CHANGES ON SERUM TROPONIN T LEVEL BEFORE AND AFTER TAKING STANDARD THERAPY MEDICATION IN HEART FAILURE PATIENTS

Yen Yen Ari Indrawijaya[1], Suharjono[2], Muhammad Aminuddin[3], Endang Retnowati[4], Gilang Mauladi Rahman[3]

[1]Master Program of Clinical Pharmacy, [2]Department of Clinical Pharmacy, Faculty of Pharmacy, Universitas Airlangga, [3]Department of Cardiology and Vascular Medicine, [4]Department of Clinical Pathology Medicine, Soetomo Teaching Hospital Surabaya, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

ABSTRACT

Patients with advanced heart failure (NYHA FC III and IV heart failure) had positive cardiac troponin levels in previous cohort studies. In heart failure, cardiac troponin T (cTnT) is a biomarker that is sensitive to myocardial damage, especially myocardial necrosis. However, there is still little information regarding changes in cTnT levels during standard therapy. This prospective observational study is aimed at evaluating changes in cTnT levels before and after the administration of standard therapy and evaluating symptom improvement before and after the administration of standard therapy in patients with severe heart failure. Measurement of cTnT levels and symptom improvement parameters before treatment was carried out on the first day of the inpatient and measurement after therapy was carried out on the last day of the inpatient. Sampling was done by consecutive sampling and found 30 patients in the inpatient room of the SMF Cardiovascular Disease, Dr. Soetomo Hospital, Surabaya during the months of May-July 2017. The results of the study obtained the average cTnT levels before therapy 33.48 ± 31.88 pg/ml and the average cTnT levels after therapy 46.32 ± 52.68 pg/ml. Based on the statistical difference test with the Wilcoxon sign-ranked test, there was no significant change in cTnT levels (p = 0.318). On the parameter of clinical symptom improvement, there was a significant decrease in pulse, respiratory rate, blood pressure, and mean arterial pressure before and after administration of therapy (p <0.05). There was no change in troponin T levels before and after the administration of therapy meant there was no worsening of myocardial necrosis.

***Keywords**: Heart failure; standard therapy; cardiac troponin T; myocardial necrosis*

ABSTRAK

Pasien dengan gagal jantung berat (gagal jantung NYHA FC III dan IV) memiliki kadar troponin jantung yang positif pada penelitian kohort sebelumnya. Pada gagal jantung, troponin T jantung (cTnT) merupakan biomarker yang sensitif pada kerusakan miokard khususnya nekrosis miokard. Namun, masih sedikit informasi mengenai perubahan kadar cTnT selama pemberian terapi standar. Penelitian observasional prospektif ini ditujukan untuk mengevaluasi perubahan kadar cTnT sebelum dan setelah pemberian terapi standar dan mengevaluasi perbaikan gejala sebelum dan setelah pemberian terapi standar pada pasien gagal jantung berat. Pengukuran kadar cTnT dan parameter perbaikan gejala sebelum terapi dilakukan pada hari pertama pasien rawat inap dan pengukuran setelah terapi dilakukan pada hari terakhir pasien rawat inap. Pengumpulan sampel dilakukan dengan consecutive sampling dan didapatkan 30 pasien di ruang rawat inap SMF Penyakit Jantung dan Pembuluh Darah RSUD Dr. Soetomo Surabaya selama bulan Mei-Juli 2017. Hasil penelitian diperoleh rerata kadar cTnT sebelum terapi 33,48 ± 31,88 pg/ml dan rerata kadar cTnT setelah terapi 46,32 ± 52,68 pg/ml. Berdasarkan uji beda secara statistik dengan Wilcoxon sign-ranked test tidak didapatkan perubahan kadar cTnT yang signifikan (p = 0,318). Pada parameter perbaikan gejala klinis terjadi penurunan yang signifikan antara nadi, laju pernafasan, tekanan darah dan tekanan arteri rata-rata sebelum dan setelah pemberian terapi (p < 0,05). Tidak terdapat perubahan kadar troponin T sebelum dan setelah pemberian terapi berarti tidak terdapat perburukan dari nekrosis miokard.

***Kata kunci**: Gagal jantung; terapi standar; troponin T jantung; nekrosis miokard*

Correspondence: Yen Yen Ari Indrawijaya, Jalan Mulyorejo, Surabaya, Indonesia 60115.
Phone: +6285931235299. E-mail: yenyen.indrawijaya@gmail.com

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INTRODUCTION

Heart failure is a complex clinical syndrome and is the result of structural and functional disorders of ventricular filling and expulsion. The main manifestations of heart failure are tightness and fatigue which can limit exercise tolerance and fluid retention, causing lung and/or splenic congestion and peripheral edema (Yancy et al 2013). Heart failure becomes a significant public health problem related to mortality, morbidity and health care costs especially in patients aged> 65 years (Roger 2013). After patients hospitalized with heart failure, patients have a high risk of returning admission with a 25% return on admission at 1 month (Krumholz et al 2012).

