a common cause for patients to seek medical counsel, visit emergency departments, and undergo hospitalization. Among the most common etiologies for dyspnea are chronic obstructive pulmonary disease (COPD), asthma, and congestive heart failure (CHF) [1]. Due to the high prevalence of co-morbidities as well as overlapping clinical signs, diagnosing the cause for acute dyspnea is challenging [1].

Brain natriuretic peptide (BNP) is a natriuretic peptide released mostly by ventricular myocytes in response to left ventricular overload. BNP assists in reducing the load on the left ventricle by means of promoting natriuresis, vasodilatation, and inhibition of the renin-angiotensin-aldosterone system [2]. BNP release is increased during left ventricular loading and has been found to be an effective indicator for acute heart failure with a high sensitivity, high specificity, and high negative predictive values [3,4]. There are a few confounding factors affecting BNP levels besides heart failure including age, sex, renal function, myocardial ischemia, mitral regurgitation, and right ventricular overload [5]. Apart from the use of BNP for diagnosing heart failure, a few other implementations have been suggested for BNP testing, among them are determining prognosis of heart failure and ischemic heart disease [2,6] as well as guiding treatment of heart failure [7].

Most studies regarding BNP as a diagnostic tool were conducted using BNP levels at presentation to the emergency department (ED). Its main use during hospitalization has been to estimate the response to treatment for heart failure [8]. As a result, very little information exists regarding the use of BNP for diagnosing heart failure in hospitalized patients.

Common co-morbidities and overlaps between symptoms makes diagnosing the etiology for dyspnea a challenge. Some patients may be hospitalized without a definitive diagnosis or, in some cases, the diagnosis changes [1].

The aim of this study was to evaluate the additive value of BNP tests in patients with dyspnea already admitted to medical wards who did not respond to the initial treatment. Can BNP in this stage affect the working diagnosis and treatment? Does it still have prognostic value? Can it help in identifying patients who need treatment adjustments?

PATIENTS AND METHODS

Data was collected from the electronic medical records (EMR) of patients who had a BNP test in the Department of Internal Medicine D, Sheba Medical Center during 2012. Data collected from the records included past morbidities, pre-hospital medical treatments, diagnosis at presentation and discharge, laboratory test results including BNP, in-hospital mortality, re-hospitalization, and mortality during the year following hospitalization. In addition, to have a better definition of the patient's heart function status, we collected data from recent echocardiography examination when was applicable. A test conducted more than 90 days after the admission was considered relevant.

The study protocol was approved by Sheba's Helsinki Committee.

BNP tests were conducted during the hospitalization using the Triage Meter-Pro system (Alere International, Sari, Switzerland) with a small sample of blood applied to the device using a transfer pipette. Time elapsed from presentation to the emergency department to the BNP test was recorded.

STATISTICAL ANALYSIS

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA). Significance levels were set at $P < 0.05$.

Baseline characteristic across BNP tertiles were presented as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Chi-square and one-way ANOVA tests were used to compare the three BNP tertiles by baseline characteristics and major risk factors.

The risk for death or hospitalization, within one year after admission, was evaluated by the Cox proportional regression model. Time to event was calculated as time from hospitalization date to death or rehospitalization within one year or time to end of follow-up (one year).

Multivariate analysis using the Cox regression model for time until death or re-hospitalization within 1 year was performed with main risk factors. The covariates were (age, sex, diabetic, hypertension, C-reactive protein [CRP], and length of stay in the hospital). The cumulative survival curves were computed using a multivariate Cox regression analysis.

RESULTS

BNP VALUES ARE CORRELATED TO PATIENT CHARACTERISTIC

After reviewing the EMR, we determined 169 patients with BNP tests. The patient anthropomorphic characteristics and co-morbidities represented the classical medical ward hospitalized patient, with an average age of 77 ± 12 years of age, weight of 77 ± 17 kg and an average of 3 ± 1 cardiovascular or respiratory co-morbidities.

