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**CONTENTS**

RESEARCH



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Rismawati Yaswir, July Kumalawati, Mansyur Arif, Rahayuningsih Dharma,
Nurhayana Sennang Andi Nanggung, AAG. Sudewa, Ninik Sukartini, Tahono, M. Yolanda Probohoesodo

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RESEARCH

# CORRELATION BETWEEN NT-PROBNP AND LEFT VENTRICULAR EJECTION FRACTION BY ECHOCARDIOGRAPHY IN HEART FAILURE PATIENTS

*(Kenasaban antara Kadar NT-proBNP dan Fraksi Ejeksi Ventrikel Kiri Secara Ekokardiografi di Pasien Gagal Jantung)*

**Mutiara DS[1], Leonita Anniwati[1], M. Aminuddin[2]**

***ABSTRAK***

*Petanda biologis $NH_2$-terminal fragment of proBrain Natriuretic Peptide (NT-proBNP) berguna untuk diagnosis dini, menyingkirkan gejala klinis yang berasal dari luar jantung serta pemantauan pengobatan dan meramalkan perjalanan penyakit pasien gagal jantung. Pemeriksaan NT-proBNP dapat dilakukan secara otomatis, sehingga hasil tidak bersifat subjektif. Pemeriksaan ekokardiografi merupakan pemeriksaan penunjang yang telah umum digunakan untuk mendiagnosis gagal jantung. Namun, pemeriksaan ekokardiografi tidak selalu tersedia di seluruh rumah sakit, khususnya rumah sakit di daerah, serta memerlukan tenaga ahli untuk melakukan pemeriksaan dan hasil pemeriksaan bersifat subjektif. Salah satu tolok ukur yang dinilai pada pemeriksaan ekokardiografi adalah fraksi ejeksi ventrikel kiri. Penelitian ini bertujuan untuk mengetahui kenasaban antara kadar NT-proBNP dengan fraksi ejeksi ventrikel kiri yang diperoleh dari pemeriksaan ekokardiografi. Penelitian bersifat quasi experimental dengan pendekatan pretest and posttest only without control. Sampel penelitian berjumlah 41 orang, dikumpulkan selama bulan Februari–April 2015 dari Ruang Perawatan Jantung RSUD Dr. Soetomo Surabaya. Pemeriksaan kadar NT-proBNP menggunakan metode chemiluminescent (Immulite 1000) dengan prinsip solid-phase two site chemiluminescent immunometric assay. Hasil dianalisis secara statistik menggunakan uji kenasaban Spearman's, uji t 2 sampel berpasangan, Kruskal Wallis dan Mann Whitney. Rentang kadar NT-proBNP sebelum dan sesudah pemberian pengobatan di pasien gagal jantung masing-masing antara 1.296–34.374 pg/mL dengan rerata 10.422,49 pg/mL (Simpang Baku (SB) 8.608,05) dan 997–34.401 pg/mL dengan rerata 8.899,41 pg/mL (SB 8.489,46). Rentang persentase fraksi ejeksi ventrikel kiri sebelum dan sesudah pemberian pengobatan di pasien gagal jantung masing-masing antara 20–62% dengan rerata 35,61% (SB 10,00) dan 22–71% dengan rerata 41,49% (SB 10,96). Didapatkan perbedaan bermakna rerata kadar NT-proBNP serta persentase fraksi ejeksi ventrikel kiri sebelum dan sesudah pemberian pengobatan di pasien gagal jantung dengan setiap nilai p=0,001. Didapatkan kenasaban negatif yang bermakna antara kadar NT-proBNP dan fraksi ejeksi ventrikel kiri di pasien gagal jantung sebelum dan sesudah pemberian pengobatan dengan masing-masing nilai p=0,001, r=-0,81 dan nilai p=0,001, r=-0,80. Didapatkan kenasaban negatif yang bermakna antara kadar NT-proBNP dengan fraksi ejeksi ventrikel kiri di pasien gagal jantung sebelum dan sesudah pemberian pengobatan. Berdasarkan hal tersebut maka pemeriksaan petanda biologis NT-proBNP dapat diusulkan untuk digunakan sebagai tolok ukur pilihan pengganti ekokardiografi untuk gagal jantung.*