Currently the severe heart failure population (NYHA FC III and IV) has a 1-year mortality rate of around 50% and requires therapeutic intervention. Treatment options for advanced heart failure include a combination of drugs, mechanical devices, and surgical procedures that can improve symptoms and survival (Friedrich & Bohm 2007). Based on studies of risk stratification using a combination of troponin T and brain natriuretic peptide in 93 patients with class III and IV heart failure, troponin T levels >33 pg/ml when Admission is associated with an increased risk of cardiac death (Ishii et al 2002).

The goal of heart failure therapy is to reduce morbidity and mortality (PERKI 2015). Administration of ACEI, ARB, beta blockers and aldosterone antagonists aims to improve morbidity and mortality while administration of diuretics, digitalis, transient inotropes and certain antiarrhythmias aims to control symptoms (Hunt 2005, Swedberg et al 2005). The standard therapy given includes ACEI, beta blockers, aldosterone antagonists, ARBs and diuretics (Yancy et al 2013, PERKI 2015).

BNP and NT-proBNP are considered as benchmarks of heart failure biomarkers compared to others (Gaggin & Januzzi 2015). Based on The Trial of TIME-CHF Randomized Trial (Pfisterer et al 2009) showed that heart failure therapy based on NT-BNP did not improve the overall clinical outcome or QoL (Quality of Life) compared to symptom-based therapy. Although symptom improvement is also the goal of therapy, symptom improvement is not the same as significant improvement in morbidity and mortality (Cotter et al 2005).

Increased levels of Troponin T are associated with higher hospital mortality, ejection fraction and lower systolic pressure, increased need for inotropics, longer intensive care (Singh et al 2015). Troponin levels in acute heart failure are higher than chronic heart failure and the percentage detected troponin T levels are higher than troponin I in chronic heart failure (Kociol et al 2010).

In the analysis of troponin T in patients with acute heart failure, showed a decrease in troponin T levels is a response to therapy and return to compensation conditions. Unchanged troponin T levels indicate a steady state of decompensation and a longer duration of hospital stay (Ferreira et al 2014). Based on this background, through this study we want to analyze how much changes in troponin T levels before and after the administration of standard therapy in patients with heart failure by taking into account the parameters of the improvement of the patient's clinical condition.

MATERIALS AND METHODS

This research is a prospective observational study with consecutive sampling techniques. In this study, researchers did not intervene in the therapeutic subjects. Subjects were adult (> 18 years) class III and IV heart failure patients who had symptoms of heart failure for more than 9 hours and were willing to sign information to consent. The study was conducted on inpatients at the heart and blood vessel disease SMF Dr.Soetomo Regional Hospital.

Patients with severe renal failure (creatinine clearance <30 ml/min), acute myocardial infarction, sepsis and pulmonary embolism were excluded from this study. The number of research subjects was 30 patients and cTnT levels were measured twice, that is before therapy or on the first day of hospitalization and after therapy or on the last day of hospitalization. Patients also recorded clinical condition parameters, including heart rate, respiratory rate (RR), blood pressure, mean arterial pressure (MAP), input volume and output volume of the body.

Measurement of cTnT levels was carried out by taking 2 ml of the patient's blood in a serum separator tube on the first and last day of hospitalization. Analysis of serum cTnT levels using the ELISA method and Human cTnT/TNNT2 reagents (Troponin T type 2, cardiac) ELISA KIT (Elabscience, Italy). The study was conducted in May-July 2017. Analysis of changes in levels and improvement of clinical symptoms of patients was carried out statistically with the Wilcoxon signed-rank test for non-parametric data while the Paired T-test for parametric data to the differential test. Ethical clearance test by the Ethics Committee Dr.Soetomo Surabaya Public Hospital and has obtained information on ethical eligibility.

RESULTS

Patient demographic data are listed in Table 1. From the demographic data, the mean age of patients was 55.13 + 11.17 years. The youngest age of the patient is 31 years and the oldest is 74 years. By age category, the largest group of patients was 50-59 while the patient group was at least> 70 years old. Most of the research subjects were male, 16 patients (53.3%) while the rest were female 14 patients (46.7%).

Patients have various clinical characteristics on the first day of hospitalization. Characteristics of these clinical conditions include classes of heart failure, shortness before hospitalization, ejection fraction, kidney function and comorbid patients.