The average time for BNP testing was 1.7 ± 2.7 days from hospitalization. BNP levels were found to positively correlate with age, creatinine, troponin, and CRP but were negatively correlate with body weight, glomerular filtration rate (GFR), and hemoglobin. BNP levels were also correlated with length of hospitalization. Dividing the patients into tertiles according to BNP levels (low ≤ 167, medium 168–530, and high ≥ 531) revealed three equally dis-

Table 1. BNP levels significantly correlate with clinical parameters

	BNP Spearman r	BNP (low tertile) ≤ 167 N=57	BNP (middle tertile) 168–530 N=56	BNP (high tertile) ≥ 531 N=56	*P* value
BNP	–	79 ± 45	315 ± 113	1170 ± 580	
Days hospitalized before BNP	-0.09	1.77 ± 2.77	1.30 ± 0.95	1.71 ± 2.77	0.515
Hospital LOS	0.163 *	4.26 ± 3.20	4.61 ± 3.62	6.30 ± 6.95	0.063
Age, years	0.249 **	72.35 ± 13.76	80.20 ± 11.52	79.63 ± 9.73	0.001
Weight	-0.240**	83.18 ± 18.29	77.06 ± 18.57	73.35 ± 12.43	0.010
Body mass index	-0.158*	29.73 ± 6.02	28.61 ± 6.53	27.24 ± 4.38	0.083
Creatinine	0.393**	1.39 ± 0.95	1.44 ± 0.75	2.09 ± 1.39	0.001
GFR	-0.343**	56.87 ± 23.51	48.75 ± 20.33	40.19 ± 17.43	0.001
pH	-0.018	7.35 ± 0.04	7.33 ± 0.06	7.34 ± 0.06	0.356
pCO2	-0. 117	50.85 ± 9.17	53.22 ± 16.19	54.20 ± 42.29	0.801
HCO3	-0.193 *	27.35 ± 3.77	70.23 ± 321.94	25.25 ± 4.35	0.364
Hemoglobin	-0.233**	12.33 ± 2.13	12.02 ± 1.61	11.53 ± 2.15	0.095
CRP	0.264**	48.48 ± 72.05	54.15 ± 62.79	69.86 ± 79.59	0.269
Troponin	0.608**	0.04 ± 0.08	0.20 ± 0.49	0.47 ± 1.12	0.016

BNP = brain natriuretic peptide, CRP = C-reactive protein, GFR = glomerular filtration rate, LOS = length of stay, pCO_2 = partial pressure of carbon dioxide
*$P < 0.05$, **$P < 0.01$

tributed groups (n=56–57 each) with a distinctive BNP level characterizing each tertile. Tertiles were significantly distinguishable in several parameters. Patients in the higher tertiles were older, had lower body weight, and worse kidney function (presented by higher creatinine and lower GFR). The length of hospitalization was longer in patients in the upper tertile. There were no differences in time to BNP tests between tertiles [Table 1].

CO-MORBIDITIES AND BNP VALUES

Mean BNP was significantly higher among patients with CHF, ischemic heart disease (IHD), atrial fibrillation (AF), valvular disease, and diabetes mellitus (DM). The presence of COPD and hypertension had no effect on BNP levels [Table 1]. The tertile division sharpened the correlation of co-morbidities and preadmission medication with BNP levels. The percentage of patients with CHF, IHD, AF, and DM was significantly higher in the upper tertiles. The prevalence of valvular disease was also higher in the upper tertiles, but did not reach a statistical significance, probably due to the small sample size. Being in the upper tertiles was also correlated with preadmission treatment with furosemide, beta blockers, and spironolactone [Supplemental Table 1].

BNP CORRELATES WITH DIASTOLIC DYSFUNCTION PARAMETERS

We found relevant echocardiography tests for 80 patients. BNP showed good correlation with systolic and diastolic dysfunction parameters. BNP levels had a strong negative correlation with left ventricular ejection fraction (EF). Patients were also distributed into BNP tertiles, with higher tertiles having a lower EF. BNP also had a good correlation with diastolic dysfunction (DD) parameters. The strongest correlation was found with left ventricular mass (LVM), but other parameters such as left atrium (LA) end systolic pressure and LA diameter had good correlation as well [Table 2].

