EDITORIAL TEAM

Editor-in-chief:
Puspa Wardhani

Editor-in-chief Emeritus:
Prihatini
Krisnowati

Editorial Boards:

Editorial Assistant:
Dian Wahyu Utami

Language Editors:
Yolanda Probohoesodo, Nurul Fitri Hapsari

Layout Editor:
Akbar Fahmi

Editorial Adress:
d/a Laboratorium Patologi Klinik RSUD Dr. Soetomo Jl. Mayjend. Prof. Dr Moestopo 6–8 Surabaya, Indonesia
Telp/Fax. (031) 5042113, 085-733220600 E-mail: majalah.ijcp@yahoo.com, jurnal.ijcp@gmail.com
Website: http://www.indonesianjournalofclinicalpathology.or.id

Accredited No. 36a/E/KPT/2016,Tanggal 23 Mei 2016
CONTENTS

RESEARCH

The Morphological Features of Erythrocytes in Stored Packed Red Cells
(Gambaran Morfologi Eritrosit di Packed Red Cells Simpan)
Dewi Sri Kartini, Rachmawati Muhiddin, Mansyur Arif .......................................................... 103–106

Correlation of Advanced Glycation End Products with Urinary Albumin Creatinin Ratio in Patients
with Type 2 Diabetes Mellitus
(Kenasaban Kadar Advanced Glycation End Products dengan Rasio Air Kemih Albumin Kreatinin di
Pasien Diabetes Melitus Tipe 2)
Debie Anggraini, Rismawati Yaswir, Lillah2, Husni .................................................................. 107–110

Monocyte Lymphocyte Ratio in Dengue Hemorrhagic Fever
(Monocyte Lymphocyte Ratio di Dengue Hemorrhagic Fever)
Dwi Retnoningrum, Purwanto AP .................................................................................................. 111–113

Correlation between NT-proBNP and Left Ventricular Ejection Fraction by Echocardiography in Heart
Failure Patients
(Kenaskan antara Kadar NT-proBNP dan Fraksi Ejeksi Ventrikel Kiri Secara Ekokardiografi di Pasien
Gagal Jantung)
Mutia DS, Leonita Anniwati, M. Aminuddin .............................................................................. 114–118

Detection of Mycobacterium Tuberculosis with TB Antigen Rapid Test in Pulmonary Tuberculosis
Patients with Four Types of Spuctum Sample Preparation
(Deteksi Antigen Mycobacterium Tuberculosis Menggunakan TB Antigen Uji Cepat di Pasien Tuberkulosis
Paru dengan 4 Cara Preparasi Dahak)
Miftahul Ilmiah, IGAA. Putri Sri Rejeki, Betty Agustina Tambunan ...................................................... 119–125

Diagnoatstic Test of Hematology Parameter in Patients Suspect of Malaria
(Uji Diagnostik Tolok Ukur Hematologi di Pasien Terduga Malaria)
Ira Ferawati, Hanifah Maani, Zelly Dia Rofinda, Desywar .................................................................... 126–130

Comparison Results of Analytical Profile Index and Disc Diffusion Antimicrobial Susceptibility Test to
Technical Dedicated Reasonable 300B Method
(Perbandingan Hasil Analytical Profile Index dan Uji Kepekaan Antibiotika Difusi Cakram dengan
Metode Technical Dedicated Reasonable 300B)
IG Eka Sugiartha, Bambang Pujo Semedi, Ruspa Wardhani, IGAA Putri Sri Rejeki ........................................ 131–137

The Agreement between Light Criteria and Serum Ascites Albumin Gradient for Distinguishing
Transudate and Exudate
(Kesesuaian Patokan Light dengan Serum Ascites Albumin Gradient dalam Membedakan Transudat dan
Eksudat)
Rike Puspasari, Lillah, Efrida ........................................................................................................ 138–140

Correlation between Serum Tissue Polypeptide Specific Antigen Level and Prostate Volume in BPH
(Kenasaban antara Kadar Tissue Polypeptide Specific Antigen Serum dan Volume Prostat di BPH)
Mahrany Graciella Bumbungan, Endang Retnowati, Wahjoe Djatisoesanto ........................................... 141–145
Correlation of Antinuclear Antibody Profile with Hematologic and Renal Disorders in Systemic Lupus Erythematosus

(Hubungan Antinuclear Antibody Profile dengan Gangguan Hematologi dan Ginjal di Systemic Lupus Erythematosus)

