Decreased cTnT Levels Heart Failure Patients with Routinely Taking Standard Therapy

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ABSTRACT

Extreme physical stressors such as thirst increase the risk of non-communicable diseases, especially heart failure (HF). Cardiac patients should ensure adequate supplies of and adherence to medications. They must avoid crowds, perform certain rituals, and report to the nearest health center if there are symptoms that indicate cardiac decompensation. However, in acute or chronic HF with reduced or preserved ejection fraction (EF), elevated cardiac troponin (cTn) levels carry prognostic value for adverse outcomes. A prospective observational study aimed to evaluate levels of cTnT before and after administration of standard therapy and treatment history in hospitalized HF patients. The samples were collected by consecutive sampling and obtained from 30 patients from May-July 2017. The results showed that the number of patients whose cTnT levels decreased by ten patients (30.68 vs. 12.96 pg/ml; p=0.005) increased by 12 patients (31.00 vs. 76.75 pg/ml; p=0.002) and persistent by eight patients (40.70 vs. 42.41 pg/ml; p=0.779). Changes in serum cTnT levels and the clinical condition of the patient, possible to consider the factors of the patient's clinical condition that affect cTnT levels. There was a decrease in levels of cTnT in patients who regularly took medication (10 patients, 29.74 vs. 17.97 pg/ml; p=0.037), while in patients who did not take medication regularly, there was an increase in levels of cTnT (20 patients, 35.35 vs. 60.51 pg/ml; p=0.025). Evaluation of patients' adherence to heart failure therapy has ruled out major risk factors, such as patients with uncontrolled heart disease, to reduce casualties during Hajj.

Keywords: cTnT, Adherence, Heart Failure, Standard therapy

INTRODUCTION

Extreme physical stressors lead people thirsty and especially patients with a risk of non-communicable diseases like heart failure (HF) (Chamsi-Pasha, Ahmed and Al-Shaibi, 2014). Heart failure is a significant public health problem associated with mortality, morbidity, and health expenditure costs, especially in patients aged > 65 years. Although there has been

progress in efforts to reduce heart failure, which is associated with mortality, the rate of patients returning to the hospital (hospitalization) continues to increase (Roger, 2013). Once a patient is hospitalized with heart failure, the patient has a high risk of returning to hospitalization, with a 25% return rate of hospitalization at one month (Krumholz *et al.*, 2009).

Standard therapy provided includes ACEI groups, beta-blockers, aldosterone antagonists, ARBs, and diuretics (Yancy *et al.*, 2013). The goal of this therapy is to relax blood vessels, reduce biological stress and improve heart function. Diuretics control symptoms of heart failure. 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). HF NYHA FC III-IV showed a 50% 1-year mortality rate (Friedrich and Böhm, 2007). Troponin T levels > 0.033 g/L at the time of hospitalization have an increased risk of cardiac mortality (Ishii, et al., 2002). Troponin T in the cytosol is released immediately after ischemic damage, followed by a longer release of troponin from myofibrils resulting in a biphasic pattern, while the amount of troponin I in the cytosol is less and has a monophasic pattern (Maynard, Menown and Adgey, 2000). Troponin levels begin to increase 4-6 hours after symptoms, so sampling should be done when the patient is admitted to the hospital. Increased troponin levels then persist, indicating slow release and degradation of troponin in the cytosol (Babuin and Jaffe, 2005).

Clinical assessment and management while the patient is undergoing treatment, is the beginning of the prevention of re-hospitalization. The key to the success of this effort is the assessment of fluid status and optimal treatment (PERKI, 2015). Optimal therapy for heart failure includes identification and correction of potentially reversible precipitation, titration of drug doses to target doses, and management of hospitalization in decompensated patients (Ramani, Uber and Mehra, 2010). The role of the clinical pharmacist in the heart failure team can influence therapy reconciliation and education, ensure management consistency in improving patient satisfaction and therapy adherence, and reduce medication errors (Milfred-laforest *et al.*, 2013). Patients with heart failure are at high risk of experiencing DNOs (Drug Related Negative Outcomes) because of polypharmacy, comorbidities, and age. The incidence of DNOs includes 45% due to not receiving drug therapy (requiring drugs) and 24% of insufficient doses (quantitatively ineffective) (Gastelurrutia *et al.*, 2011). Based on this background, this study wanted to depict troponin T levels changed before and after standard therapy was given to heart failure patients and different factors of each group of changes in serum troponin T levels.

