

Value of serum NT-ProBNP concentration in the diagnosis of some acquired heart diseases in children

Ngo Anh Vinh¹, Lai Thuy Thanh¹

ABSTRACT

Objective: Research the value of plasma NT - ProBNP in diagnosing acquired heart diseases in children. **Objects and methods of the study:** Cross-sectional descriptions of 107 patients included myocarditis, dilated cardiomyopathy, supraventricular tachycardia, and Kawasaki disease at the Vietnam National Children's Hospital. Quantify plasma NT-ProBNP concentrations and compare between these pathological groups and the control group. **Results:** NT-ProBNP concentrations in cardiovascular diseases were higher than in the control group with a statistically significant difference ($p < 0.05$). NT-ProBNP concentration was highest in the myocarditis group, followed by supraventricular tachycardia and dilated cardiomyopathy, and lowest in the Kawasaki group ($p < 0.05$). The optimal cut-off points of NT-ProBNP in diagnosing myocarditis, dilated cardiomyopathy, and Kawasaki are 1195, 943.6 and 176.4 pg/ml, respectively. NT-ProBNP concentration in the group with systolic dysfunction ($EF < 50\%$) was statistically significantly higher than the group with normal systolic function ($EF \geq 50\%$) with $p < 0.001$. **Conclusion:** NT-ProBNP concentrations increase in some acquired heart diseases such as myocarditis, dilated cardiomyopathy, supraventricular tachycardia, and Kawasaki. NT-ProBNP concentration correlates with left ventricular systolic function

Keywords: NT-ProBNP, acquired heart diseases, children.

¹ Vietnam National Children's Hospital

* Corresponding author

Ngo Anh Vinh
Email: Drngovinh@gmail.com

Received: October 12, 2023

Reviewed: October 15, 2023

Accepted: November 11, 2023

INTRODUCTION

Type B-type Natriuretic Peptide is a protein secreted by the ventricular myocardium in response to volume or pressure overload of the heart chambers, especially the left ventricle. B-type Natriuretic Peptide plays a role in improving volume homeostasis, osmolality, and regulating circulatory system pressure [1].

Currently, B-type Natriuretic Peptide, especially NT-ProBNP, has been widely

used in the diagnosis and prognosis of cardiovascular diseases in adults and has been shown to have high sensitivity and specificity. However, the application of NT-ProBNP in cardiovascular diseases in children is still limited. This is partly due to differences in cardiovascular diseases in children compared to adults as well as changes in NT-ProBNP concentrations according to children's age [2], [3].

Currently, a number of studies around the world also show that NT-ProBNP concentration is increased in children with

congenital heart disease, and this is also a very valuable indicator in predicting surgery for congenital heart disease [3], [4]. However, in Vietnam, there have not been many studies on the role of B-type Natriuretic Peptide in diagnosing acquired heart diseases in children. Therefore, in order to support the diagnosis of cardiovascular diseases in children, we conducted the study: "Value of plasma NT - ProBNP concentration in the diagnosis of some acquired heart diseases in children".

OBJECTS AND METHODS

Objects of the study

Criteria for selection

- Disease group: Patients were diagnosed with cardiovascular diseases including myocarditis, dilated cardiomyopathy, paroxysmal supraventricular tachycardia, and Kawasaki disease.

Diagnosis criteria:

+ Myocarditis: diagnosed according to Sagar criteria [5].

+ Dilated cardiomyopathy: diagnosis is based on echocardiography.

+ Supraventricular tachycardia (SVT): diagnosed by cardiologists based on electrocardiogram.

+ Kawasaki disease: based on the diagnostic criteria of the Japanese Kawasaki Research Committee and the American Heart Association [6].

+ Pulmonary hypertension: determined when systolic pulmonary artery pressure on echocardiography is ≥ 25 mmHg.

+ Systolic dysfunction: when cardiac function (EF) on ultrasound $< 50\%$.

- Control group: are healthy children similar in age and gender to the disease group.