***Kata kunci:*** *NT-proBNP, fraksi ejeksi ventrikel kiri, gagal jantung*

**ABSTRACT**

Biological marker $NH_2$-terminal fragment of pro-Brain Natriuretic Peptide (NT-proBNP) is useful for early diagnosis, to role out the clinical symptoms originating from outside the heart, monitoring treatment and predicting prognosis in heart failure patients. NT-proBNP eaxamination can be done automatically, so the results are not subjective. Echocardiography is the examination commonly used to help diagnosing heart failure. However, echocardiography is not always available in all hospitals, especially small hospitals in the rural areas and requires expertise in conducting examination and the results are subjective. One of the parameters assessed by echocardiography is the left ventricular ejection fraction (LVEF). The study design was quasi-experimental with pre-test and post-test approach only without control. Samples consisted of 41 subjects collected from February to April 2015 from the

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Cardiology Unit, Dr. Soetomo Hospital, Surabaya. NT-pro BNP was examined using a solid-phase two-site chemiluminescent immunometric assay as the principle. The results were statistically analyzed using Spearman's correlation test, two sample paired t test, Kruskal Wallis and Mann Whitney test. NT-proBNP levels before and after therapy in heart failure patients were each between 1,296–3,474 pg/mL, mean 10,422.49 pg /mL (SD 8,608.05) and 997–3,401 pg/mL, mean 8,899.41 pg/mL (SD 8,489.46). The range of the percentage of LVEF before and after therapy in heart failure patients was etween 20–62%, mean 35.61% (SD 10.00) and 22–71%, mean 41.49% (SD 10.96). Significant differences in mean levels of NT-proBNP and LVEF before and after therapy in heart failure patients with each value of p=0.001 were found. A significant negative correlation between levels of NT-proBNP with LVEF in heart failure patients before and after therapy with the values of p=0.001, r=-0.81 and p=0.001, r=-0. 80, respectively was also shown. A significant negative correlation between the levels of NT-proBNP with LVEF in heart failure patients before and after therapy was found. Based on these conditions, examination of biological markers NT-proBNP can be suggested to be used as an alternative to echocardiography parameters for heart failure.

**Key words:** NT-proBNP, left ventricular ejection fraction (LVEF), heart failure

## INTRODUCTION

Changes in lifestyle causes a disease patterns change, from infectious diseases and malnutrition disease becoming chronic degenerative diseases such as heart disease and blood vessels. Heart failure is a complex clinical syndrome known as caused by damage to the structure or function of the heart so that the filling and ejection ability becomes impaired. Incidence and prevalence of heart failure tend to increase at this time. Heart failure patients who were treated at Dr. Soetomo Hospital during 2014, based on data obtained through the fields of marketing and medical records listed 673 people.[1–4]

Echocardiography is the examination that has been commonly used to diagnose heart failure. One of the parameters was assessed on echocardiography wasleft ventricular ejection fraction Left Ventricle Ejection Fraction (LVEF). Heart failure patients will generally experience a decrease in the percentage of LVEF to <50%. Echocardiography is not always available in all hospitals and requires expertise in conducting examination. The results of echocardiography can be subjective, because it depends on the interpretation of experts who perform the examination. Some of these limitations become the reason of the research on biological markers for heart failure. Biological markers for heart failure is expected to have a high sensitivity and specificity as well as to correlate well with echocardiography as the examination that has been more commonly used to diagnosis and monitoring of therapy for heart failure patients.

A laboratory examination of parameter group natriuretic peptide neurohormones, especially Brain