MATERIALS AND METHODS

Study design

We used analytical observational with a longitudinal study design. The population of this study is patients diagnosed with heart failure without comorbid infarct myocardial acute, sepsis, lung emboly, acute kidney injury, and chronic kidney disease stage V. These inclusion criteria are male or female patients> 18 years old, hospitalized patients with a diagnosis of NYHA class III-IV heart failure and presenting with symptoms of heart failure > 9 hours. We conducted consecutive sampling with a minimal sample size of 25 patients based on paired T-test analysis. Independent variables are standard therapy for heart failure during hospitalization and history of

adherence to treatment. The dependent variable is cTnT levels. All the patients or their families signed the informed consent. We collect clinical manifestation data for each patient from patient medical records at the Department of Cardiology and Vascular Medicine, Soetomo Teaching Hospital's Surabaya. Ethical clearance by the Ethics Committee of RSUD Dr. Soetomo Surabaya No. 303/Panke.KKE/IV/2017.

cTnT measurement levels

We used sandwich Enzyme-linked Immunosorbent Assay (ELISA) protocol to analyze Human cTnT/TNNT2 (Troponin T Type 2, Cardiac) with ELISA Kit (Elabscience, Italy) at the Department of Clinical Pathology Medicine, Soetomo Teaching Hospital Surabaya. cTnT measured twice each patient on day one hospitalized and before being in charge of the hospital. We collect the blood serum of patients and analyze ELISA simultaneously.

History of adherence patients

Prior to hospitalization, there was a history of patient drug therapy which was also observed during the study. The patient stated that he regularly took medication, and there was a history of medication during outpatient care in the medical record showing that the patient was obedient and took medication regularly. Patients do not take medication regularly if the patient says they have never taken medication or have not taken medication regularly before.

RESULT AND DISCUSSION

Based on the demographic characteristics of the study subjects, the mean age of the patients was 55.13 + 11.17 years, with an age range of 31-74 years. There were more male patients than female patients (16 vs. 14).

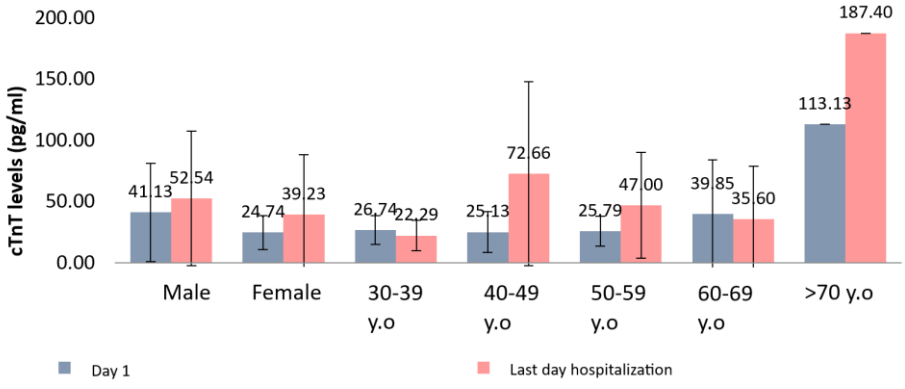

Figure 1. Profile of serum cTnT levels and patient demographics. Total patients = 30 patients. 16 male patients and 14 female patients. 5 patients 30-39 years, three patients 40-49 years, 11 patients 50-59 years, ten patients 60-69 years, and one patient 70-79 years.

cTnT serum levels after therapy experienced an increase and decreased from serum cTnT levels before therapy. Therefore, to determine the factors that influence the increase and decrease in research subjects, cTnT serum level profiles and patient demographics were made. Based on the average cTnT serum level for each patient demographic parameter, cTnT serum levels were higher in male patients than in female patients and in the age group > 70 years. Decreased cTnT serum levels occurred in the age group 30-39 years and 60-69 years.

Clinical symptom data, including pulse, RR, systolic blood pressure, diastolic blood pressure, MAP, and the volume of fluid in and volume of fluid out, were then analyzed to see the significance of the changes. There were changes in the clinical symptom parameters pulse, RR, systolic blood pressure, diastolic blood pressure, and MAP based on mean values and statistical tests with a significance of $p < 0.05$ (Indrawijaya *et al.*, 2020). This shows that the clinical improvement after the administration of therapy was stated to be significant. Based on the average cTnT serum levels and clinical symptoms before and after administration of therapy, it showed an improvement in clinical symptoms not accompanied by a decrease in cTnT serum levels.

Correlation analysis of changes in troponin T levels and changes in clinical symptoms was carried out by linking all troponin T data and clinical symptoms of patients before and after therapy and their changes. This was done to determine the level of association between troponin T levels and clinical symptoms. If the data is normally distributed, a correlation test is performed using the Pearson correlation test with a correlation value in the correlation coefficient (r). If the distribution is not normal, Spearman's rho test is performed with a correlation value in rho (ρ).