Criteria for exclusion

Excluded from the study if patients have kidney failure, endocrine diseases, severe infections, pneumonia, obesity, or severe anemia.

Time and location of the study

Time: from April 2018 to May 2020.

Location: Clinic, Emergency department, Cardiovascular department, Intensive care department – Vietnam National Children's Hospital.

Method of study

Design of the study: Cross-sectional description, Selecting convenient samples. In this study, we selected 107 patients who met the criteria for selection of the study.

Steps to conduct the study: Patients with cardiovascular disease (disease group) had plasma NT-ProBNP concentration measured right at the time of admission when no treatment was used. For the control group, quantify plasma NT-ProBNP concentration at the time the child came for medical examination. Quantification of NT-ProBNP concentration by electrochemiluminescence immunoassay on Roche's Cobas e601 machine at the Department of Biochemistry, National Children's Hospital. We compared plasma NT-ProBNP concentrations between the patient group and control group and between cardiovascular disease groups.

Data processing and analysis

Data in the study were processed using SPSS software version 22. Variables in the study are expressed as numbers (n) and percentages. Data are presented as median with the 25th and 75th Interquartile range (25th, 75th Interquartile Range - IQR) for non-standard distribution. We use the Mann - Whiney test to compare the median of 2 independent samples for non-standard distribution.

Ethical considerations in the study

The study was approved by the Ethics Council of Hanoi Medical University. The child's family explained the study content and agreed to participate. The

study aims to improve the value of disease diagnosis without affecting the patient's health.

RESULTS

General characteristics of the study objects

Table 1. General characteristics

Characteristics	Quantity	Percentage (%)
Gender	Boy	59
	Girl	48
Age	< 1 year old	48
	1- 5 years old	30
	5 -15 years old	29
Types of disease	Myocarditis	32
	SVT	18
	Dilated cardiomyopathy	35
	Kawasaki	22
Average age (months)	15 ± 13.12	

Regarding gender, there are more men than women at the rate of 55.1% and 44.9%. Regarding age, it mainly occurs in the group under 1 year old (accounting for 45.9%). The average age of study subjects was 15 months. Dilated cardiomyopathy is the most common disease (accounting for 32.7%).

NT-ProBNP concentration in diagnosing some acquired heart diseases

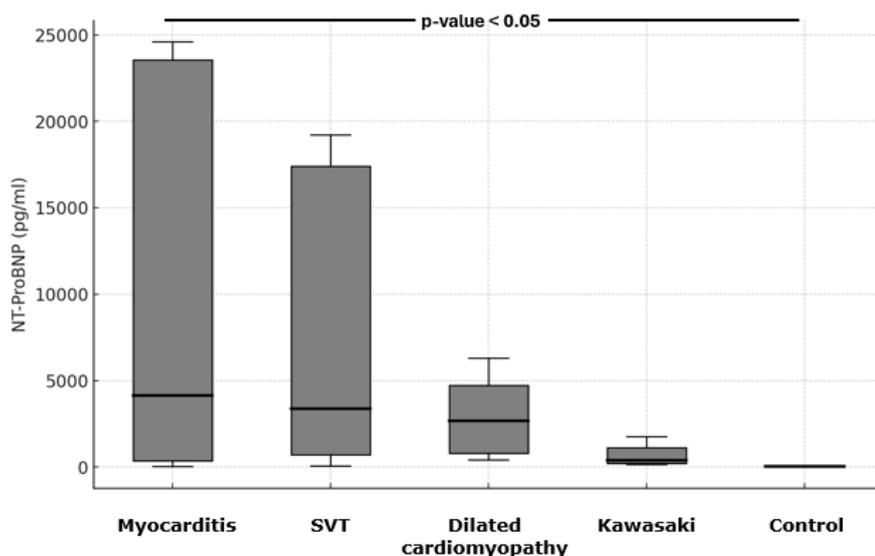


Figure 1. NT-ProBNP concentrations in some acquired heart diseases

NT-ProBNP concentration was highest in the myocarditis group, followed by paroxysmal supraventricular tachycardia and dilated myocardium, and lowest in the Kawasaki disease group ($p < 0.05$). NT-ProBNP concentrations in cardiovascular diseases were higher than in the control group with a statistically significant difference ($p < 0.05$).