Table 1. Patients' demographic data

Variables		n (%) or mean ± SD
Age		55.13 ± 11.17
-	30 – 39 years old	5 (16.7)
-	40 – 49 years old	3 (10.0)
-	50 – 59 years old	11 (36.7)
-	60 – 69 years old	10 (33.3)
-	≥ 70 years old	1
Sex		
-	Male	16 (53.3)
-	Female	14 (46.7)

The characteristics of drug therapy given to patients are presented in Table 5.3, including: diuretics, aldosterone antagonists, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II type I receptor blockers (ARB), beta blockers, digitalis, ISDN, warfarin, amiodarone and inotropic (dopamine and dobutamine).

Of the 30 patients subjected to the study, 10 patients (33.3%) had a history of drug therapy and regularly took medication while 20 patients (66.7%) did not have a history of drug therapy or did not take medication regularly. Kinds of history of drug therapy can vary from patient to patient. Blood sampling for each patient for measurement of serum troponin T (cTnT) levels was carried out twice, namely on the first day of hospitalization (before administration of therapy) and finally of hospitalization (after administration of therapy).

The mean serum cTnT level before administration of therapy was 33.48 + 31.88 pg/ml with a minimum level of 9.27 pg/ml and a maximum level of 141.99 pg/ml. The mean serum cTnT level after administration of therapy was 46.32 + 52.68 pg/ml with a minimum level of 5.59 pg/ml and a maximum level of 187.40 pg/ml. The cut off point of cTnT is 12 pg/ml (Latini, et al., 2007) and serum cTnT levels prior to the administration of therapy that exceeded this value were 28 patients (93.3%). Based on the average serum cTnT levels and clinical symptoms before and after administration of therapy showed improvement in clinical symptoms not accompanied by a decrease in serum cTnT levels.

Before hospitalization, there was a history of taking the patient's medication therapy which was also observed during the study. Patients said taking medication regularly and there was a history of medication during outpatient care in the medical record showed patients were obedient and regularly took medication. Patients do not routinely take medication if the patient says he has never taken medication or not routinely taking medication before. During hospitalization, patients get standard therapy ranging from 1-5 kinds of standard therapy drugs. Based on variations in the standard therapy of each patient, can be grouped into 6 variants with each consisting of 5 patients.

Mean cTnT serum levels from each variant and mean serum levels of adherence taking medication were then displayed to find out whether therapeutic and adherence variation factors influenced changes in troponin T levels. There was a decrease in levels in the variant group (Fur + Spi + Cap/Val +/- Bis) and (Fur + Spi + Lis +/- Val +/- Bus). There was a decrease in levels in patients who regularly took medication (10 patients) whereas in patients who did not routinely take drugs there was an increase in levels (20 patients).

Serum cTnT levels before and after administration of therapy based on significance did not change ($p = 0.318$), but based on the average results of both there were increased levels. This shows that the increase in cTnT levels before and after therapy is not significant. In the parameters of the clinical symptoms of pulse, RR, systolic blood pressure, diastolic blood pressure, and MAP there are changes based on mean values and statistical tests with a significance of $p < 0.05$. This shows the clinical improvement after the administration of therapy was declared significant. Changes in and out of fluid based on the results of the mean decreases but the change is not significant ($p > 0.05$).

DISCUSSION

This study aims to analyze standard therapy for heart failure by measuring changes in serum troponin T levels and improvement of symptoms (blood pressure, MAP, pulse, RR, volume of fluid in and out) before and after standard therapy. The study was conducted on 30 patients with NYHA FC III and IV heart failure who were treated at the IRNA of the Heart and Blood Vessels of RSUD Dr. Soetomo Surabaya. The mean age of patients was 55.13 + 11.17 years with an age range of

31-74 years. More male patients than female patients. Based on epidemiological studies in Spain with 88,195 patients have an average age of 77 years and the majority of women, but in patients younger than 74 years the prevalence of men is higher than women (Farre et al 2011). Estrogen plays a role in women before menopause by preventing the activation of RAAS (the renin-angiotensin-aldosterone system). If menopause is associated with ovarian estrogen loss, pathogenesis of diastolic dysfunction will occur, resulting in an increase in angiotensin II and NOS (nitric oxidase synthase), and ROS (reactive oxygen species) that contribute to hypertension (Zhao et al 2014).