Table 1. Correlation of changes in troponin T levels and changes in clinical symptoms

Parameter	**p**	**Spearman's rho Test**		**Pearson Correlation Test**
		cTnT before therapy	**cTnT after therapy**	**Change cTnT**
Pulse before Therapy	0.774	ρ = -0.055		
Pulse after Therapy	0.134		ρ = 0.280	
Pulse changes	0.488			r = 0.132
RR before Therapy	0.903	ρ = 0.023		
RR after Therapy	0.838		ρ = 0.039	
RR changes	0.772			r = -0.055
Systolic pressure before Therapy	0.036	ρ = 0.385		
Systolic pressure after Therapy	0.299		ρ = -0.196	
Changes in systolic pressure	0.734			r = -0.065
Diastolic pressure before Therapy	0.051	ρ = 0.360		
Diastolic pressure after Therapy	0.850		ρ = -0.036	
Changes in Diastolic Pressure	0.700			r = -0.073
MAP before Therapy	0.029	ρ = 0.398		
MAP after Therapy	0.520		ρ = -0.122	
MAP changes	0.659			r = -0.075

cTnT serum levels in pg/ml, Pulse and RR in x/minute, systolic and diastolic blood pressure, and MAP in mmHg.

Correlation test results showed a weak correlation between troponin T serum levels before therapy and systolic blood pressure ($\rho = 0.385$; $p = 0.036$) and MAP ($\rho = 0.398$, $p = 0.029$). This shows an increase in troponin T serum levels before therapy, followed by an increase in systolic blood pressure and MAP and vice versa.

During hospitalization, patients receive standard therapy with varied for each patient, and it can be grouped into six types of variants with five patients each. Type 1 standard therapy Furosemide +/ Spironolactone +/ Ramipril +/ Candesartan +/ Bisoprolol. Type 2 standard therapy Furosemide + Spironolactone + Captopril/Valsartan +/Bisoprolol. Type 3 standard therapy Furosemide + Spironolactone + Captopril/Valsartan +/Bisoprolol. Type 4 standard therapy Furosemide + Spironolactone + Ramipril + Bisoprolol. Type 5 standard therapy Furosemide + Spironolactone + Lisinopril. Type 6 standard therapy Furosemide + Spironolactone + Captopril + Bisoprolol. All patients received furosemide to treat fluid and salt retention, but not all patients received all standard therapies.

cTnT serum levels after administration of therapy exceeded the cut-off point of 12 pg/ml in 22 patients (73.3%). Based on previous research (Felker *et al.*, 2015), to assess troponin T levels increasing, decreasing, or continuing to categorize changes. An increase in troponin T levels is defined as an increase in troponin T levels above 20% of the previous level. A decrease in troponin T levels is defined as a decrease in troponin T levels above 20% of the previous level. Troponin T levels are defined as stable if the increase or decrease in levels is within 20% (Felker et al., 2015). Based on this categorization, the number of patients whose levels decreased was ten patients (33.3%), increased by 12 patients (40%), and remained constant by eight patients (26.7%). Decreased cTnT levels indicate treatment response, return to compensation, improved wall stress, and reduced myocardial damage (Ferreira *et al.*, 2014; Takashio *et al.*, 2017). Increased cTnT levels indicate a mismatch of supply and demand, turn over cardiomyocytes, and ongoing myocyte injury (Groding dan Tang, 2013; Meredith et al., 2016). Remained cTnT indicated persistent decompensation, and processes associated with cTnT on day 1 continued (Kociol *et al.*, 2010; Ferreira *et al.*, 2014).

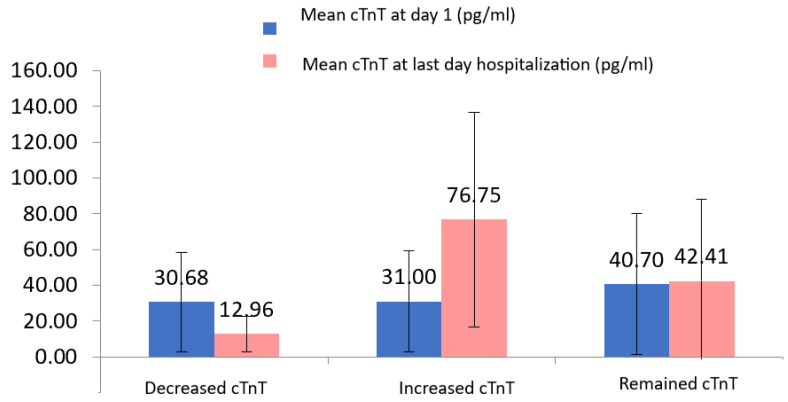

Figure 2. Profile of serum cTnT levels that decreased, increased, and remained constant. Total patients = 30 patients, ten patients had decreased levels, 12 patients had increased levels, and eight patients had constant levels.