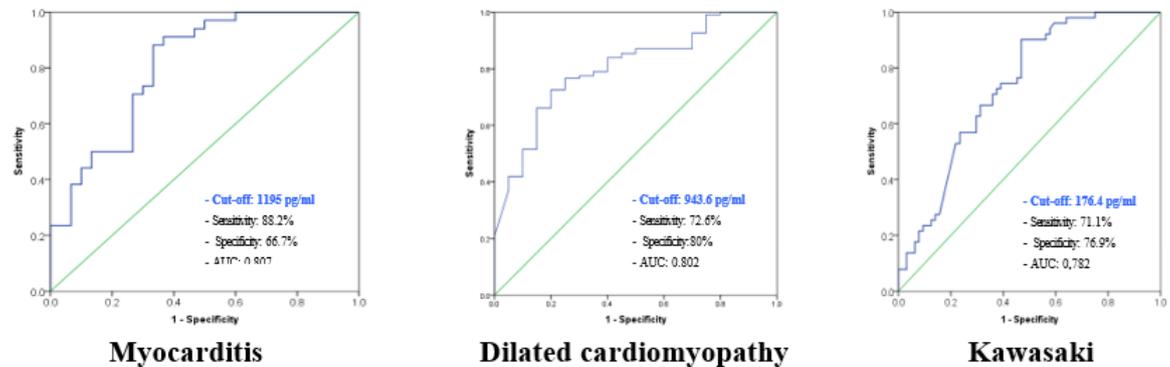


Figure 2. Roc curve of NT-ProBNP in diagnosing some heart diseases

The optimal cutoff point of NT-ProBNP is 1195 pg/ml, which is valuable for diagnosing myocarditis with other diseases with a sensitivity of 88.2% and a specificity of 66.7%. The optimal cutoff point of NT-ProBNP concentration is 943.6 pg/ml, which has a diagnostic value of dilated cardiomyopathy with a sensitivity of 72.6% and specificity of 80%. The optimal cutoff point of NT-ProBNP concentration is 176.4 pg/ml, which has diagnostic value for Kawasaki disease with a sensitivity of 71.1% and specificity of 76.9%.

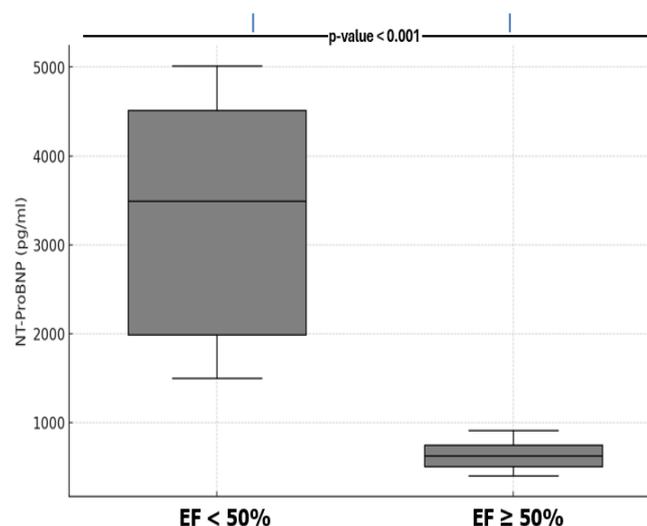


Figure 3. Relationship between NT-ProBNP and left ventricular ejection fraction

NT-ProBNP concentration in the group with systolic dysfunction ($EF < 50\%$) was statistically significantly higher than the group with normal systolic function ($EF \geq 50\%$) with $p < 0.001$.