Table 2. Profile characteristics of clinical conditions of research subjects

Variables	n (%) or mean ± SD	Min	Max
Heart Failure Class			
- NYHA FC III	16 (53.3)		
- NYHA FC IV	14 (46.7)		
Shortness before hospitalization (days)	3 ± 2.28	1	7
- 1 day	12 (40.0)		
- >1 day	18 (60.0)		
Length of stay (days)	5.27 ± 1.67	2	8
- <5 days	19 (63.3)		
-> 5 days	11 (36.7)		
Ejection Faction (%)	35.33 ± 15.90	17	71
- HFrEF (<40%)	21 (70.0)		
- HFpEF (>40%)	9 (30.0)		
Creatinine serum (mg/dl)	1.17 ± 0.34	0.76	1.83
- <1 mg/dl	13 (43.3)		
-> 1 mg/dl	17 (56.7)		
estimated GFR (ml/minute/1.73m2)	60.01 ± 21.31	34.72	118.40
- 30-59 ml/minute/1.73m2	20 (66.7)		
-> 60 ml/minute/1.73m2	10 (33.3)		
Comorbid (each patient)	2.37 ± 0.99	1	6
- Ischemic cardiomyopathy	14 (46.7)		
- Valvular heart disease	11 (36.7)		
- Diabetes mellitus type II	11 (46.7)		
- Coronary heart disease	10 (33.3)		
Old Myocard Infarct			
- Rheumatic heart disease	7 (23.3)		
- Atrial fibrillation	7 (23.3)		
- hypertension	5 (16.7)		
- Left ventricular thrombus	4 (13.3)		
- Post cardiogenic shock	1 (3.3)		
Improvement of symptoms			
- Admission heart rate (x/minute)	100.27 ± 21.22	50	168
- Discharge heart rate (x/minute)	86.73 ± 15.20	65	135
- RR Admission (x/minute)	25.40 ± 4.34	20	40
- RR Discharge (x/minute)	19.87 ± 1.04	16	22
- Admission systolic pressure (mmHg)	120.07 ± 25.71	80	180
- Discharge systolic pressure (mmHg)	109.67 ± 15.20	90	140
- Admission diastolic pressure (mmHg)	76.33 ± 12.59	60	100
- Discharge diastolic pressure (mmHg)	72.00 ± 9.61	60	100
- MAP Admission (mmHg)	90.91 ± 16.19	66.67	126.67
- MAP Discharge (mmHg)	84.56 ± 10.98	70	113,33
- Admission inlet fluid volume (ml)	1045.00 ± 226.42	500	1300
- Admission fluid volume out (ml)	1820.00 ± 1135.45	400	6000
- The volume of fluid entering the Discharge (ml)	986.67 ± 367.17	500	2000
- Discharge liquid volume out (ml)	1383.33 ± 651.30	400	3000

Note: n = number of patients, SD = standard deviation, total patients = 30 patients, NYHA = New York Heart Association Functional Class, GFR = glomerular filtration rate, Admission = hospital admission, Discharge = hospital discharge, RR = respiratory rate, MAP = mean arterial pressure.

Table 3. Characteristics of drug therapy study subjects

Drug Therapy (daily dose range)	n = 30	Percentage (%)
Standard therapy for heart failure:		
Furosemide (20-240 mg)	30	100.0
- Furosemide 10 mg/hour infusion pump	5	16.7
- Furosemide 5 mg/hour infusion pump	23	76.7
- Furosemide 2.5 mg/hour infusion pump	14	46.7
- Furosemide 3x20 mg IV	19	63.3
- Furosemide 2x20 mg IV	7	23.3
- Furosemide 1x20 mg IV	4	13.3
- Furosemide 1x40 mg PO	5	16.7
Hydrochlorothiazide (100 mg)	1	3.3
Spironolactone (25-100 mg)	27	90.0
- Spironolactone 2x50 mg PO	2	6.7
- Spironolactone 1x50 mg PO	4	13.3
- Spironolactone 1x25 mg PO	27	90.0
Captopril (18.75-37.5 mg)	9	30.0
- Captopril 3x12.5 mg PO	5	16.7
- Captopril 3x6.25 mg PO	4	13.3
Ramipril (2.5-5 mg)	11	36.7
- Ramipril 1x5 mg PO	6	20.0
- Ramipril 1 x 2.5 mg PO	9	30.0
Lisinopril (2.5-10 mg)	5	16.7
- Lisinopril 1x10 mg PO	1	3.3
- Lisinopril 2x5 mg PO	2	6.7
- Lisinopril 1x5 mg PO	3	10.0
- Lisinopril 1 x 2.5 mg PO	1	3.3
Valsartan (40-80 mg)	4	13.3
- Valsartan 1x80 mg PO	1	3.3
- Valsartan 1x40 mg PO	4	13.3
Candesartan (16 mg)	1	3.3
Bisoprolol (1.25-5 mg)	14	46.7
- Bisoprolol 1x5 mg PO	2	6.7
- Bisoprolol 1 x 2.5 mg PO	7	23.3
- Bisoprolol 1x1,1,25 mg PO	8	26.7
Other heart failure therapies:		
Digoxin (0.25-1 mg)	17	56.7
ISDN (5-24 mg)	13	43.3
Warfarin (2-4 mg)	11	36.7
Dobutamine (3 mcg/kgBB)	3	10.0
Dopamine (3 mcg/kgBB)	2	6.7
Amiodarone (150-1200 mcg)	1	3.3
Compliance with taking medication before hospitalization:		
Routine taking medication and control at Poly	10	33.3
Not routinely taking medicine or never taking medicine before	20	66.7

Note: 1 patient can receive more than 1 drug regimen, IV = intravenous, PO = orally. Standard therapy includes diuretics, aldosterone antagonists, ACEI, ARB, & beta blockers. Poly = Outpatient installation.