HIGH BNP LEVELS MAY PREDICT ONE-YEAR RE-HOSPITALIZATION AND MORTALITY

There were threefold more cases of one-year re-hospitalization and death in the upper BNP tertile than in the lower one. The unadjusted risk for the composite events of re-hospitalization

Table 2. Echocardiography within 90 days of hospitalization

	BNP Spearman r	BNP (low tertile) ≤ 167 N=57	BNP (middle tertile) 168–530 N=56	BNP (high tertile) ≥ 531 N=56	*P* value
EF, n=78	-0.586**	58.70 ± 6.10	52.70 ± 12.00	38.90 ± 15.80	< 0.001
EndDias, n=80	0.387**	4.64 ± 0.57	4.56 ± 0.64	5.23 ± 0.71	< 0.001
EndSyst, n=80	0.420**	3.50 ± 3.14	3.08 ± 0.78	3.95 ± 1.10	0.282
IVsep, n=80	0.386**	1.07 ± 0.15	1.11 ± 0.15	1.21 ± 0.19	0.004
PW, n=80	0.117	1.00 ± 0.16	0.99 ± 0.16	1.03 ± 0.18	0.451
LVM, n=75	0.614**	92.10 ± 22.10	91.70 ± 30.90	132.9 ± 25.5	< 0.001
LAAP, n=80	0.411**	3.98 ± 0.65	7.05 ± 15.40	4.53 ± 0.57	0.399
LAendsy, n=78	0.444**	21.40 ± 6.00	22.20 ± 6.60	26.60 ± 4.60	0.003
sysPA, n=73	0.345**	38.10 ± 10.60	47.20 ± 22.60	48.90 ± 15.30	0.043
EAratio, n=61	0.365**	0.88 ± 0.30	1.57 ± 1.20	6.56 ± 20.30	0.232
DeceR, n=72	-0.376**	221 ± 66	188 ± 66	180 ± 64	0.073
E/e' septal, n=65	0.441**	13.90 ± 5.80	16.80 ± 7.90	24.80 ± 13.60	0.001
E/e' lateral, n=67	0.249*	11.40 ± 7.00	14.30 ± 10.50	13.90 ± 6.50	0.404

BNP = brain natriuretic peptide, DeceR = deceleration rate, EF = ejection fraction, EndDias = end diastolic diameter, EndSyst = end systolic diameter, IVsep = intra ventricular septum, LAAP = left atrial anterior posterior diameter, LAendsy = left atrial end systolic diameter, LVM = left ventricular mass, PW = posterior wall, sysPA = sustolic pulmonary artery pressure
*$P < 0.05$, **$P < 0.01$

Table 3. Multivariate analyses for death or hospitalization within one year

	BNP (low tertile) ≤ 167 N=57	BNP (middle tertile) 168–530 N=56	BNP (high tertile) ≥ 531 N=56	*P* value
Re-hospitalization and Mortality rates	10 (18%)	25 (45%)	33 (59%)	< 0.001
Unadjusted HR	1.0	3.1 (1.5–6.4)	4.5 (2.2–9.3)	< 0.001
Age and sex HR	1.0	2.7 (1.3–5.8)	4.1 (2.0–8.5)	0.001
Multivariate* HR	1.0	2.8 (1.3–6.2)	3.9 (1.8–8.2)	0.002

HR = heart rate
*Adjusted to age, sex, diabetic, hypertension, CRP and length of stay

and mortality increased significantly in each tertile increment. The significance remained after adjusting for related variables like age or sex and after multivariate analyses [Table 3]. It is noteworthy that the confidence intervals are wide due to the relatively small sample size, but the trend is clear.

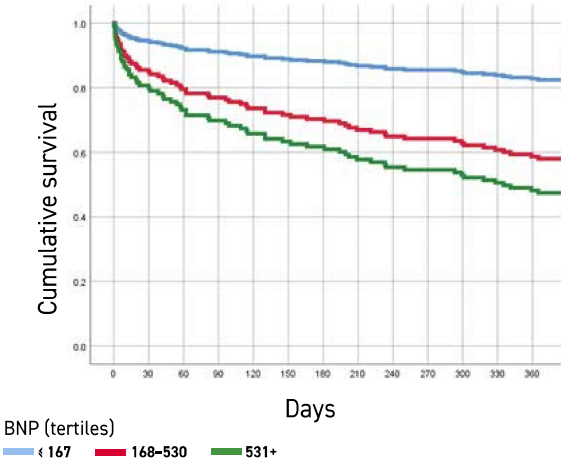
The survival curves for one-year survival and readmission and for one-year survival demonstrated that the difference between tertiles became obvious soon after first admission [Figure 1A and 1B, respectively].

