Diagnostic Importance of N-Terminal B-Type Natriuretic Peptide (NT-PRO-BNP)

Dr. R. Dhananjayan

Professor, Consultant & Head, Department of Biochemistry, Apollo Speciality Hospitals, Vanagaram, Chennai, India
Corresponding Author Email: *doctordhananjayan[at]gmail.com*
Mob: +91-9629429414

Abstract: *Early clinical diagnosis of heart failure (HF) is challenging because the signs and symptoms are neither sensitive nor specific for diagnosis. The determination of type-B natriuretic peptide (BNP) and its amino terminal fragment N-terminal B-type natriuretic peptide (NT-proBNP) represents an advance in the management of heart failure. The concentration of these molecules strongly reflects ventricular functions and is of prognostic value. BNP and NT-proBNP are cardiac neurohormones secreted from cardiac myocytes in response to cardiac wall stress caused by pressure or volume overload and its release is triggered by physiological and pathological stimuli. There are many randomized trials and systemic reviews conducted over a decade to research the potential value of BNP for diagnosis of HF.*

Keywords: BNP, NT-pro BNP, neurohormones, heart failure, natriuretic peptide, biomarker

1. Introduction

Brain natriuretic peptide (BNP) and N-terminal B-type natriuretic peptide (NT-proBNP) are cardiac neurohormones secreted from cardiac myocytes in response to cardiac wall stress caused by pressure or volume overload and its release is triggered by physiological and pathological stimuli [1]. The cardiac hormone relaxes vascular smooth muscle and increases capillary permeability. In the kidney, it increases the glomerular filtration, inhibits the release of renin and reduces sodium reabsorption in the collecting ducts. It also inhibits the release of aldosterone and antidiuretic hormone, while reducing sympathetic nervous activity. By promoting vasodilatation, natriuresis and diuresis, BNP reduces preload and after load [2]. The natriuretic peptides (NPs) are commonly used in the evaluation of heart failure (HF), but their role extends beyond diagnosis [3]. BNP and NT-proBNP have become important diagnostic tools for assessing patients with acute [4] breathlessness and both of these NPs are helpful in the diagnosis, prognosis, risk satisfaction and management of HF [5]. The determination of BNP and NT-proBNP represents an advance in the management of HF [6, 7]. The concentrations of these molecules strongly reflect ventricular function and are of prognostic value [8]. This paper is focused on the diagnostic importance of NT-proBNP

In Emergency Departments
NT-proBNP testing plays an important role to standard clinical assessment for the identification and exclusion of acute Congestive Heart Failure (CHF) in emergency department. ECG, BNP and NT-proBNP all have high sensitivities [9]. A chest X-ray is moderately specific but insensitive. BNP was found to be more accurate than ECG. Few studies stated that NT-proBNP appears superior to BNP for the evaluation of suspected acute HF with preserved LV ejection fraction (LVEF) [10].

There are various guidelines across the world in relation to NT-proBNP values in Emergency Departments. The NICE

(National Institute for Health and Care Excellence) guidelines of UK is as follows [11].
1) NT-proBNP>2000 pg/mL: patient should have an echocardiography and specialist clinical assessment within 2 weeks from the time of presentation.
2) NT-proBNP 400-2000 pg/mL: patient should have echocardiography and clinical assessment by the specialist within 6 weeks from the time of presentation.
3) NT-proBNP < 400 pg/mL, in the absence of HF therapy: HF is an unlikely cause for the presentation.

The ESC (European Society of Cardiology) guidelines for the diagnosis and treatment of acute and chronic HF is as follows: The upper limit of normal in non-acute setting for NT-proBNP is 125 pg/mL, while in acute setting, the cutoff value for NT-proBNP is 300 pg/mL [12].

In Primary Care
NT-proBNP is better than BNP when used for screening asymptomatic at-risk populations [13, 14]. An earlier study stated the effect of NT-proBNP on the accuracy of HF diagnosis in primary care [15] and shows that the availability of NT-proBNP measurement to the physicians significantly improves the diagnostic accuracy of HF in primary care by decreasing over diagnosis of HF.

As a Prognostic Biomarker in HF Patients
There are several studies performed to evaluate prognostic significance of natriuretic peptide. The prospective Copenhagen Hospital Heart Failure (CHHF) study showed that the measurements of NT-proBNP gave the prognostic information independent of LVEF and is a strong predictor of one year mortality in hospitalized patients with HF regardless of systolic dysfunction [16]. Another study investigated the prognostic value of NT-proBNP in a large number of patients with severe CHF. NT-proBNP was consistently associated with increased risk for all cause mortality and or hospitalization for HF in patients with severe CHF [17].

NT-proBNP increases with the severity of ventricular systolic as well as diastolic dysfunction [18, 19, 20]. The measurement of NT-proBNP level is useful to predict the probability of death within 12 months after hospital admission in patients with systolic dysfunction as well as in those with preserved systolic function [21]. Similarly, NT-proBNP values at discharge or changes in NT-proBNP concentration during hospitalization are useful to identify patients at risk of adverse outcomes regardless of systolic function [22].

NT-proBNP levels are a rapid and good predictor of morbidity and mortality within 30 days. A single determination of the NT-proBNP level was sufficient to identify high risk patients with a poor prognosis at the time of admission in ED [23].

In Covid 19
NT-pro BNP is an independent risk factor of in-hospital death in patients with severe COVID-19. An earlier study suggested that the prognostic effect of plasma NT-pro BNP in severe COVID-19 patients could not fully ascribe to heart failure induced by the virus or hypoxia. Further understanding of physiological and pathological significance of plasma NT-proBNP elevation in severe COVID-19 patients might help clinicians make corresponding decisions to reduce the risks of adverse outcome [24, 25].

The elevated NT-proBNP in these cases was believed owing to the cardiac complications resulted from complex interactions among preexisting conditions, relative ischemia, up-regulation of the sympathetic system, systemic inflammation and direct pathogen mediated damage to the cardiovascular system [26].

2. Conclusion

NT-proBNP is recognized as a potential biomarker in ruling out the heart failure in multiple clinical settings and is recommended in the diagnostic pathways of national and international guidelines for detection of heart failure. Measurements of plasma NT-proBNP concentrations provide important prognostic information on cardiovascular mortality and morbidity in patients with heart failure.

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