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PROGNOSTIC CORRELATION OF CARDIAC TROPONIN T (cTnT) AND CARDIAC TROPONIN I (cTnI) ESTIMATION IN ACUTE DECOMPENSATED HEART FAILURE PATIENTS ADMITTED IN DMCH, LAHERIASARAI, BIHAR

Medicine

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ABSTRACT

Background : Heart failure is a common condition worldwide and it is a frequent cause of hospitalisation. It is the only common cardiovascular disease increasing in prevalence and incidence. Five year mortality rates for this condition are as high as 50% and it is the most frequent cause and hospitalization in patients older than 65 years.

Purpose: The purpose of the study is to investigate the prognostic value of admission high sensitivity troponins in patients with acute decompensated heart failure.

Material and Methods : 100 consecutive patients with acute decompensated heart failure admitted to wards of DMCH, Laheriasarai, Bihar from September, 2017 to September, 2019 (20 months approximately).

Results : In hospital mortality was higher in the hsTnT positive group(34.8%,n=23) than in negative group(8.8%,n=3). Death outside hospital was nil in troponin T negative patients but it was 9.1% in troponin positive group.

Conclusion : The patients with troponin T positivity show higher mortality(both in hospital and outside) and recurrent hospitalization in comparison with troponin T negative patients. Duration of stay in hospital is higher for hsTnT positive patients when compared with troponin negative patients. NYHA class and ejection fraction changed in a negative direction in patients of ADHF who are troponin positive.

KEYWORDS

INTRODUCTION

Heart failure is defined as cardiac dysfunction resulting in an inability to meet systemic metabolic demands, at rest or with exertion at normal ventricular filling pressure[1].

Acute heart failure is the term used to describe the rapid onset of signs and symptoms of pulmonary Congestion and/or Peripheral hypoperfusion due to cardiac and/or vascular dysfunction needing urgent therapy.

Acute heart failure includes both acute exacerbations of chronic heart failure (acutely decompensated chronic heart failure)or appearance of signs and symptoms without a prior history of heart failure (acute or denovo or new onset heart failure[2].

Heart failure is a common condition worldwide and it is a frequent cause of hospitalisation. It is the only common cardiovascular disease increasing in prevalence and incidence. Five year mortality rates for this condition are as high as 50% and it is the most frequent cause and hospitalization in patients older than 65 years.

Acute heart failure is one of the most common conditions encountered in emergency care and it is the single most costly medical syndrome in cardiology.

The use of biomarkers to guide therapy and indicate prognosis of heart failure patients is known since last 2 decades. In 2001, an NIH working group standardized the definition of a biomarker as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmalologic responses to a therapeutic intervention and defined types of biomarkers[3].

Multiple biomarkers to diagnose heart failure as well as to define adverse prognostic effect of their presence and increased titres have been used since last 2 decades. New and newer biomarkers are coming in the market with each one of them are released in the circulation due to some pathobiologic sequence of heart failure. NTProBNP, C-reactive protein, Endothelin-1, Arginine vasopressin, Cardiac Troponin are few examples. Very recently ChromagraninA, Galectin3, Osteoproterin, Adiponectin and Growth Differentiation Factor-15 have been introduced as biomarkers and newer molecules are on the offing's as innovative research and newer development are ongoing extensively.

Abnormal Concentrations of circulating Cardiac Troponins are found in patients with advance heart failure or acute decompensated states often without obvious myocardial ischemia and frequently in those without underlying CAD[4].

AIMS AND OBJECTIVES

The purpose of the study is to investigate the prognostic value of admission high sensitivity troponins in patients with acute decompensated heart failure.

SPECIFIC OBJECTIVES OF THE STUDY

1. To correlate the prognosis of ADHF (acute decompensated heart failure) patients with high admission cTnT and cTnI level.
2. To evaluate the adverse outcome of cTnT and cTnI positive patients in 3 months follow-up period.

MATERIALS AND METHODS

This prospective observational study was conducted at Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Bihar. Patients admitted in the indoor department of Medicine, DMCH with acute heart failure who are willing to be enrolled in the study.

100 consecutive patients with acute decompensated heart failure admitted to wards from September, 2017 to September, 2019 (20 months approximately).

Inclusion criteria - Male and female patients admitted with acute decompensated heart failure whose age is>=18 years and who will be giving informed consent for the study.