BNP LEVELS ARE ASSOCIATED WITH DIAGNOSIS CHANGE DURING HOSPITALIZATION

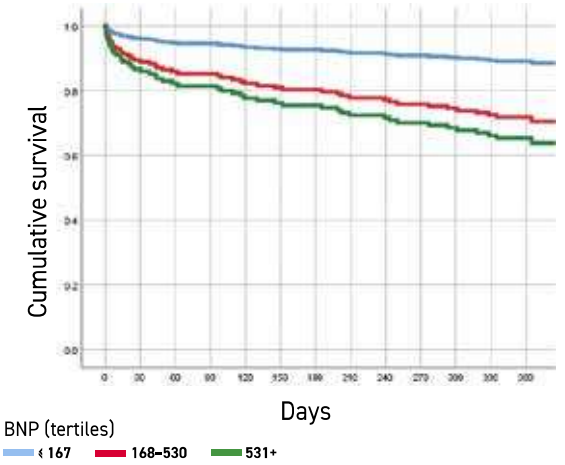
Higher tertiles of BNP showed a higher frequency of CHF as the diagnosis at admission and discharge. Interestingly, higher levels of BNP were also associated with higher rates of in-admission diagnosis change, as the two higher tertiles had a significantly higher rate of change in diagnosis to CHF (33% and 34.5%, respectively) than the lowest BNP value tertile (14%) ($P < 0.05$).

Figure 1. Multivariate survival curves

[A] Survival until death or readmission on a one year follow up for the different BNP tertiles. BNP = brain natriuretic peptide



[B] Survival until death in a one year follow up for the different BNP tertiles



DISCUSSION

Measuring plasma BNP is recommended by several medical society guidelines and is widely used for diagnosing CHF [9,10]. There are numerous studies focusing on its use in the acute care setting, ED, and urgent care centers. However, the recommendations are based mainly on the Breathing Not Properly Multinational Study [11] in which the investigators measured BNP in more than 1500 dyspneic patients in an acute setting, that is, emergency departments [11].

Our study is unique in that the test was performed in the subacute setting, after admission to an internal medicine department and after emergency treatment. Reassessment of a patient's diagnosis and treatment is crucial during hospitalization, yet often overlooked. Occasionally, a patient does not respond to treatment and remains dyspneic and so physicians must decide whether to increase the current treatment, replace it, or reconsider the working diagnosis. A BNP measurement at this stage can provide valuable decision supporting information.

Our study is not the first in which BNP levels were taken during hospitalization. Cheng et al. [12] demonstrated that serial BNP measurements during hospitalization provide some prognostic data. However, in their study, like in others, the baseline BNP test was taken in the ED and following BNP measurements were compared to this baseline. Even without baseline ED BNP measurements, measuring BNP during hospitalization is of considerable value for determining risk for re-hospitalization and death at one year as well as for ascertaining the cause for dyspnea during hospitalization.

The precise BNP cutoff for CHF is another controversial issue. Traditionally, according to the Breathing Not Properly Multinational Study [11], a BNP level lower than 100 pg/ml is considered a reliable means for ruling out CHF as the cause of dyspnea, while levels above 400 pg/ml are indicative of acute CHF exacerbation. Noteworthy, different studies used different cutoffs for making clinical decisions. Shah and colleagues [13] used a cutoff of 500 pg/ml for diagnosing CHF. Dao et al. [3] found that the average BNP in patients without CHF was approximately 40 pg/ml. Patients with an acute decompensated CHF in their study had an average BNP level higher than 1000 pg/ml. Thus, choosing the cutoff has a major impact on the sensitivity and specificity of the test.

Another advantage of our study is that the patients were spontaneously split to three equal groups. This division revealed distinct BNP levels and clinical characterization of the groups. Despite our relatively small group of patients, we demonstrated robust correlations between different BNP levels and prognosis and hospitalization, suggesting that our cut-offs were reliable and a powerful marker of an adverse prognosis for hospitalized patients.