Based on the patient's length of stay, the mean cTnT serum level after therapy can represent the cTnT serum level during hospitalization, and the cTnT serum level before giving therapy can represent the baseline cTnT serum level. The average cTnT serum level in this study decreased on the second and fifth days and then rose again after that. All mean cTnT serum levels based on length of stay were above the cut-off point of 12 pg/ml (Latini *et al.*, 2007). An increase in cTnT levels indicates ongoing myocyte injury associated with remodeling rather than infarction.

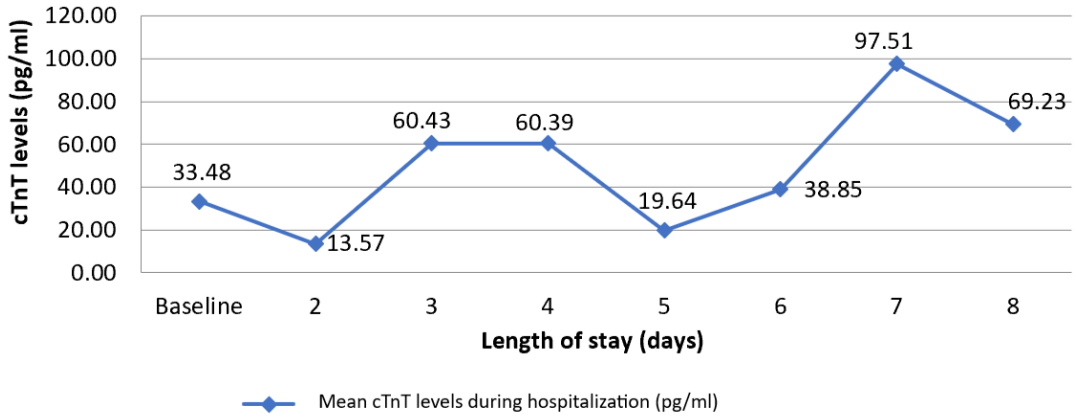

Figure 3. Profile of cTnT serum levels during hospitalization. The total baseline patients were 30 patients; one patient was hospitalized for one day, four patients were hospitalized for three days, four patients were hospitalized for four days, ten patients were hospitalized for five days, four patients were hospitalized for six days, two patients were hospitalized seven days and five patients were hospitalized eight days.

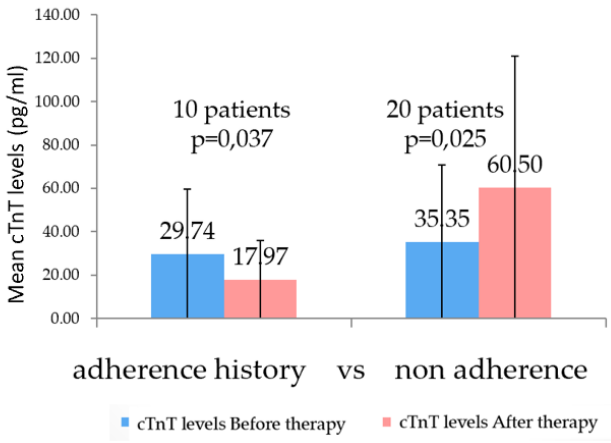

Figure 4. Changes of cTnT serum levels on HF patients with adherence history and non-adherence history to standard therapy before hospitalization.

In (Miller *et al.*, 2009), the more frequent cTnT examinations in outpatients with chronic heart failure showed an increase in cTnT (> 10 pg/ml) associated with an increased risk of short-term mortality or heart transplantation and also patient hospitalization. Troponin T levels after therapy in inpatients in this study can be a baseline for measuring troponin T levels in patients during their next outpatient stay. When the patient's volume status and symptoms are stable, the patient's heart failure condition is said to be compensatory. When volume overload occurs, or symptoms worsen, the patient is considered decompensated. Acute decompensation can be triggered by several etiologies, which have the potential to reversibly worsen heart failure, including prescription and non-prescription drug therapy, food, and medication non-adherence. Non-compliance with dietary restrictions or drug therapy for chronic heart failure requires special attention because it is a major cause of acute decompensation and is preventable (Parker & Cavallari, 2011). Social support is needed to help patients take medication regularly. Decreased social support is associated with an increased risk of re-hospitalization and mortality (Luttik *et al.*, 2005). Evaluation of patients' adherence to heart failure therapy has ruled out major risk factors, such as patients with uncontrolled heart disease, to reduce casualties during Hajj.

CONCLUSION

Patients with a history of taking the medication routine had a lower worsening of heart failure in this study.

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