Original article

Correlation between NT proBNP and left ventricular ejection fraction in elderly patients presenting to emergency department with dyspnoea

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KEY WORDS

Echocardiography
LV dysfunction
NT proBNP
Shortness of breath

A B S T R A C T

Objective: Shortness of breath is a common complaint for which the elderly seek medical attention in the emergency department (ED). Differentiating cardiac from respiratory causes of dyspnoea in this population is quite a challenge. N Terminal pro brain-natriuretic-peptide (NT proBNP) has been studied extensively as a biomarker of left ventricular (LV) failure.

Methods: The NT proBNP was measured in 100 patients above 60 years of age who presented to the ED with shortness of breath. The level was compared with echocardiographic findings to assess correlation with ejection fraction (EF).

Results: The NT proBNP values increased significantly as the functional severity of heart failure (HF) increased ($P < 0.001$). The mean NT proBNP level was 1503.33 pg/mL. Patients with respiratory causes of dyspnoea had a mean NT proBNP level of 309.28 pg/mL with normal LV function.

Conclusion: The NT proBNP levels had a good correlation with worsening LVEF.

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Introduction

Elderly people are affected with several morbidities like hypertension (HTN), ischaemic heart disease (IHD), diabetes mellitus (DM), bronchial asthma (BA), and chronic obstructive pulmonary disease (COPD), often being seen in combination, with breathlessness being a common symptom.¹

Left ventricular (LV) dysfunction is a common consequence of the morbid states in the elderly.² Cardiac disorders are often misdiagnosed in the elderly because clinical manifestations can be significantly different from those in younger patients with the same disorder.³

After evaluating a patient's symptoms and conducting a physical examination, the clinician is often left with considerable diagnostic uncertainty, which results in misdiagnosis and delay the initiation of appropriate therapy.^{4,5}

In addition, the misdiagnosis of heart failure (HF) causes morbidity, increases the time to discharge and the cost of treatment because the use of a treatment strategy for other conditions, such as COPD, may be hazardous to patients with HF, and vice versa.⁶

N Terminal proBNP is a cardiac neurohormone which is secreted from the myocardium in response to increased intracardiac volume or pressure.^{7,8} Increased NT proBNP levels would help differentiate cardiac from respiratory causes of dyspnoea.

We performed a prospective study to test the hypothesis that a diagnostic strategy guided by the rapid measurement of NT proBNP levels would improve the evaluation and care of elderly patients who present to the emergency department (ED) with acute dyspnoea.

Aim of the study

To evaluate the usefulness of NT proBNP levels in the diagnosis of LV dysfunction in the elderly and to correlate NT proBNP levels with echocardiographic findings.

Materials and methods

A prospective study was conducted on 100 elderly patients who presented to the ED of M.S. Ramaiah Hospitals with shortness of breath. Eligible patients were those above the

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age of 60 years who had acute onset of dyspnoea as the primary symptom. Patients with severe renal disease (defined by a serum creatinine level of $>250 \mu\text{mol/L}$ [2.8 mg/dL]), patients on therapy with angiotensin-converting enzyme inhibitors, beta-blockers and diuretics were excluded from the study.

One hundred and twenty-six patients were screened. Of these, 100 patients were enrolled in the study. All the patients underwent an initial clinical assessment that, in general, included a clinical history taking, a physical examination, electrocardiography, pulse oximetry, blood tests, chest radiography, and echocardiography. Pulmonary function tests were carried out when indicated. The NT proBNP was measured with the use of a rapid fluorescence immunoassay.

The NT proBNP value of $<1000 \text{ pg/mL}$ was taken as the cut-off.

Statistical analysis

The statistical analyses were performed with the use of the statistical presentation software SPSS (version+ 10.0). A P value of <0.01 was considered statistically significant. Comparisons were made with the use of the student t -test, χ^2 test, Pearson's correlation coefficient, as appropriate.

Results

A total of 100 patients who presented to the ED with shortness of breath were enrolled in the study. Majority of the patients were in the age group 60–69 years (50%). Medical history included HTN in 73%, followed by diabetes in 51%, IHD in 48%, COPD in 23% and BA in 15%.

The NT proBNP levels were estimated in all the patients. Thirty-seven patients had levels $<1000 \text{ pg/mL}$, 22 patients had levels between 1000 – 2000 pg/mL , and 41 patients had levels between 2000 – 3000 pg/mL .