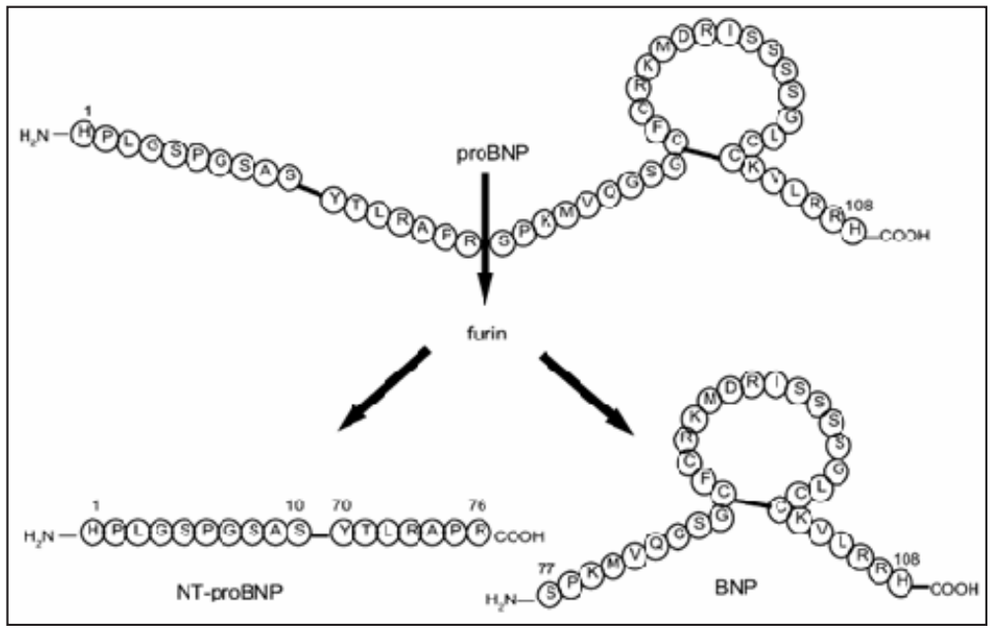


**Figure 1.** ProBNP schematic of showing the enzymatic breakdown into NT-proBNP.[5]

Natriuretic Peptide (BNP) and the $NH_2$-terminal fragment of pro-Brain Natriuretic Peptide (NT-proBNP), has been developed since the last few years.Biological marker $NH_2$-terminal fragment of pro-Brain Natriuretic Peptide (NT-proBNP) is useful for early diagnosis, to role out the clinical symptoms that originate from outside the heart, monitoring treatment and predicting prognosis in heart failure patients. NT-proBNP eaxamination can be done automaticly, so the result are not subjective.[5–7]

NT-proBNP levels are associated with the degree of heart failure functional classification according to the New York Heart Association (NYHA). Some literature mentions the possibility of heart failure when levels of NT-proBNP >300 pg/mL. The level of NT-proBNP in serial data is useful for monitoring therapy, supporting the clinical improvement indicators, define more aggressive treatment and predict prognosis in heart failure patients.NT-proBNP levels decreased by 30% or more, had a better prognosis than when the levels rise.[8–10]

Research on NT-proBNP has been done, but until now there is no data to explain the NT-proBNP in patients with heart failure in the Dr. Soetomo Hospital. This study aimed to determine the correlation between the levels of NT-proBNP and LVEF by echocardiography. Levels of NT-proBNP in this study are expected to have a strong correlation with LVEF, so that it later can be used as a surrogate parameter for echocardiography to diagnosis, monitoring therapy and supporting indicators of clinical improvement in patients with heart failure.

## METHODS

The study design was quasi-experimental with pre-test and post-test approach only without control.

This study used samples of cubital vein blood examined for NT-proBNP examination. NT-proBNP was examined using a solid-phase two-site chemiluminescent immunometric assay as the principle. The samples were 41 subjects collected from February to April 2015 from the Cardiology and Vascular Unit, Dr. Soetomo Hospital, Surabaya.

NT-proBNP examination was conducted at the Laboratory of Clinical Pathology in the Dr. Soetomo Hospital, while ecocardiography examined in the Cardiology and Vascular unit in the Dr. Soetomo Hospital. The samples were heart failure patients treated in the cardiology unit collected from February to April 2015.

## RESULTS AND DISCUSSION

In this study, the samples were obtained from 22 males (53.66%) and 19 females (46.34%) with the mean age of 54.46 years and range between 40 to 71 years old.

Based on Body Mass Index (BMI), the mean BMI was 25.26 kg/$m^2$ and the range between 23 to 27.8 kg/$m^2$. This result was based on the WHO classification (2000), including criteria for obesity I. This is in consistance with one of the risk factors associated with heart failure that is obesity. Obesity showns a correlation with the high incidence of cardiovascular disease. Obesity can raise triglyceride levels that would be bad for heart health and lowers levels of High Density Lipoprotein (HDL), which is cardioprotective. Moreover, with increasing obesity, increasing numbers are also hypertensive. Obesity can also lead to diastolic dysfunction and is associated with wosening systolic function.[11]

The mean systolic and diastolic blood pressure in this study were 126.58 mmHg with a range between 90 to 160 mmHg and 77.07 mmHg with a range between 60 to 100 mmHg. The results of this study are not consistance with hypertension as one of the risk factors of heart failure. This condition could be caused by most patients having regularly taking antihypertensive drugs, so that the patient's blood pressure was well controlled.

