Journal of Medicinal and Chemical Sciences 6 (2023) 970-975

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Understanding NT-proBNP as One of Useful Marker for Cerebral Perfusion and Venous Congestion in Intensive Care Unit

Adityo Prabowo[1], Azwar Iwan Tona[1], Agus Prima[2], Bastian Lubis[2]*

[1]*Department of Emergency, Ibnu Sina Hospital, Aceh, Indonesia*
[2]*Department of Anesthesiology and Intensive Care, Faculty of Medicine, Universitas Sumatera Utara*

ARTICLE INFO

Article history

Receive: 2022-07-13
Received in revised: 2022-08-10
Accepted: 2022-10-14
Manuscript ID: JMCS-2209-1777
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatimah Ramezani
Editor who approved publication:
Dr. Ali Delpisheh

DOI:10.26655/JMCHEMSCI.2023.5.3

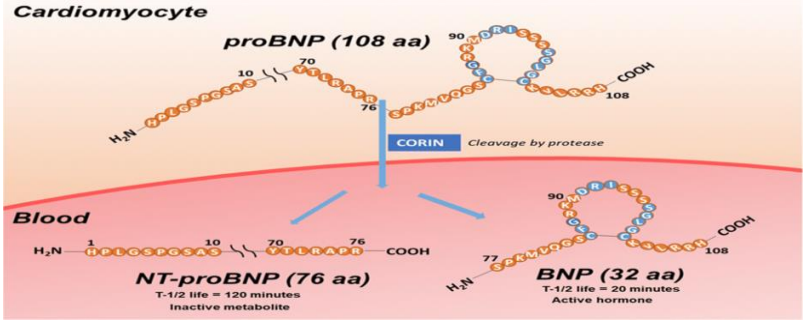
KEYWORDS

NT-proBNP
Hb
CVP
rSO_2
procalcitonin
cerebral perfusion
venous congestion

ABSTRACT

Background: N terminal pro B type Natriuretic Peptide (NT-proBNP) is an inactive pro-hormone that is used as a biomarker to evaluate our heart's condition. It is secreted due to stretching of venctricles. Increment of NT-proBNP levels usually signifies worse cardiac condition. NT-proBNP has been also used to assess the other indirect conditions that have an impact on cardiomyocytes such as sepsis and dehydration.
Objective: NT-proBNP is one of the functional cardiac markers that could be used as one of the markers in critical condition patients to measure cerebral perfusion and venous congestion. The better and the sooner understanding about NT-proBNP could help intensivists for relating with sepsis condition, resuscitation, and volume overload and prevent the multi organ failure.
Methods: 30 unconscious intensive care unit (ICU) patients with various sources of infection and sepsis as a working diagnosis from q-SOFA criteria were selected. All of the patients were intubated with mechanical ventilation and oxygenation. The blood sample was taken from the jugular vein to measure NT-proBNP, haemoglobin, procalcitonin and frontal rSO_2 are measured by using Near-Infrared Spectroscopy. The collected data include central venous pressure and mean arterial pressure.
Results: Significant correlation between NT-proBNP and other markers such as, haemoglobin (p=0.001), right rSO_2 (p=0.001), left rSO_2 (p=0.001), and mean arterial pressure (p=0.001). NT-proBNP result also has a correlation with procalcitonin (p=0.011) and central venous pressure (p=0.011).
Conclusion: NT-proBNP has a correlation with the other markers, such as procalcitonin, as one of the sepsis markers, haemoglobin, mean arterial pressure, and central venous pressure as components of delivery oxygen, and rSO_2 as the recent brain oxygenation parameter that has been used. NT-proBNP definitely could be developed in the future as a useful marker in critical condition patients to support the primary organ sepsis patients in the intensive care unit.

GRAPHICAL ABSTRACT



* Corresponding author: Bastian Lubis
✉ E-mail: Email: bastian.lubis@usu.ac.id

Introduction

NT-proBNP is the N-terminal part of the prohormone BNP (Brain Natriuretic Peptide) which appears as a biochemical marker of cardiac function. An important causative stimulus for the NT-proBNP formation results from stretching of cardiac myocytes, while the other hormones such as catecholamines, angiotensin II, endothelin via paracrine, and possibly endocrine mechanisms. Under these conditions, stretching can occur; hormones and hypoxia can alter the state of plasma peptide concentrations [1].

NT-proBNP increases due to anemia every 1 g/dL decrease in hemoglobin, and is useful for the diagnosis of heart failure in addition to echocardiography. Furthermore, the acute respiratory infections are also associated with an increase in NT-proBNP [2].