Several factors can influence BNP levels in CHF patients. Several authors demonstrated that BNP levels are directly correlated with the degree of kidney dysfunction [5]. However, even in chronic kidney disease, BNP levels remain a reliable diagnostic marker of CHF [14].

The effect of age on BNP results is controversial. Data suggest that older people have higher BNP levels. Nevertheless, BNP is still helpful in making clinical decisions in the elderly. Knudsen and co-authors [15] showed that BNP discriminates between dyspneic patients presenting with CHF and dyspneic patients not presenting from CHF, regardless of their age and BNP cutoff.

In agreement with existing literature, in our study population, BNP levels had a strong correlation with the presence of cardiac and non-cardiac co-morbidities like DM, renal failure, and anthropomorphic characteristics of patients, thus enhancing the accuracy and relevance of the results.

Another characteristic feature of internal medicine patients is the high prevalence of diastolic dysfunction. Obviously, most BNP studies have focused on patients with reduced EF CHF, and diastolic dysfunction data are usually a byproduct and derived from small studies. Redfield et al. [16] looked for markers for pre-clinical CHF. Correlation between BNP and diastolic dysfunction parameters were goals of some of the studies, but they concluded that BNP was not a good marker for this purpose [16]. Other studies found good correlation between BNP and some classical diastolic dysfunction (like E/Ea ratio) parameters [17], and some tried to establish new diastolic dysfunction parameters and used the BNP test to support their results [18]. Goda and colleagues [19] examined BNP levels in hypertensive patients without overt CHF. Like in our study, they found strong correlation with LVM. This finding is not surprising as left ventricle hypertrophy and diastolic dysfunction are early signs of hypertension induced organ damage. Palazzuoli et al. [20] conducted a study in which they looked at BNP and systolic and diastolic parameters in 310 patients. In concordance with our results, they concluded that BNP levels correlate with the degree of diastolic dysfunction as well as with pulmonary artery pressure. Hence, our results support existing data on BNP and diastolic dysfunction and may contribute to better clinical assessment of these patients.

The interpretation and relevance of BNP measurement in COPD patients is challenging. Some studies determined whether BNP measures during an acute exacerbation of COPD (AECOPD) contribute to treatment and establishing a prognosis. Adrish and colleagues [21] reported that elevated BNP levels during AECOPD were associated with both prolonged hospital stay and admission to intensive care units. In their retrospective study, the authors excluded patients with any degree of systolic heart failure and moderate diastolic dysfunction. Consequently, higher BNP levels were associated with higher right ventricle pressure, suggesting some degree of right-sided heart failure. Despite this, the study showed no clinical differences between patients with low versus high BNP. A systemic review from 2017 concluded that BNP reflected diverse aspects of the cardiopulmonary continuum, which limits utility when applied in isolation. This result is due to the difficulty in separating the respiratory from cardiac complaints [22]. Still, in a comprehensive review, Le Jemtel et al. [23] recommended the use of BNP to uncover CHF during AECOPD [23].

In our study, the presence of COPD had no impact on BNP results. In addition, the deviation of COPD patients was equal across groups. Thus, it seems that BNP can distinguish between CHF and COPD during hospitalization and can be an important surrogate marker in clinical decision-making. In this regard, the use of point-of-care ultrasound (POCUS) is also mentioned as an evolving tool for the assessment of both cardiac function and volume status in the 2022 heart failure guidelines of the American college of cardiology [9]. While POCUS was found to be more accurate than the standard physical exam, chest X-ray, and laboratory work (including natriuretic peptides in some cases), it remains user dependent. Moreover, there is no consensus on training recommendations and a wide array of training curricula exists [24]. It is also noteworthy that volume status evaluation using POCUS may be hindered by bowel gas, adipose tissue, and patient discomfort [25]. It can therefore be concluded that while POCUS is gradually gaining importance as a decision-supporting tool in the workup of dyspneic patients, its place remains like that of BNP: a decision-supporting tool.