The mean hemoglobin (Hb) level in the study was 12.82 g/dL with a range between 10 to 15.6 g/dL. The results of this study are not consistance with anemia as one of the trigger factors of heart failure. Level range Blood Urea Nitrogen (BUN) and creatinine patients in the study, respectively between 11 to 36 mg/dL, with the mean of 24.05 mg/dL and 0.7 to 1.2 mg/dL with the mean of 0.97 mg/dL. The results in this study showed there was little increase in mean BUN levels with a normal mean serum creatinine. It has not been able to show any abnormalities in kidney function. Several factors can cause this condition such as a high-protein diet or dehydration.

The mean Glomerular Filtration Rate (GFR) of patients in the study was 72.32 mL/min/1,73$m^2$, with a range between 60.2 to 123.6 mL/min/1,73$m^2$. Calculation of GFR in this study used the formula GFR (Estimated Glomerular Filtration Rate) Cockroft-Gault. Patients in this study mostly had a mild decreased GFR with normal serum creatinine levels. It can be caused due to aging. Because after 30 years of age, GFR values fell about 1 mL/min/year, so with age, the GFR values would decrease. This situation would be accompanied

by normal creatinine serum levels, because the serum creatinine level was influenced by muscle mass. Muscle mass will generally decrease with age, so levels of serum creatinine would appear normal or lower at older ages.[12]

Heart failure patients in this study consisted of patients with heart failure class DCFC II, DCFC III and DCFC IV. The highest percentage of patients with heart failure was DCFC IV (58.53%).

The mean of NT-proBNP levels before therapy in heart failure patients in the study was 10,422.49 pg/mL (SD 8,608.05), with the range between 1,296 to 34,374 pg/mL. These results were consintent with the criteria contained in the diagnosis of heart failure algorithm based on examination of natriuretic peptides.

Therapy in patients with heart failure is expected to reduce stress and dilatation of the myocardium, which will reduce levels of biological markers, including NT-proBNP. The results of this study showed that the mean levels of NT-proBNP in patients with heart failure after therapy was 8,899.41 pg/mL (SD 8,489.46), with the range between 997 to 34,401 pg/mL. There were differences between the mean levels of NT-proBNP before and after therapy (delta NT-proBNP) in heart failure patients in this study, which was 1,523.08 pg/mL. Differences in mean levels of NT-proBNP before and after therapy in this study was statistically significant, with p=0.001.

NT-proBNP levels also correlated with heart failure class according to the NYHA classification system. The results of this study showed that the mean levels of NT-proBNP for each class of heart failure according to NYHA was 5,390.33 pg/mL for DCFC class II, 6,720.57 pg/mL for DCFC class III and 13,210.95 pg/mL for class DCFC IV. There was a significant difference statistically using the Wilcoxon Signed Ranks Test, between NT-proBNP levels before and after treatment in each class heart failure DCFC III and DCFC IV with p=0.001. This showed that the treatment given to samples of heart failure patients in this study was quite effective, so that it could reduce stress and dilatation of the myocardium, which resulted in lower levels of NT-proBNP.

The results of this study showed that the average percentage of LVEF in heart failure patients before therapy was 35.61%. These results were consistent with the literature that stated that in patients with heart failure will usually decrease LVEF to less than 50%. Therapy in patients with heart failure is expected to increase the percentage of LVEF. This was consistent with the results obtained in this study, for the mean percentage of LVEF after therapy was 41.49%. The mean difference in the results of serial LVEF before and after treatment obtained in this study were statistically significant, with p=0.001.

Data levels of NT-proBNP and the percentage of LVEF before and after therapy that has been obtained,