NT-proBNP also helps diagnose heart failure in acute dyspnoe [3]. NT-proBNP does not help assess fluid responsiveness effectively, while NT-proBNP does increase in septic patients. We recommend that NT-proBNP levels are not expected to be an indicator to pospone fluid administration [4].

The higher levels of NT-proBNP can lead to a poor prognosis, the higher risk of death, the risk stratification, and predictor of myocardial ischemia [5].

Materials and Method

The sample of this study included patients who were treated at the intensive care unit of the H. Adam Malik Hospital in Medan who met the inclusion and exclusion criteria. The basic data were recorded such as name, gender, height, weight, BMI, and ventilator settings used. The examination of vital signs carried out in the form of assessing the consciousness level based on GCS and FOUR, blood pressure, MAP, heart rate, and SpO_2. Before using NIRS, the patient's forehead was cleaned first with wet gauze and alcohol, and then dried so that was cleaned from disturbances such as an oily or watery face. The measurable results on the NIRS (at the time the jugular vein sample was taken, described in the next point) were recorded on the study sheet. The blood collection area was cleaned, on the right and left neck with betadine, after a while with alcohol, and then it was dried with gauze. Ultrasonography was used as a guide for taking blood samples using a 3 mL syringe on the internal jugular vein and internal carotid artery, and then inserted into a vacuum tube containing lithium heparin accompanied by the NT-proBNP examination, Arterial and Venous Blood Gas Analysis, routine blood, current blood sugar, and lactate.

After the required data was collected, the data was checked for completeness before being tabulated and processed, and then the data is coded to make it easier to tabulate. The data was tabulated into a master table using SPSS software. The numerical data that is normally distributed was presented in the mean value of SD (Standard Deviation), while the numerical data that was not normally distributed, was presented in the median value (the minimum to the maximum values). The categorical data was displayed in numbers (percentages). The normality test used with a sample size of less than 50 was the Shapiro-Wilk test. Normality test was mentioned to be normal if the p-value is greater than 0.05. The hypothesis testing was used to assess the relationship between NT-proBNP and other various parameters.

Results and Discussion

In this study, several parameters listed in Table 1. The taken parameters include, age, gender, weight and height, body mass index (BMI), the fraction of oxygen given to the patient, GCS score, and FOUR as a benchmark to assess the patient's decreased level of consciousness, mean arterial pressure, pulse oximetry, cerebral oximetry, jugular venous saturation, blood sugar level, lactate level, hemoglobin, blood gas analysis, and NT-proBNP.

Then, a correlation test was conducted on some of these parameters with NT-proBNP as the main topic of the study. We found that the only parameter which has a correlation with NT-proBNP was the procalcitonin level. NT-proBNP has been shown to have a positive correlation with the procalcitonin level and the result was statistically significant (Table 2).

Table 1: Characteristics of research parameters

Characteristics	n=30
Age	47,06 ±17,63
Gender, n (%)	
Male	18 (60,0)
Female	12 (40,0)
Weight	64,66 ±15,30
Height	1,62 ± 0,08
IMT	24,19 ± 4,71
FiO2	70,16 ± 26,98
GCS	7,16 ± 2,91
Mean Arterial Pressure	87,46 ± 19,97
SpO_2	95,70 ± 7,47
Right StO_2 (rSO_2)	53,86 ±19,99
Left StO_2 (rSO_2)	56,26 ± 18,66
$SjvO_2$	92,33 ± 8,00
Lactate serum	0,05 ± 0,32
$AVDO_2$	1,51 ± 1,52
Hb	10,96 ± 2,98
CaO_2	15,73 ±4,00
$CjvO_2$	14,22 ±3,50
PvO_2	93,06 ± 40,79
NT-proBNP	5461,93 ± 11076,67
CVP	5,26 ± 6,66
Procalcitonin	20,57 ± 79,43

Table 2: Correlation of research parameters with the NT-proBNP levels

	NT-proBNP	p-value
	Correlation coefficient (r)	
MAP	0,073	0,703
rSO_2 (R)	-0.194	0.304
rSO_2 (L)	-0.216	0.251
$SjvO_2$	0.201	0.287
SpO_2	-0.108	0.569
GCS	-0.206	0.274
Procalcitonin	0.435	0,016[a]
Hemoglobin	-0.273	0,144
CaO_2	-0.280	0.134
CjO_2	-0.228	0.226
CVP	-0.191	0.312
Laktat	-0.221	0.24

[a] *Wilcoxon test, Correlation coefficient test with Pearson's tes*

Brain Natriuretic Peptide (BNP) and N-terminal proBNP (NT-proBNP) are useful biomarkers for the management of heart failure, coronary heart disease, and acute coronary syndrome due to their good prognostic ability [6]. BNP circulates in the blood as an active component and is actively cleared of the neutral endopeptidase and natriuretic peptide receptors. NT-proBNP as an initial form of BNP has a more stable form with a half-life of 120 minutes and can survive in vacuum tubes for 72 hours [7]. As a marker, NT-proBNP is able to provide better clinical predictions than natriuretic peptides [6]. NT-proBNP with a value above 826.7 pg/mL has a poor prognosis, and can even predict death, as

well as for risk stratification and predictor of myocardial ischemia [5].

