Original Article

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Clinical Profile of Cardiac Failure and Its Correlation with Lab Markers and Outcome

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Abstract

Background: Cardiac failure carries a high mortality and morbidity. Cardiac troponins and brain natriuretic peptide (BNP), are useful in the diagnosis and risk stratification of patients with heart failure (HF), are a better predictor of death. Both biomarkers are secreted directly, and almost exclusively by cardiac tissue and thought to be more sensitive than imaging or even invasive hemodynamics.

Objectives: The present study was done to assess the significance of troponin T and BNP levels in cardiac failure and their correlation with outcome.

Materials and Methods: The study included 196 patients with HF. Complete blood count, renal function test, liver function test, electrolytes, urine examination, electrocardiography, Chest X-ray, two-dimensional echo, cardiac troponin T, and serum BNP levels on admission were done for all patients. The study population was divided into 3 groups based on troponin T levels.

Results: 150 patients were in Group I with troponin T levels <0.03 ng/ml, 35 patients in Group II between 0.03 and 0.1 ng/ml, and Group III included 11 patients with levels more than 0.1 ng/ml. Mean duration of intensive care unit stay was 1.91 days in Group I, 4.03 in Group II, and 3.82 in Group III. Mean BNP values (957.3 in Group I, 2378 in Group II, and 3931.4 in Group III), systolic blood pressure (BP) (104 mm Hg in Group I, 96.4 in Group II, and 94 in Group III), and ejection fraction (41.92 in Group I, 34.18 in Group II, and 34.2 in Group III) were high in patients with higher troponin T values. All patients in group III required inotropic support and 45.5% patients had death.

Conclusion: An elevated cardiac troponin T values are associated with higher in-hospital mortality, lower ejection fraction and systolic BP, increased requirement of inotropes and prolonged intensive care.

Key words: Brain natriuretic peptide, Cardiac failure, Intensive care unit stay, Inotropic support, Troponin T

INTRODUCTION

The incidence of heart failure (HF) is increasing because of improved survival after myocardial infarction. It is important to recognize that HF is a clinical syndrome arising from various causes. The American Heart Association and European Society of Cardiology have recognized the importance of simple and reproducible criteria and have developed guidelines for the diagnosis of HF. According to these recommendations, the diagnosis is based on clinical parameters and other laboratory tests to determine the etiology and degree of functional impairment. As an example, the task force of The European Society of Cardiology for the diagnosis and treatment of acute congestive HF (CHF) recommended that a cardiac natriuretic hormone (brain natriuretic peptide [BNP]) assay should be included as a first step of in the diagnosis of HF along with electrocardiography (ECG) and chest X-rays. Missov *et al.*,[1] Missov and Mair[2] first reported the association between troponin and HF. Studies have indicated that elevated troponin concentrations in patients with HF are associated with more severe disease[3,4] and a worse prognosis.[5-7]

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Reversible injury, from myocardial strain or subendocardial ischemia, could lead to transient changes in cell membrane

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permeability and leakage of cytosolic troponin. Troponin in cells is mostly bound to myofibrils suggesting the presence of more severe injury. Troponins are released in response to myocyte necrosis in patients with HF.[8] Cardiac troponins and BNP are secreted directly and almost exclusively by cardiac tissue. They indicate wall stress and injury which could be more sensitive than imaging or invasive hemodynamics. Both the biomarkers are clinically significant in view of the above features.

The need to counsel patients and select appropriate candidates for advanced therapies makes the proper assessment of HF prognosis very important. Prior small studies have suggested that routine measurement of cardiac troponins could help to identify HF patients in need of escalation of therapy. High troponin T is associated with adverse outcomes in chronic HF especially in patients with lower ejection fraction.[9] The role of troponin-T and BNP levels are being evaluated for population-based screening programs and prediction of prognosis in ambulatory CHF patients[10,11] and in chronic kidney disease for determining outcome and prognosis.

The present study was aimed at evaluating the significance of troponin-T levels in patients presenting with acute CHF in relation to diagnosis and assessment of prognosis. Also we wanted to study the correlation of troponin T with of left ventricle function, in-hospital mortality, BNP, duration of intensive care unit (ICU) stay, and systolic blood pressures (BP).