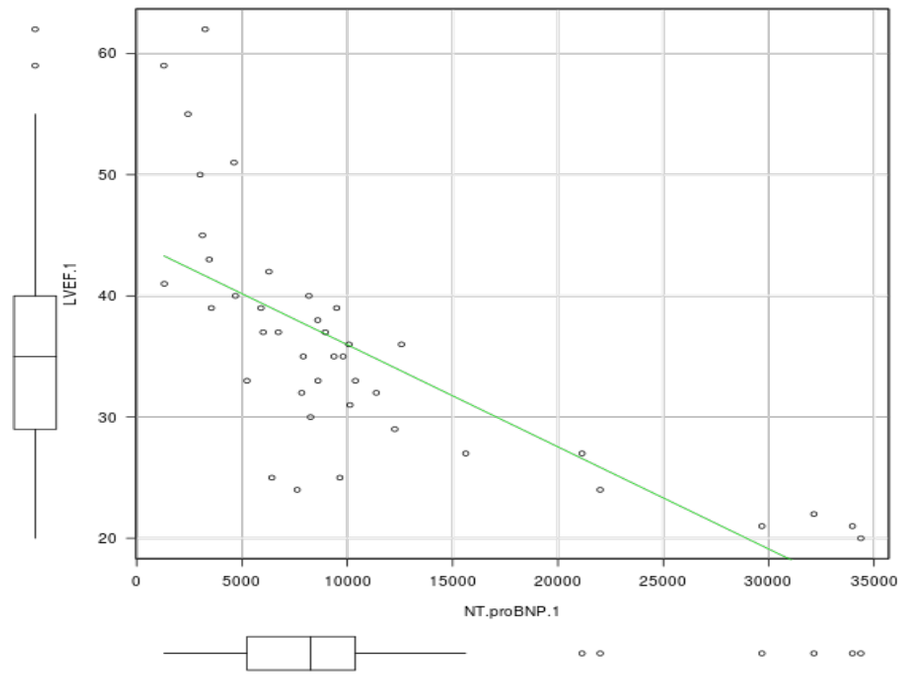


**Figure 2.** The correlation between the levels of NT-proBNP and LVEF by echocardiography before therapy (p=0.001; r=-0.81).

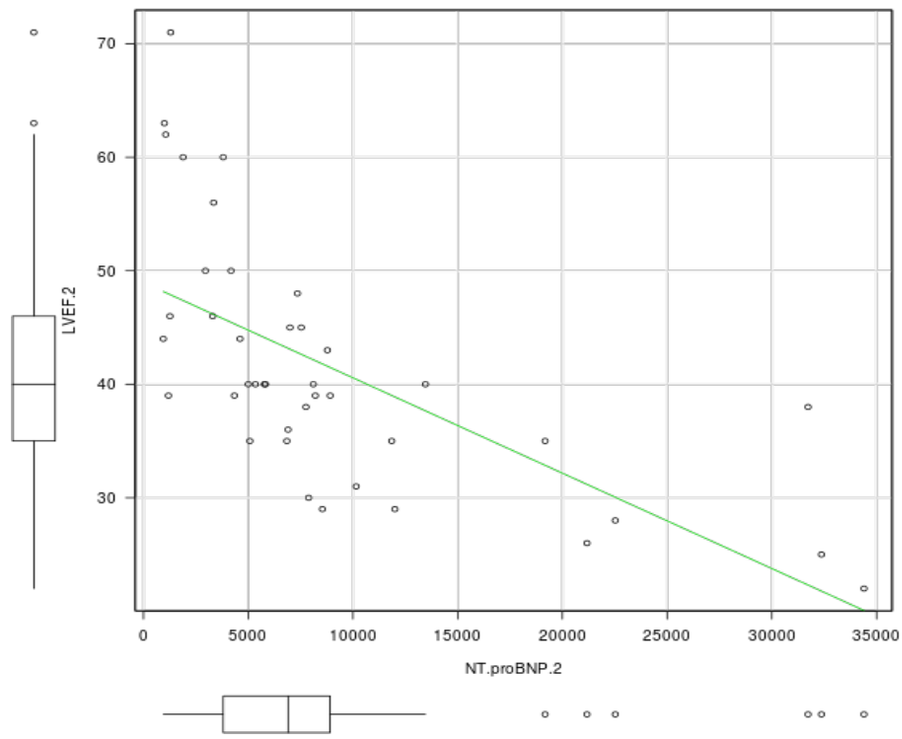


**Figure 3.** The correlation between the levels of NT-proBNP and LVEF by echocardiography after therapy (p=0.001; r =-0.80).

then performed correlation test, respectively showed a asignificant negative correlation with p=0.001, r=-0.81 and p=0.001, r=-0.80.

Based on the analysis in this study, a strong correlation between levels of NT-proBNP with LVEF in heart failure patients both before and after therapy was obtained, the examination of biological markers NT-proBNP can be proposed to be used as an alternative parameter instead of LVEF examination in echocardiography for heart failure. Both in terms of helping diagnosis of heart failure and for monitoring therapy in heart failure patients. However, based on these results, it can not yet use the levels of NT-proBNP as a parameter to predict the percentage of LVEF by echocardiography in the general population. This is due to the fact that the sample size was too small.

## CONCLUSIONS AND SUGESTION

The results showed a significant negative correlation between the levels of NT-proBNP with the percentage of LVEF in heart failure patients before and after therapy each with p=0.001, r=-0.81 and p=0.001, r=-0.80. Based on these conditions, examination of biological markers NT-proBNP can be suggested to be used as an alternative for echocardiography parameters in heart failure.

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