NT-ProBNP has a significant correlation with various parameters such as hemoglobin (p=0.001). The correlation is negative where the higher level of NT-ProBNP is associated with lower levels of hemoglobin, or vice versa, the higher the level of hemoglobin, the lower the level of NT-ProBNP. Hemoglobin is an important component of the oxygen delivery, and according to the theory that decreased levels of hemoglobin will be associated with an increase in NT-ProBNP. One of the symptoms experienced by patients with heart failure and of course the NT-ProBNP is increased. If we look further, this relationship can lead to kidney failure, where the association between heart and kidney failures is quite significant in the presence of anemia [2].

Patients with hypovolemia had the lower NT-proBNP values than patients with euvolemia [7]. In contrast to the results in this study, that there is a statistically significant correlation, with a weak correlation and in a negative direction. However, the higher the NT-proBNP value was associated with a low CVP value or vice versa, the lower the NT-proBNP value was associated with a high CVP value, although it was explained by further bioimpedance analysis that these measurements could not differentiate intravascular and extravascular volumes [7]. Huang *et al.* also confirmed that NT-proBNP showed the poor prediction of body responsiveness to fluids. A high value of NT-proBNP is indeed associated with septic shock, and it is advisable not to use the baseline value of NT-proBNP as the only indicator to delay fluid challenge but caution in fluid resuscitation. NT-proBNP may not be used as a marker of cardiac filling pressure in critically ill patients [4]. The increased value of NT-proBNP in the septic patients is also consistent with this study, that NT-proBNP has a significant and positive correlation with procalcitonin as a marker of sepsis. In summary, an increase in NT-proBNP is also accompanied by an increase in procalcitonin in the septic patients.

The results of NT-proBNP have a significant positive correlation with MAP, which means that an increase in one parameter is also followed by an increase in other parameters. This is related to the Left Ventricular Ejection Fraction (LVEF), where an increase in NT-proBNP is also associated with the heart wall tension, with an increase in LVEF over 40%, increasing the NT-proBNP value above normal [8-10]. In addition, NT-proBNP is associated with diastolic function, BMI, creatinine clearance, and with diastolic function and fluid balance. However, NT-proBNP could not differentiate between TRALI and TACO, but increased in both cases [11]. NT-proBNP shows the sufficient information about the condition of the heart, especially in patients on dialysis and is able to predict mortality due to cardiovascular problems so that it should be continued as a routine examination [6]. MAP is also related to the oxygen delivery which will greatly affect the perfusion value.

Likewise, study examined the relationship between NT-proBNP and CaO_2 values, CjO_2 which was significantly correlated and in a negative direction, where the high CaO_2 and CjO_2 values were correlated with low NT-proBNP values, which it means if perfusion is good, then the NT-proBNP values will be desired. Meanwhile, the relationship between NT-proBNP and NIRS value is denoted by right and left rSO_2, in a positive direction, which means that the NT-proBNP value will increase where the NIRS value will also increase, and if NT-proBNP decreases, the NIRS value will also be low. However, this is a little confusing, where the NIRS has a standard value between 60-80% with an increase over 80% influenced by various factors, including decreased oxygen uptake, whereas if it is less than 60%, the oxygen uptake will increase. Therefore, actually when it is going to be concluded, the relationship between NIRS and NT-proBNP cannot be drawn a clear relationship, but there is a correlation and requires more data and further research, where the NIRS also assesses the arterial: vein ratio of 75%:25%. Of course this will be different in the normal anatomical variations [12].

Conclusion

As a marker, NT-proBNP is quite good for assessing the state of sepsis and assessing prognostication in septic patients, which found a significant relationship between NT-proBNP with sepsis parameters such as procalcitonin, MAP, CaO_2, $CjvO_2$, and hemoglobin. In addition, NT-proBNP has a good relationship with NIRS and CVP. Furthermore, the relationship between NIRS and CVP was analysed in which there is a statistically significant correlation, but the relationship pattern needs to be discussed further. This is because the NIRS value has a fairly wide normal limit value in patients, while the CVP value is taken only once and of course it cannot dynamically assess the pressure in the central vein. Concerning the above mentioned points, it can actually be concluded that NT-proBNP can be further developed as a good marker to assess critical organ conditions in the septic patients, especially the heart and brain. However, further research is needed with a larger sample to accommodate the need to describe the pattern of the association between NT-proBNP and the other hemodynamic parameters.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