DISCUSSIONS

In our study, NT-ProBNP concentrations in acquired heart diseases were statistically

significantly higher than the control group ($p < 0.05$) (Figure 1). Hemodynamic changes in cardiovascular diseases affect ventricular volume and pressure, especially the left

ventricle, causing increased plasma NT-ProBNP concentrations. Specifically, in acute myocarditis and dilated cardiomyopathy, hemodynamic disorders are caused by acute or chronic myocardial damage. In paroxysmal supraventricular tachycardia, hemodynamic disorders caused by too fast heart rate also increase the pressure and volume of the heart chambers, especially the left ventricle. In the pathogenesis of Kawasaki disease, there is no direct damage to the ventricles. Differences in pathogenesis are also the cause of differences in NT-ProBNP concentrations in these cardiovascular diseases. Specifically, NT-ProBNP concentrations increased highest in the myocarditis group, followed by paroxysmal supraventricular tachycardia, dilated myocardium, and the lowest in Kawasaki disease with a statistically significant difference ($p < 0.05$) (Figure 1).

According to Mlczoch E et al., in myocarditis in children, NT-ProBNP concentrations are elevated and have value in disease monitoring and prognosis. NT-ProBNP concentration decreased corresponding to the degree of improvement of the disease. Although diagnosis of the disease needs to be based on electrocardiogram, acute echocardiogram, and cardiopulmonary X-ray, these results show that NT-ProBNP is valuable in monitoring and treating acute myocarditis in children [7]. In dilated cardiomyopathy, Koura et al. also showed that there was a clear increase in NT-ProBNP concentration in patients compared to the control group, so it has diagnostic value [8]. Meanwhile, Mazurek B et al. showed that in pediatric arrhythmias, increases in NT-ProBNP concentration corresponded with arrhythmia severity. The author believes that quantifying NT-ProBNP concentrations is valuable for diagnosing and classifying the severity of arrhythmias [9]. In Kawasaki disease, some studies also show that NT-ProBNP concentrations are higher than in the control group and are valuable in diagnosing the disease. Specifically, Yu J et al. performed a

controlled study on 330 children with Kawasaki disease and the results showed that NT-proBNP concentrations were higher in the patient children [10]. Similarly, a study by Banerjee P et al. showed that NT-ProBNP concentrations in children with Kawasaki disease were higher than in age- and gender-matched infected children. Therefore, the author believes that NT-ProBNP is a valuable biomarker in the diagnosis of Kawasaki disease [11]. However, author Wen JX believes that the NT-ProBNP indicator cannot be used alone to diagnose the disease, but it needs to be combined with many other clinical and paraclinical factors [1].

According to our results, in the diagnostic value of cardiovascular diseases, the optimal cutoff point of NT-ProBNP is 1195 pg/ml, which has a suggestive value in diagnosing myocarditis with a sensitivity of 88.2% and specificity is 66.7%. This is the cutoff point to determine the boundary of NT-ProBNP concentration due to myocarditis with the control group of children without cardiovascular disease. Also, according to the study results, the optimal cut-off point of NT-ProBNP is 943.6 pg/ml, which has a suggestive value for dilated cardiomyopathy with a sensitivity of 72.6% and specificity of 80%. Meanwhile, the optimal cutoff point of NT-ProBNP concentration is 176.4 pg/ml, which has a diagnostic value for Kawasaki disease with a sensitivity of 71.1% and specificity of 76.9% (Chart 2). Other studies also provide some cut-off points for NT-ProBNP concentrations in diagnosing acquired heart diseases. Specifically, Zoair et al. reported that the NT-ProBNP cutoff point of 1500 pg/ml has a sensitivity of 85% and a specificity of 100% in diagnosing dilated cardiomyopathy [9].