On echocardiographic evaluation, 58% with normal ejection fraction (EF) were found to have a mean NT proBNP level of 891.75 pg/mL , 3% with mild LV dysfunction with EF between 40–49% had a mean NT proBNP of 1359 pg/mL , 17% with moderate LV dysfunction with EF 30–39% had mean NT proBNP of 2092.35 , and 19% with severe LV dysfunction with EF $<30\%$ had a mean NT proBNP of 2763.95 pg/mL . It was seen that the NT proBNP levels increased significantly as the severity of LV systolic dysfunction increased. The Pearson correlation comparing NT proBNP levels with echocardiographic findings was -0.721 ($P<0.001$). Three percent with normal EF had elevated NT proBNP. This may be attributed to diastolic HF.

Patients with COPD and BA constituted 38% and the mean NT proBNP level was 309.28 pg/mL . The remaining 62% of the patients with co-morbidities like IHD and HTN had mean NT proBNP of 2345.07 pg/mL . This finding would help differentiate dyspnoea due to cardiac causes from respiratory causes.

Ten patients who expired had a significantly higher mean NT proBNP of 2887 pg/mL .

Discussion

Although the causes of HF in elderly patients are generally the same as those in younger patients, the clinical presentation can be different. Because of the sedentary lifestyle, many elderly patients with HF do not experience progressive exertional dyspnoea, which is considered the classical symptom of LV dysfunction in younger patients.⁹

The NT proBNP is a powerful biomarker for the diagnosis and prognosis of HF in the elderly. It is elevated in conditions of increased ventricular wall stress and is most commonly used to rule out HF in dyspnoeic patients.¹⁰

Our study was designed to assess the diagnostic value of plasma NT proBNP level as a non-invasive indicator of LV dysfunction and to differentiate it from other causes of dyspnoea in the elderly. Also, to correlate the NT proBNP values with echocardiographic ejection fraction.

The NT proBNP is related to age and gender; levels increase with age and are more elevated in females than males.¹¹ The value of $>900 \text{ pg/mL}$ of proBNP is taken as suggestive of HF in patients >60 years of age.¹²

The NT proBNP seems to be affected more by worsening renal function than BNP. So patients with creatinine $>2.8 \text{ mg/dL}$ were excluded from the study.

In the BNP study, the optimal cut point for BNP of 100 pg/mL had a negative predictive value (NPV) of 89%, while a cut point of 50 pg/mL , which is still higher than the upper limit of normal (20 pg/mL) for healthy subjects, showed a NPV of 96%.⁴

In the NT proBNP Investigation of Dyspnea in the Emergency Department (PRIDE) study, the data were even more impressive. At a cut point for all persons (900 pg/mL), the NPV was 94%, while a 'rule out' cut point of 300 pg/mL yielded a NPV of 99%. Both the BNP and PRIDE studies also had high positive predictive values with markedly elevated levels.¹³

In the landmark BNP study, BNP levels $<100 \text{ pg/mL}$ carried an 89% NPV for ruling out HF.⁴ Similar diagnostic accuracy was shown for NT proBNP in the recent PRIDE study.¹³

The well-designed B-type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) study showed that BNP is cost-effective.¹⁴

Although echocardiography is considered the gold standard for the detection of LV dysfunction, it is expensive, not easily accessible, and may not always reflect an acute condition.¹⁵ In our study NT proBNP levels correlated well with reduced LVEF. Patients with a final diagnosis of LV dysfunction had significantly higher levels of NT proBNP than those without LV dysfunction ($P<0.001$).

Chronic obstructive pulmonary disease and BA constituted 38% of the patients in our study and the mean NT proBNP level was 309.28 pg/mL , with normal LV function. This finding corresponds well with a recent observation that acute exacerbation of COPD frequently escapes recognition in the ED making the correct diagnosis of congestive heart failure (CHF) in only 37% of these patients.¹⁶ It can be used as a rapid screening test to distinguish cardiac from respiratory causes of dyspnoea.

In addition to its role in the diagnosis of CHF, NT proBNP has been shown to have strong prognostic utility in patients with

HF and is clearly a strong independent predictor of morbidity and mortality in patients with CHF.¹⁷

Conclusion

The NT proBNP provides a rapid and reliable marker for accurate and early diagnosis of CHF. The values correlate well with the severity of LV dysfunction and its outcome.

The results demonstrate that rapid measurement of the NT proBNP level in the blood will improve the ability of clinicians to differentiate patients with dyspnoea due to CHF from those with dyspnoea due to other causes in acute care settings. This is especially true among the elderly in whom the diagnosis of CHF is not clinically straightforward.

Low NT proBNP levels on admission rule out HF and high-risk patients. Any increase in NT proBNP levels have to be interpreted in the clinical context and do not replace echocardiography for assessing cardiac abnormalities and dysfunction.

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