MATERIALS AND METHODS

This was a cross-sectional study of 196 patients with HF admitted in Sri Ramachandra Medical College and Hospital from the year 2008 to 2010. All patients fulfilling inclusion criteria (acute cardiac failure as per Framingham criteria) were screened and investigations done. The patients with age <18 years, serum creatinine more than 2.0 mg/dl, sepsis, acute coronary syndrome, liver disease, and malignancy were excluded from the study. A detailed history was taken from all patients, and a thorough physical examination was done.

Framingham criteria were used for the admission diagnosis of all patients - diagnosis of CHF requires the simultaneous presence of at least two major criteria or one major criterion in conjunction with two minor criteria. Minor criteria are acceptable only if they cannot be attributed to another medical condition (such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or nephrotic syndrome).

Complete blood count, renal function test, liver function test, electrolytes, urine examination, ECG, chest X-ray, and two-dimensional echo were done for all patients. Cardiac troponin T and serum BNP levels on admission were done. Cardiac troponin T was measured by the Roche cardiac T quantitative test which is an immunological test for the detection in venous blood for use with COBAS h 232 instrument. The study population was divided into three groups based on troponin T levels. Group I included 150 patients with troponin T levels <0.03 ng/ml, 35 patients in Group II with levels between 0.03 and 0.1 ng/ml, and Group III included 11 patients with levels more than 0.1 ng/ml.

The collected data was analyzed using the Statistical Package of Social Sciences (SPSS) software. Data were expressed as the mean ± standard deviation. A $P < 0.05$ was considered statistically significant.

RESULTS

The study included 196 patients (168 males and 28 females). Eight patients were in the age group of 18-40 years, 69 patients between 41 and 60 years, and 119 patients above 60 years of age.

Out of 196 patients, 76.5% patients had troponin T levels <0.03, 17.9% patients had troponin T levels between 0.03 and 0.1, and 5.6% patients had troponin T levels >0.1, thus the majority of patients had low troponin T levels (Table 1).

Mean duration of ICU stay was 1.91 days in Group I, 4.03 in Group II, and 3.82 in Group III. Mean BNP values (957.3 in Group I, 2378 in Group II, and 3931.4 in Group III), systolic BP (104 mm Hg in Group I, 96.4 in Group II, and 94 in Group III), and ejection fraction (41.92 in Group I, 34.18 in Group II, and 34.2 in Group III) were high in patients with higher troponin T values. All patients in Group III required inotropic support and 45.5% patients had death. All were statistically significant except for systolic BP (Table 2).

DISCUSSION

Troponin T values on admission correlate well with morbidity and mortality. Out of 196 patients, 76.5% patients

Table 1: The study group

Groups	Troponin T	Frequency	Percentage
I	<0.03	150	76.5
II	0.03-0.1	35	17.9
III	>0.1	11	5.6

Table 2: Clinical and lab parameters with outcome

Parameter	Group I	Group II	Group III	*P* value
Systolic BP - Mean value (mm Hg)	104	96.4	94	0.319
Inotropic support - Oral (N)	90	4	0	0.001
Inotropic support - Intravenous (N)	23	27	11	0.001
Ejection fraction - Mean value (%)	41.92	34.18	34.2	0.001
BNP mean value (pg/ml)	967.53	2378	3934.94	0.001
ICU stay (mean duration days)	1.91	4.03	3.82	0.001
Death (N)	2	7	5	0.001

BP: Blood pressure, BNP: Brain natriuretic peptide, ICU: Intensive care unit

had troponin T levels <0.03, 17.9% patients had troponin T levels between 0.03 and 0.1, and 5.6% patients had troponin T levels>0.1, thus the majority of patients had low troponin T levels. In a study by Peacock *et al.*,[12] Troponin was measured at the time of admission in 84,872 of 105,388 patients (80.5%) who were hospitalized for acute decompensated HF. Of these patients, 67,924 had a creatinine level of <2.0 mg per deciliter. Cardiac troponin I was measured in 61,379 patients, and cardiac troponin T in 7880 patients (both proteins were measured in 1335 patients). Overall, 4240 patients (6.2%) were positive for troponin. Thus, the frequency correlated well with the present study.