LIMITATIONS

The main study limitations of our study are the relatively small sample size and the fact it is based on BNP tests taken in 2012. These pitfalls are because the test is not routinely available in many internal departments in Israel and so results had to be acquired from a very specific time frame when the test was available for the routine workup of dyspnea in hospitalized patients. Indeed, we think that the test should be introduced for routine use in internal departments as it may contribute to clinical decision making.

CONCLUSIONS

Testing BNP during hospitalization in internal medicine wards can stratify the patients into distinct CHF related categories, which predict rehospitalization and mortality. In addition, BNP tests can help in clinical decision making in patients needing reassessment due to unsatisfied clinical improving despite therapy. BNP testing is recommended even late after the hospitalization and even after directed treatment initiation.

ACKNOWLEDGMENTS

The authors thank Dr. Mechael Kanovsky for his editorial services.

Correspondence

Dr. A. Leibowitz
Dept. of Internal Medicine D, Sheba Medical Center, Tel Hashomer 5262000, Israel
Phone: (972 3) 530-2834
Fax: (972-3) 530-2835
email: avshalom.leibowitz@sheba.health.gov.il

References

1. Mulrow CD, Lucey CR, Farnett LE. Discriminating causes of dyspnea through clinical examination. *J Gen Intern Med* 1993; 8 (7): 383-92.
2. Uddin MH, Rashid T, Chowdhury SM. Role of B-type natriuretic peptide (BNP) in heart failure. *Int J Disabil Hum Dev* 2017; 16 (162): 3-9.
3. Dao Q, Krishnaswamy P, Kazanegra R, et al. Utility of B-type natriuretic peptide in the diagnosis of congestive heart failure in an urgent-care setting. *J Am Coll Cardiol* 2001; 37 (2): 379-85.
4. Lainchbury JG, Campbell E, Ons BSCH, et al. Brain natriuretic peptide and n-terminal brain natriuretic peptide in the diagnosis of heart failure in patients with acute shortness of breath. *J Am Coll Cardiol* 2003; 42 (4): 728-35.
5. Tang WH. B-type natriuretic peptide: a critical review. *Congest Heart Fail* 2007; 13 (1): 48-52.
6. Richards M, Nicholls MG, Espiner EA, et al. Comparison of B-type natriuretic peptides for assessment of cardiac function and prognosis in stable ischemic heart disease. *J Am Coll Cardiol* 2006; 47 (1): 52-60.
7. Jourdain P, Jondeau G, Funck F, et al. Plasma brain natriuretic peptide-guided therapy to improve outcome in heart failure. The STARS-BNP Multicenter Study. *J Am Coll Cardiol* 2007; 49 (16): 1733-9.
8. Silver MA, Maisel A, Yancy CW, et al; BNP Consensus Panel. BNP Consensus Panel 2004: a clinical approach for the diagnostic, prognostic, screening, treatment monitoring, and therapeutic roles of natriuretic peptides in cardiovascular diseases. *Congest Heart Fail* 2004; 10 (5 Suppl 3): 1-30.
9. Heidenreich PA, Bozkurt B, Aguilar D, et al; Writing Committee Members 2022 American College of Cardiology/American Heart Association/Heart Failure Society of America Guideline for the Management of Heart Failure: Executive Summary. *J Card Fail* 2022; 28 (5): 810-30.
10. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failureDeveloped by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2021; 42 (36): 3599-726.
11. Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002; 347 (3): 161-7.
12. Cheng V, Kazanagra R, Garcia A, et al. A rapid bedside test for B-type peptide predicts treatment outcomes in patients admitted for decompensated heart failure: a pilot study. *J Am Coll Cardiol* 2001; 37 (2): 386-91.
13. Shah KB, Kop WJ, Christenson RH, et al. Natriuretic peptides and echocardiography in acute dyspnoea: implication of elevated levels with normal systolic function. *Eur J Heart Fail* 2009; 11 (7): 659-67.
14. Takami Y, Horio T, Iwashima Y, et al. Diagnostic and prognostic value of plasma brain natriuretic peptide in non-dialysis-dependent CRF. *Am J Kidney Dis* 2004; 44 (3): 420-8.
15. Knudsen CW, Riis JS, Finsen A V, et al. Diagnostic value of a rapid test for B-type natriuretic peptide in patients presenting with acute dyspnoe: effect of age and gender. *Eur J Heart Fail* 2004; 6 (1): 55-62.
16. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA* 2003; 289 (2): 194-202.
17. Dokainish H, Zoghbi WA, Lakkis NM, Quinones MA, Nagueh SF. Comparative accuracy of B-type natriuretic peptide and tissue Doppler echocardiography in the diagnosis of congestive heart failure. *Am J Cardiol* 2004; 93 (9): 1130-5.
18. Park H-J, Jung HO, Min J, et al. Left atrial volume index over late diastolic mitral annulus velocity (LAVi/A') is a useful echo index to identify advanced diastolic dysfunction and predict clinical outcomes. *Clin Cardiol* 2011; 34 (2): 124-30.
19. Goda A, Nakao S, Tsujino T, et al. Determinants of plasma brain natriuretic peptide levels in untreated hypertensive patients. *J Echocardiogr* 2011; 9 (3): 103-8.
20. Palazzuoli A, Beltrami M, Ruocco G, Franci B, Campagna MS, Nuti R. Diagnostic utility of contemporary echo and BNP assessment in patients with acute heart failure during early hospitalization. *Eur J Intern Med* 2016; 30: 43-8.
21. Adrish M, Nannaka VB, Cano EJ, Bajantri B, Diaz-Fuentes G. Significance of NT-pro-BNP in acute exacerbation of COPD patients without underlying left ventricular dysfunction. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 1183-9.
22. Hawkins NM, Khosla A, Virani SA, McMurray JJ, FitzGerald JM. B-type natriuretic peptides in chronic obstructive pulmonary disease: a systematic review. *BMC Pulm Med* 2017; 17 (1): 11.
23. Le Jemtel TH, Padeletti M, Jelic S. Diagnostic and therapeutic challenges in patients with coexistent chronic obstructive pulmonary disease and chronic heart failure. *J Am Coll Cardiol* 2007; 49 (2): 171-80.
24. Kovell LC, Ali MT, Hays AG, et al. Defining the role of point-of-care ultrasound in cardiovascular disease. *Am J Cardiol* 2018; 122 (8): 1443-50.
25. Tzadok B, Shapira S, Tal-Or E. Ultrasound of jugular veins for assessment of acute dyspnea in emergency departments and for the assessment of acute heart failure. *IMAJ* 2018; 20 (5): 308-10.