Chelvi Wijaya, Asvin Nurulita, Uleng Bahrun

Identification of Dengue Virus Serotypes at the Dr. Soetomo Hospital Surabaya in 2016 and its Correlation with NS1 Antigen Detection

(Identifikasi Serotipe Virus Dengue di RSUD Dr. Soetomo Surabaya Tahun 2016 serta Kenasabannya dengan Deteksi Antigen NS1)

Jeine Stela Akualing, Aryati Puspa Wardhani, Usman Hadi

Correlation of Coagulation Status and Ankle Brachial Index in Diabetes Mellitus Patients with Peripheral Arterial Disease

(Hubungan Status Koagulasi terhadap Nilai Ankle Brachial Index Pasien Penyakit Arteri Perifer dengan Diabetes Melitus)

Lany Anggreani Hutagalung, Adi Koesema Aman, Syanti Syafri

The Difference of Plasma D-dimer Levels in Acute Myocardial Infarction with and without ST Elevation

(Perbedaan Kadar D-dimer Plasma di Infark Miokard Akut dengan ST Elevasi dan Tanpa ST Elevasi)

Desi Kharina Tri Murni, Adi Koesoema Aman, Andre Pasha Ketaren

Fructosamine and Glycated Albumin in Patients with Type 1 Diabetes Mellitus During Ramadhan Fasting

(Fruktosamin dan Albumin Glikat di Pasien Diabetes Melitus Tipe 1 yang Menjalankan Puasa Ramadhan)

Vinzy Yulina, Sidarti Soehita, Muhammad Faizi, Budiono

Diagnostic Test on the Fourth Generation Human Immunodeficiency Virus in HIV Suspects

(Uji Diagnostik Human Immunodeficiency Virus Generasi Keempat di Terduga HIV)

Sofitri, Ellyza Nasrul, Almurdy, Efriida

Correlation of Neutrophils/Lymphocytes Ratio and C-Reactive Protein in Sepsis Patients

(Kenasaban antara Rasio Neutrofil/Limfosit dan C-Reactive Protein di asien Sepsis)

Henny Elfira Yanti, Fery H Soedewo, Puspa Wardhani

Differences of Lymphocyte Proliferation Index After Culture Filtrate Protein 10 Stimulation in Patients with Active and Latent Tuberculosis and Healthy Individuals

(Perbedaan Indeks Proliferasi Limfosit Pascastimulasi Culture Filtrate Protein 10 di Pasien Tuberkulosis Aktif, Laten dan Orang Sehat)

Binar R. Utami, Betty Agustina T, Suprapto Ma'at

LITERATURE REVIEW

Glycated Hemoglobin A1c as a Biomarker Predictor for Diabetes Mellitus, Cardiovascular Disease and Inflammation

(Glikasi Hemoglobin A1c sebagai Petanda Biologis Peramal Diabetes Melitus Penyakit Kardiovaskular dan Inflamasi)

Indranila KS

CASE REPORT

Erythroleukemia

(Airitroleukemia)

Allinda Theodora Tedja, Riadi Wirawan
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 DS1, Leonita Anniwati1, M. Aminuddin2

Biological marker NH2-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 examination 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 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 kadar NT-proBNP serta persentase fraksi ejeksi ventrikel kiri sebelum dan sesudah pemberian pengobatan 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 pengganti ekokardiografi untuk gagal jantung.

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

1 Department of Clinical Pathology, Faculty of Medicine, Airlangga University-Dr. Soetomo Hospital, Surabaya, Indonesia.
2 Department of Cardiology and Vascular Medicine, Faculty of Medicine, Airlangga University, Surabaya, Indonesia

E-mail: dr.moethi@yahoo.co.id
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 between 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 was left 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 natriuretic peptide neurohormones, especially Brain
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 rule out the clinical symptoms that originate from outside the heart, monitoring treatment and predicting prognosis in heart failure patients. NT-proBNP examination can be done automatically, 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 1. This is in consistence with one of the risk factors associated with heart failure that is obesity. Obesity shows 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 worsening 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 consistence 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 consistence 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/1.73m$^2$, with a range between 60.2 to 123.6 mL/min/1.73m$^2$. Calculation of GFR in this study used the formula GFR (Estimated Glomerular Filtration Rate) Cockcroft-Gault. Patients in this study mostly had a mild decreased GFR with normal serum creatinine levels. It has not been 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 consistent 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, then performed correlation test, respectively showed a significant negative correlation with p=0.001, r=-0.81.

![Figure 2](image.png)
then performed correlation test, respectively showed a significant 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.

**REFERENCES**