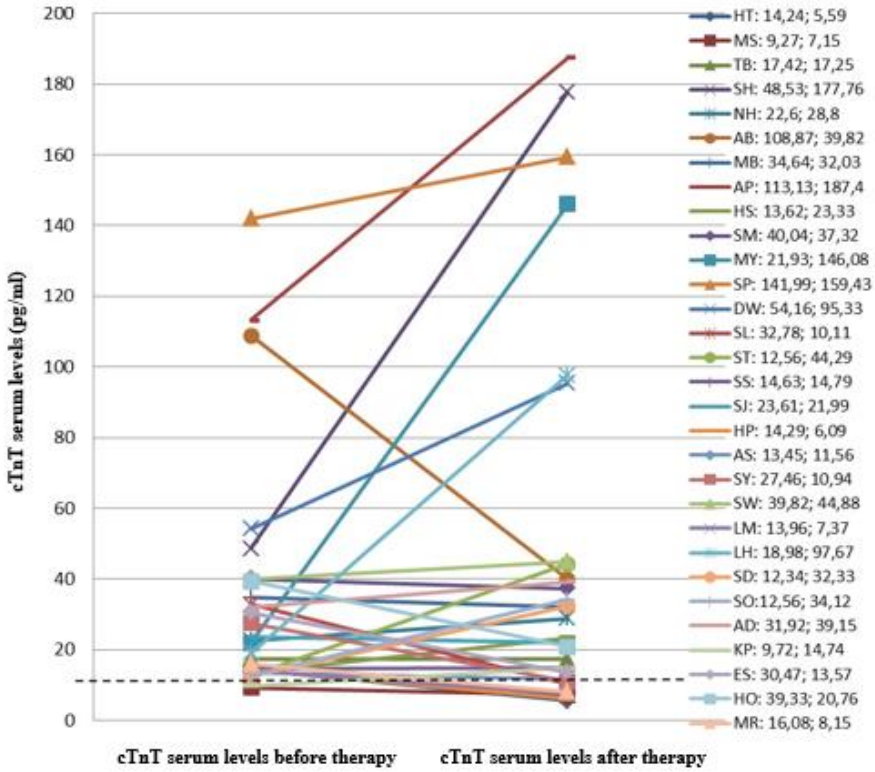

Fig. 1. Profile of cTnT serum levels before and after therapy. Note: total of patients = 30 patients, cut off point cTnT = 12pg/ml, cTnT = cardiac Troponin T.

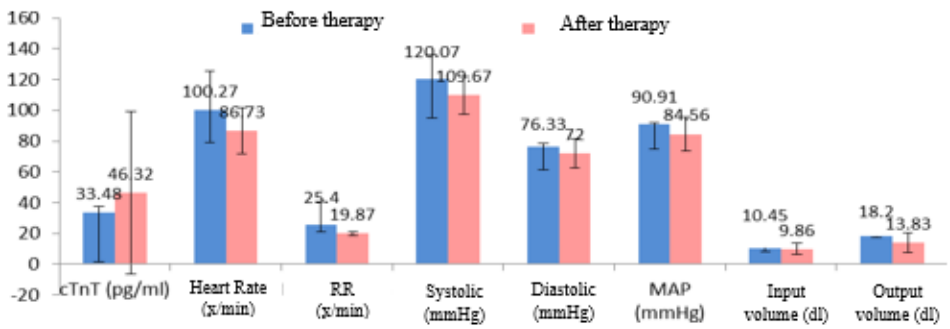

Fig. 2. Profile of cTnT serum levels and symptoms improvement.

Table 4. Characteristics of variations of standard therapy on study subjects

Variant	Standard Therapy	n
(Fur+/-Spi/Ram/Can/Bis)	Furosemide, with or without Spinorolactone/Ramipril/Candesartan/Bisoprolol	5
(Fur+Spi+Cap/Val+/-Bis)	Furosemide, Spironolactone, Captopril/Valsartan, with or without Bisoprolol	5
(Fur+Spi+Lis+/-Val+/-Bis)	Furosemide, Spinorolactone, Lisinopril, with or without Valsartan and Bisoprolol	5
(Fur+Spi+Lis)	Furosemide, Spironolactone, and Lisinopril	5
(Fur+Spi+Ram+Bis)	Furosemide, Spironolactone, Ramipril, and Bisoprolol	5
(Fur+Spi+Cap+Bis)	Furosemide, Spironolactone, Captopril, and Bisoprolol	5

Note: total patients = 30 patients, total variants = 6 and each variant consists of 5 patients.