The mean duration of ICU stay was lower (1.91 days) in patients with low troponin T value (<0.03 ng/ml), and was highest (4.03 days), for the patient group whose troponin T were between 0.03 and 0.1 ng/ml. The mean duration for ICU care for patients with troponin T above 0.1 ng/ml was 3.82 days. The lower value of mean for the patient group with troponin T above 0.1 ng/ml was 3.82 days can explained by the fact that early deaths in this subgroup resulted in shorter ICU stay compared to the patients group whose troponin T were between 0.03 and 0.1 ng/ml. In the study done by Peacock *et al.*, the median ICU stay was 4.1 for patients who were positive for troponin and 3.7 who were negative for troponin.

In the present study, patients with high troponin levels (>0.1 ng/m) had low mean systolic pressures of 94 mm Hg and patients with low troponin levels (<0.03 ng/ml) had higher mean systolic pressures of 103.9 mm Hg. Thus, patients with higher troponin T values were associated with lower systolic pressures and the results correlated well with the above studies. In the study done by Peacock *et al.*, patients with high troponin had lower systolic BP on admission, than those who had normal troponin. In one small study by Koide *et al.*,[13] there was no significant differences of BP between the two groups. In another small study by Angheloiu *et al.*,[14] systolic BP correlated well with troponin levels.

We measured serum troponin T, plasma BNP, and left ventricular ejection fraction (LVEF) on admission. In the present study, the mean BNP for patients with troponin T values <0.01 ng/ml was 967.53 and for the patients with troponin T values above 0.1 ng/ml was 3934.94. The mean BNP rise is proportional to an elevation of troponin T values. We hypothesize that an increase in troponin T concentrations is an expression of ongoing myocyte injury unmitigated by treatment of CHF and associated with a greater rise in BNP concentrations. Similar observations were in a study by Sato *et al.* In a small study by Koide *et al.*, patients in high troponin T group were significantly older and had a higher BNP on admission, as well as a higher prevalence of diabetes, and worse NYHA functional class at discharge. They also had higher discharge levels of BNP.

The measurement of troponin levels in patients who present with HF could provide independent prognostic information regarding in-hospital death and other clinical outcomes and can be useful for risk stratification of such patients. Ishii *et al.* reported a weak correlation between troponin T and BNP concentrations and suggested that markers specific for ongoing myocardial damage and left ventricular overload reflect different aspects of the pathophysiology of CHF and may identify different groups of patients at risk.

In the present study, the ejection fraction was highest (41.92) for patients with troponin <0.03 ng/ml and lower (34.18) for patients with troponin T value more than 0.1 ng/ml, elevated levels were associated with decline in LVEF and higher mortality rates. Increased wall stress and myocyte death may explain the mechanisms. Increased wall stress may directly activate intracellular signaling cascades and decreased subendocardial perfusion even in the absence of coronary artery disease, resulting in a decline in systolic function. In the study done by Peacock *et al.*, patients with high troponin had lower ejection fraction on admission.

In the present study, 45.5% of patients died in the subgroup of patients with higher troponin T (more than 0.1 ng/ml) and 20% of died in subgroup of patients with troponin T (0.03-0.1 ng/ml), whereas only 3.1% deaths were observed in patients with low troponin T (<0.03 ng/ml). Mortality was higher as the troponin T value increased. As per the available literature, persistently elevated levels were associated with a decline in LVEF and higher mortality rates. Additional factors, including activation of the renin-angiotensin system, sympathetic nervous system, and inflammatory cytokine system, have been implicated in provoking myocyte injury and cell death in HF.

The strength of the study is that we had observed a reasonable number to have a specific conclusion, but the

limitations remain. Our study differs from most of the prospective design by other studies and targeted focus on hospitalized patients. We did not do serial monitoring of troponin T and BNP levels and could not determine the persistence or variability of troponin T and BNP elevations during hospital stay. Furthermore, we could not do other available markers of cardiac failure.

CONCLUSION

There is an association between elevated cardiac troponin levels and adverse events in hospitalized patients with acute decompensated HF. In patients with acute decompensated HF, an elevated cardiac troponin T values are associated with higher in-hospital mortality, lower ejection fraction and systolic BP, increased requirement of inotropes, and need for prolonged intensive care. The combination of measuring cardiac troponin levels, a marker for ongoing myocardial damage, and BNP, a marker for left ventricular overload, represents a highly effective means of risk stratification of patients with acute decompensated HF.

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