In our study, NT-ProBNP concentrations at admission in the group with left ventricular systolic dysfunction ($EF < 50\%$) were higher than in the group with normal cardiac function ($EF \geq 50\%$) with a statistically significant difference ($p < 0.01$) (Figure 3). This result showed that NT-ProBNP concentration is related to left ventricular

systolic function status. Specifically, increased NT-ProBNP concentration was associated with decreased left ventricular systolic function and vice versa. Many studies also suggest that serum NT-ProBNP concentration can serve as a diagnostic and prognostic tool for left ventricular dysfunction in children. Therefore, regularly quantifying NT-ProBNP concentration helps detect ventricular dysfunction [2], [8]. According to Rusconi et al., the cutoff point of serum NT-ProBNP concentration of 1000 pg/ml is valuable for diagnosing left ventricular dysfunction in children. The study shows that, for children with NT-proBNP concentrations between 450 and 1000 pg/ml, it is necessary to quantify this index serially (at least 3 times) to assess heart function more accurately [2]. Currently, assessment of left ventricular systolic function in children is still mainly based on echocardiography. However, the accuracy of echocardiography depends on the cardiologist and is difficult to perform regularly and quickly. Therefore, the application of the method to quantify serum NT-ProBNP concentration is very important clinically to monitor cardiac function during treatment.

CONCLUSIONS

Researching the diagnostic value of NT-ProBNP in 107 patients with acquired heart disease at the Vietnam National Children's Hospital, we concluded: NT-ProBNP concentrations increase in myocarditis, dilated cardiomyopathy, supraventricular tachycardia, and Kawasaki diseases. NT-ProBNP concentration correlates with left ventricular systolic function.

REFERENCES

1. Wen JX, Bai X, Niu Y, Hu ZD (2021). Diagnostic accuracy of N-terminal pro-brain natriuretic peptide for Kawasaki disease: An updated systematic review

- and meta-analysis. *Int J Clin Pract.* 75(11):e14538.
2. Rusconi P.G., Ludwig D.A., Ratnasamy C., et al. (2010). Serial Measurements of Serum NT-proBNP as Markers of Left Ventricular Systolic Function and Remodeling in Children with Heart Failure. *Am Heart J*, 160(4), 776–783.
3. Koura H.M., Abdalla N.M., Hamed Ibrahim M., et al. (2016). NT-proBNP in Children With Left to Right Shunt and Dilated Cardiomyopathy. *Iran J Pediatr*, 26(3); e4485.
4. Zhou F.-J., Zhou C.-Y., Tian Y.-J., et al. (2014). Diagnostic value of analysis of H-FABP, NT-proBNP, and cTnI in heart function in children with congenital heart disease and pneumonia. *Eur Rev Med Pharmacol Sci*, 18(10), 1513–1516.
5. Sagar S, Liu PP, Cooper LT (2012). Myocarditis. *The Lancet.*;379(9817):738-47.
6. Japanese Circulation Society Joint Research Group (2005). Guidelines for diagnosis and management of cardiovascular sequelae in Kawasaki disease. *Pediatr Int*; 47(6), 711-32.
7. Mlczoch E, Darbandi-Mesri F, Luckner D, et al (2012). NT-pro BNP in acute childhood myocarditis. *J Pediatr*;160(1):178-9.
8. Koura HM, Abdalla NM, Hamed Ibrahim M, et al (2016). NT-proBNP in Children With Left to Right Shunt and Dilated Cardiomyopathy. *Iran J Pediatr* ;26(3):e4485.
9. Mazurek B., Szydłowski L., Giec-Fuglewicz G., et al. (2009). N-terminal prohormone brain natriuretic peptide-proBNP levels in ventricular arrhythmias in children. *Clin Cardiol*, 32(12), 690–694.
10. Yu J., Li H.-H., and Dong L. (2016). Meta-analysis: Diagnostic Value of N-Terminal Pro-brain Natriuretic Peptide for Kawasaki Disease. *Clin Lab*, 62(10), 1903–1910.

11. Banerjee P, Pal P, Chakravarti S, Basu S, Ahmed N (2023). N-Terminal Pro-Brain Natriuretic Peptide Levels in Kawasaki Disease, Sepsis and Other Febrile Illnesses. *Indian Pediatr*;60(10):826-828.
12. Zoair, Amr M, Mawlana, Wegdan H et al (2014). Serum levels of aminoterminal of probrain natriuretic peptide (NT-Pro BNP) as a diagnostic and prognostic biomarker in children with dilated cardiomyopathy. *Tanta Medical Journal*; 42(2):p 53-57.