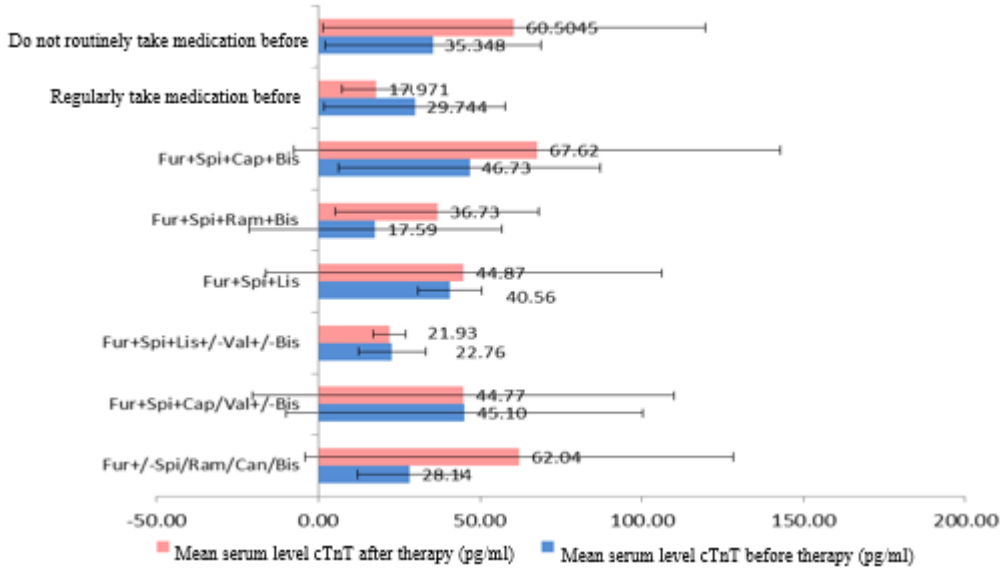

Fig. 3. Profile of variations in standard therapy, medication adherence and cTnT levels. Note: total patients = 30 patients. There are 6 variants of standard therapy and each drug variant consists of 5 patients. 10 patients regularly take medication and 20 patients do not routinely take medication before hospitalization.

Table 5. Test results for different levels of troponin T data using the Wilcoxon signed ranks test

N	Parameter	Mean ±	SD	Signficance (p)
30	CTnT levels before therapy vs	33.48 ±	32.42	0.318
	CTnT levels after therapy	46.33 ±	46.32	

Table 6. Results of different clinical symptoms with the Paired T test

N	Parameter	Mean ±	SD	Significance (p)
30	Pulse before therapy	100.27 ±	21.22	0.003
	Pulse after therapy	86.73 ±	15.20	
30	Systolic before therapy	120.07 ±	25.71	0.018
	Systolic after therapy	109.67 ±	15.20	
30	Diastolic before therapy	76.33 ±	12.59	0.019
	Diastolic after therapy	72.00 ±	9.61	
30	MAP before therapy	90.91 ±	16.20	0.011
	MAP after therapy	84.56 ±	10.99	
30	Fluid enters before therapy	1045.00 ±	228.23	0.470
	Fluid comes in after therapy	986.67 ±	367.17	
30	Fluid comes out before therapy	1820.00 ±	1135.45	0.114
	Fluid comes out after therapy	1383.33 ±	651.30	

Note: the decrease in incoming and outgoing fluids is not statistically significant.

Table 7. Results of different clinical symptoms data using the Wilcoxon signed ranks test

N	Parameter	Mean ±	SD	Significance (p)
30	RR before therapy	25.40 ±	4.34	0.000
	RR after therapy	19.87 ±	1.04	

Note: the decrease in RR is statistically significant

Based on the characteristics of the patient's clinical condition, the mean pulse on the first and last day of hospitalization decreased from 100.27 + 21.22 to 86.73 + 15.20. The pulse target to return to a stable condition is <100x/minute (Valle et al 2011) and based on the reduction in the pulse rate has been fulfilled. In heart failure patients an increase in pulse at rest is caused by a continuous inhibition of vagal nerve activity which further increases sympathetic activity. A decrease in pulse 5x/minute can reduce the risk of mortality by 14% on the use of beta-blocker therapy. Decreased pulse can restore damage to left ventricular function so providing tachycardia in heart failure significantly improves heart function. Pulses above 100x/minute can cause cardiac dilatation due to increased ventricular filling pressure and activate neurohormonal (Hori & Okamoto 2012).

The average respiratory rate (RR) on the first and last day of hospitalization decreased from 25.4 + 4.34 to 19.86 + 1.04. The normal RR range in adults is 18-20x/minute and based on the average RR last hospitalization has returned to normal. Patients with acute heart failure (NYHA FC III and IV) often with volume overload and discharge with diuretics can improve symptoms. An increase in RR at the time of hospitalization is consistent with a high class of heart failure patients and a decrease in RR is followed by a decrease in heart failure class. This is consistent with the results of the correlation test significantly in previous studies (Forleo et al 2015) namely the higher the RR the higher the NYHA class and the lower the left ventricular ejection fraction.