ORCID:

Adityo Prabowo
https://orcid.org/0000-0002-4200-3782
Bastian Lubis
https://orcid.org/0000-0002-1839-4146

References

[1]. Hall C., NT-ProBNP: the mechanism behind the marker, *Journal of cardiac failure,* 2005, **11**:81 [Crossref], [Google Scholar], [Publisher]
[2]. Widyanto D., Priyatno A., Tamam M., Faktor yang Memengaruhi Kadar NT-proBNP pada Anak dengan PJB Pirau Kiri ke Kanan yang Mengalami Gagal Jantung, *Sari Pediatri*, 2016, **17**:216 [Google Scholar]
[3]. Lainchbury J.G., Campbell E., Frampton C.M., Yandle T.G., Nicholls M.G., Richards A.M., Brain natriuretic peptide and N-terminal brain natriuretic peptide in the diagnosis of heart failure in patients with acute shortness of breath, *Journal of the American College of Cardiology*, 2003, **42**:728 [Crossref], [Google Scholar], [Publisher]
[4]. Huang H.B., Xu B., Liu G.Y., Du B., N-terminal pro-B-type natriuretic peptide for predicting fluid challenge in patients with septic shock, *Annals of Translational Medicine*, 2019, **7**:264 [Crossref], [Google Scholar], [Publisher]
[5]. Tandhana F.I., Noormartany N., Aprami T.M., Tristina N., Kadar N-Terminal Pro-Brain Natriuretic Peptide sebagai Prediktor Luaran Klinis Sindrom Koroner Akut, *Majalah Kedokteran Bandung*, 2012, **44**:106 [Crossref], [Google Scholar], [Publisher]
[6]. Cavoli G.L., Passanante S., Schillaci O., Zagarrigo C., Servillo F., Cavoli T.V.L., Palmeri M., Rotolo U., The NT-proBNP: A useful marker of cardiac dysfunction in chronic hemodialysis patients, *Diálisis y Trasplante,* 2015, **36**:40 [Crossref], [Google Scholar], [Publisher]
[7]. Tobin G., Chacko A., Simon R., Evaluation of NT-ProBNP as a marker of the volume status of neurosurgical patients developing hyponatremia and natriuresis: A pilot study, *Neurology India*, 2018, **66**:1383 [Crossref], [Google Scholar], [Publisher]
[8]. Bay M., Kirk V., Parner J., Hassager C., Nielsen H., Krogsgaard K., Trawinski J., Boesgaard S., Aldershvile J., NT-proBNP: A new diagnostic screening tool to differentiate between patients with normal and reduced left ventricular systolic function, *Heart*, 2003, **89**:150 [Crossref], [Google Scholar], [Publisher]

[9]. Okkonen M., Varpula M., Linko R., Perttilä J., Varpula T., Pettilä V., Finnali Study Group, N-terminal-pro-BNP in critically ill patients with acute respiratory failure: A prospective cohort study, *Acta anaesthesiologica scandinavica*, 2011, **55**:749 [Crossref], [Google Scholar], [Publisher]

[10]. Pudjiadi A.H., Rahayu T., Wijaya S., Alatas F.S., Serum NT-Pro-BNP versus Noninvasive Bedside Inotropic Index in Paediatric Shock: A Contest of Myocardial Performance in Response to Fluid Loading, *Critical Care Research and Practice*, 2021, **2021**:7458186 [Crossref], [Google Scholar], [Publisher]

[11]. Li G., Daniels C.E., Krpata T., Wilson G.A., Winters J.L., Moore S.B., Gajic, O., The accuracy of Natriuretic Peptides (Bnp and Nt-Pro-Bnp) in the Differentiation Between Transfusion-Related Acute Lung Injury (Trali) and Transfusion-Related Circulatory Overload (Taco) in the Critically Ill, *Chest*, 2008, **134**:89P [Crossref], [Google Scholar], [Publisher]

[12]. Murkin J.M., Arango M., Near-infrared spectroscopy as an index of brain and tissue oxygenation, *British journal of anaesthesia*, 2009, **103**:3 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Adityo Prabowo, Azwar Iwan Tona, Agus Prima, Bastian Lubis. Understanding NT-proBNP as One of Useful Marker for Cerebral Perfusion and Venous Congestion in Intensive Care Unit. *J. Med. Chem. Sci*., 2023, 6(5) 970-975
https://doi.org/10.26655/JMCHEMSCI.2023.5.4
URL: http://www.jmchemsci.com/article_159225.html