Supplemental Table 1. Frequencies and percent of chronic disease by BNP groups

	ALL N=169	BNP (low tertile) ≤ 167 N=57	BNP (middle tertile) 168–530 N=56	BNP (high tertile) ≥ 531 N=56	*P* value
Male sex	98 (58)	40 (70)	26 (46)	32 (57)	0.038
Atrial fibrillation	47 (28)	7 (12)	17 (30)	23 (41)	0.003
IHD	77 (46)	19 (33)	26 (46)	32 (57)	0.039
CHF	53 (31)	8 (14)	18 (32)	27 (48)	< 0.001
VAL dis	16 (10)	3 (5.3)	4 (7.1)	9 (16)	0.112
COPD	44 (26)	15 (26)	18 (32)	11 (20)	0.321
Diabetes mellitus	71 (42)	25 (44)	15 (27)	31 (55)	0.011
Hypertension	119 (70)	40 (70)	41 (73)	38 (68)	0.824
Death 1 year	39 (23)	6 (11)	14 (25)	19 (34.5)	0.011
Hospitalization 1 year	30 (18)	4 (7)	11 (20)	15 (27)	0.018
Furosemide	97 (57)	23 (40)	33 (59)	41 (73)	0.002
ACEi / ARB	91 (54)	28 (50)	31 (55)	32 (57)	0.732
B blocker	92 (55)	22 (39)	33 (59)	37 (66)	0.013
Aspirin	85 (50)	29 (52)	27 (48)	29 (52)	0.909
Spironolactone	30 (18)	5 (9)	10 (18)	15 (27)	0.048

ACEi / ARB = angiotensin-converting enzyme inhibitors / angiotensin receptor blockers, BNP = brain natriuretic peptide, CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, IHD = ischemic heart disease