The mean systolic blood pressure on the first and last day of hospitalization decreased from 120.07 + 25.71 to 109.67 + 15.19. The target of systolic blood pressure to return to a stable compensation condition is 90-120 mmHg (Valle et al 2011) and based on average, the decrease in systolic blood pressure has met the target. At the time of hospital admission, congestive symptoms more often cause increased systolic blood pressure. Increased systolic associated with neurohormonal activation and cytokines thereby increasing afterload. Patients with increased systolic blood pressure upon admission have a better therapeutic response during hospitalization in acute heart failure. The higher the systolic blood pressure, the more therapies used such as ARB, ACEI, and beta blockers with antihypertensive effects (Gheorghiade et al 2006).

The mean diastolic blood pressure on the first and last day of hospitalization decreased from 76.63 + 12.59 to 72 + 9.61 mmHg. The target of reducing diastolic blood pressure is <80 mmHg (Manickasavagam et al 2009) and based on the average, the reduction in diastolic blood pressure has been fulfilled.

The decrease in systolic blood pressure is greater than the decrease in diastolic blood. This is influenced by age, with increasing age, decreasing diastolic blood pressure will be smaller (Wang et al 2005). Systolic pressure, diastolic and mean arterial pressure (MAP) are important predictors of cardiovascular risk in patients younger than 60 years whereas patients over 60 years only systolic blood pressure and pulse pressure are associated with these risks (Domanski et al 1999).

The mean of MAP on the first and last day of hospitalization was decreased from 90.91 + 16.19 mmHg to 84.56 + 10.98 mmHg. Based on the results of the MAP calculation on the target of reducing blood pressure that is <130/80 (Manickasavagam et al 2009) obtained the MAP target <96.67 mmHg. Each reduction in MAP of 10 mmHg from the previous MAP predicted an 11% increase in mortality (Domanski et al 1999). Based on the average MAP, the reduction in MAP has met the MAP reduction target and no more than 10 mmHg.

Based on the profile of the volume of incoming and outgoing fluid (Figure 5.2), the mean volume of incoming fluid during the first and last day of hospitalization decreased, from 1045.00 + 226.42 to 986.67 + 367.17. The average volume of discharge came out on the first day and the last day of hospitalization also decreased, namely from 1820.00 + 1135.45 to 1383.33 + 651.30. Target diuresis to return to a stable condition (compensation) ie >1000 ml/24 hours and repair fluid overload (Valle et al 2011). Based on the mean, diuresis (volume of fluid out) on the first and last day of hospitalization has met the target diuresis. Decrease in the volume of fluid in and out on the first and last day of hospitalization is affected by a decrease in diuretic dose on the last day of hospitalization adjusted for the response of diuresis of each different patient.

According to Valle et al 2011, hydration status and myocardial performance in patients with complex heart failure. Based on an analysis of case by case shows each patient has its own hydration range for hyper or hypohydration which causes instability. The majority of patients with acute heart failure show good loop diuretic and vasoactive responses (Valle et al 2011).

All patients received furosemide to treat fluid and salt retention, but not all patients received 5 standard therapeutic drugs. Some patients did not get spinorolactone due to hyperkalemia, some patients did not get ACEI because previous therapy (when outpatient) had received ARB or patients experienced coughing during hospitalization, and some patients did not get bisoprolol because there was still ronkhi and pulse and blood pressure which tended to be low.

Beta blockers (bisoprolol) are given to patients with mild to moderate symptoms but their use is not preceded when symptoms are severe (Nohria et al 2002). A combination of furosemide and hydrochlorothiazide is also given to patients with low urine volume to increase output to the optimum. In addition to standard therapy, patients also get additional heart failure therapy. Digoxin is used to slow down rapid ventricular beats in atrial fibrillation or there is sinus rhythm (Ponikowski et al 2016). Warfarin as an oral anticoagulant is also given to patients with atrial fibrillation and LV thrombus to reduce mortality/morbidity and reduce the risk of venous thromboembolism (PERKI 2015, Ponikowski et al 2016). Amiodarone is also indicated for atrial fibrillation in heart failure patients. Amiodarone controls heart rhythm and maintains sinus rhythm in patients with moderate-severe left ventricular dysfunction. Amiodarone is considered to control the pulse if the combination of beta-blockers and digoxin is inadequate (Khan et al 2013).

Giving ISDN as a vasodilator in heart failure with comorbid coronary heart disease or LV thrombus and combined with ACEI/ARB because blood pressure remains high so that it requires more aggressive vasodilator therapy. Dopamine and dobutamine as inotropes and vasopressors are aimed at patients with a severe decrease in cardiac output (CO) which results in compromise of vital organ perfusion, where patients often show hypotension during acute heart failure (Ponikowski et al 2016).

Dobutamine and dopamine both increase the cardiac index but dopamine results in a fairly long increase in pulse compared to dobutamine. Dopamine is not effective in reducing left-ventricular end-diastolic pressure but increases MAP while dobutamine does not increase MAP (Stoner et al 1977).

Serial cTnT measurement can inform the therapeutic response and risk of further adverse events compared to a one-time check (baseline). Measurement of cTnT levels in heart failure can also look for the presence of acute myocardial infarction (IMA) type 1 although an increase and/or decrease in cTnT does not guarantee the presence of type 1 IMA (Mallick & Januzzi, 2015). According to Grodin and Tang 2013, an increase in cTnT levels in chronic heart failure is caused by a temporary or permanent mismatch of myocardial supply and needs so that cardiac troponin is released in acute and chronic conditions, the release of cTnT indicates an increase in cardiomyocyte changes that are worsening myocardial supply and needs so that cardiac troponin is released in acute and chronic conditions. an increase in cTnT explains how troponin T can be detected under conditions when metabolic requirements increase in supply (acute non-infarct myocardial) (Grodin & Tang 2013).

The limited number of patients in this study made a different test performed on troponin T levels before and after the therapy was done in a ratio. An increase in cTnT levels indicates ongoing myocyte injury associated with remodeling compared to infarction (Meredith et al 2016). In this study, there were no patients who used mechanical circulatory support so that the increase in troponin T after therapy showed a continuous myocyte damage toward remodeling. Decreased troponin T and NTproBNP levels may reflect improvements in ventricular wall stress and fewer myocardial damage (Takashio et al 2017). Unchanged troponin T levels indicate a steady state of decompensation and a longer duration of hospital stay (Ferreira et al 2014).

Based on the different test on clinical symptom parameters, the mean decrease was statistically significant ($p < 0.05$) from the pulse, RR, systolic blood pressure, diastolic blood pressure, and MAP. The decrease in these parameters shows a significant clinical improvement of heart failure (compensation). This is in accordance with the criteria for the return of the clinical condition of heart failure patients to a stable condition, namely systolic blood pressure 90-120 mmHg, pulse <100 x/min, diuresis> 1000ml/24 hours and improvement in fluid overload (Valle et al 2011). In the parameters of the volume of fluid in and out there is a decrease after therapy but the decrease is not statistically significant ($p > 0.05$). This is caused by the response of each patient's diuresis is individual while based on the mean there is a decrease in the volume of fluid in and out due to a decrease in the dose of furosemide until the end of hospitalization.

Overload volume that develops into hemodynamic and congestive has a complex pathophysiological process. Several factors are involved in the accumulation and redistribution of fluid with a longer time in the interstitial and intravascular compartments, causing congestion. Water and salt retention in the kidney initiates mechanisms that contribute to fluid accumulation but are redistributed by the abdominal venous reservoir due to changes in cardiopulmonary vascular capacity (Miller 2016).

Based on the profile variation of standard therapy, medication adherence, and serum cTnT levels, patients with a history of regularly taking medication have decreased levels and patients with a history of not routinely taking medication have increased levels of cTnT. In the study of Wal et al in 2005, non-compliance with medication/diet is a factor with a large enough

percentage (15-64%) to worsen the condition of heart failure.

Patients with a routine history of taking medication had lower heart failure worsening in this study. This was indicated by a significant decrease in cTnT levels in 10 patients in this study. In the study of Miller et al (2009), the more frequent cTnT examination in outpatients with chronic heart failure that showed an increase in cTnT (> 10 pg/ml) was associated with an increased risk of short-term mortality or heart transplantation and also hospitalization of patients. Troponin T levels after therapy in hospitalized patients in this study can be a baseline for measuring patients troponin T levels at the next outpatient.

There was a slight decrease in cTnT levels in some standard therapy variants that received ARB. Comparison of ACEI and ARB in heart failure patients with LVEF <40% does not show a significant mortality difference between the two. In addition, the comparison of ACEI and ARB also did not differ significantly on length of stay, but drug withdrawal due to side effects on ARB was significantly smaller than ACEI (Heran et al 2012). Based on Val-HeFT and CHARM studies, the addition of ARBs to a single ACEI in patients with heart failure does not improve survival. There were no significant differences in total mortality, cardiovascular mortality or non-cardiovascular mortality

CONCLUSION

There were no significant changes between troponin T levels before and after treatment. Insignificant changes mean no worsening of myocardial damage. There are significant changes, namely a decrease between blood pressure, MAP, pulse, and RR before and after administration of therapy. Significant reduction means improvement in symptoms.

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