Exclusion criteria –

1. Myocardial infarction in the last 4 weeks.

2. Serum creatinine >2.5.
3. Age<=18 years.

Study Design

In this study 100 patients of Acute Decompensated Heart Failure who were admitted in the medicine indoor between September 2017 to September 2019, were enrolled and a detailed history taking, clinical examination and laboratory evaluation was done according to case record format. They were given adequate treatment for their condition. Within 24 hours of admission quantitative serum analysis of troponinT was done and the patients were categorized as troponin T positive(>50ng/l) or troponin T negative(<50ng/l).They were evaluated for diabetes and impaired renal function by testing admission fasting blood sugar and creatinine respectively. Other laboratory investigations like hemoglobin%, urea, serum sodium and potassium were performed At the start of the study on admission, NYHA class of the patients done according to NYHA criteria based on symptoms(83).Admission cardiac function were analysed by doing two dimensional, m-mode and colour Doppler echocardiography using ASE (American society of echocardiography) diagnostic criterion of echocardiography[82]. Measurement of LV dimensions and function was determined by the use of average of 3 cycles. All patients of acute heart failure patients received standard treatment of heart failure with diuretics, ACE inhibitors, betablockers, spironolactone in optimum dosage. Digoxin was added if required Some patients were initially presented with shock and hypotension for which ionotropic drugs like dopamine, dobutamine, noradrenaline had been used. Hospital course were followed up and those patients improved or alive were discharged in a stable condition. Before discharge clinical examinations and echocardiography were repeated. LVIDd, LVIDs, EF and NYHA class noted and the patients were advised to attend the cardiology outpatient department for follow up evaluation after three months. Some patients lost during follow-up and they were excluded from the study. At follow up the patients were again went for intensive clinical examination and NYHA class determined. Echocardiographic parameters were evaluated and same paramerters as of admission noted for comparison. Some patients were hospitalized again and the number of hospitalization and the number of days stayed in the hospital were noted. A number of patients had died in the hospital during their in hospital treatment and a few patients died outside hospital which were informed by the patient party or local attending doctor over telephone-those had been noted for future analysis. The aim of the study is to investigate the prognostic value of high sensitivity troponin T and predicting future events like death and rehospitalisation.

Laboratory test employed

1. Serum troponin T(quantitative) concentration were measured using Roche Cardiac T quantitative test strip(04877722190) and tested with Cobas h-232 POC system.
2. Echocardiographic examination was done using Siemens ACUSON CV 70 machine following ACC/AHA guideline, two dimensional, M mode and color Doppler evaluation done[82].
3. ECG strips are taken from BPL CARDIART machines in the ECG lab and other blood parameters were analysed according to case record format in the pathology and or biochemistry laboratory of our hospital.

Definitions and calculations:

1. Diabetes according to ADA criteria(FBS>126mg/dl).
2. Troponin T(quantitative)<50ng/l is negative and >50 ng/l is considered as positive. (detectable level by Roche quantitative test kit is more than 50 ng/l).
3. LVIDd is considered to be increased when it is beyond 54mm in female and more than 60 mm in male and, LVIDs when elevated over 41mm.
4. EF is normal when above 55%, mildly reduced below 55 to 44%, moderately reduced between 30 to 44% and when it is below.
5. Below 30 it is definitely poor[82].
6. NYHA CLASS-inversely related with cardiac function[83].

Plan for analysis of data

1. To describe the central tendency, mean is calculated for variability standard deviation is calculated for groups.
2. To compare one group to a hypothetical value chi square or binominal test is used.
3. To compare two unpaired groups, unpaired T test is used.
4. To compare two paired group, paired T test is used.
5. To compare 3 or more unmatched group ANOVA test is used.
6. To quantify association between two variables, Spearman correlation test is used.
7. To predict value from another measured variables,simple or multiple regression analysis is done.

Pooled data is analysed using STATA 11.2 version statistical software.

RESULTS AND ANALYSIS

In this study, a total of 100 patients who were admitted in DARBHANGA MEDICAL COLLEGE AND HOSPITAL indoors for Acute Decompensated Heart Failure were enrolled as per selection criteria. All the patients were subjected to detailed history taking, clinical examination and different laboratory investigations including fasting blood sugar, serum creatinine and admission high sensitivity quantitative troponin T estimation. Echocardiographic examination was done and different parameters were taken for analysis. The patients were afforded standard treatment. Their hospital course were analysed and the patients who were improved and stabilized, were discharged after noting their clinical condition, NYHA class and echocardiographic findings at that time. The patients who were dead had been noted. The stable patients were advised to come for follow up after 3(three) months to the cardiology outpatient department and detailed clinical analysis and echocrdiograhic examination were done as per study protocol. Collected data were analysed using suitable statistical methods and inferred in the following manner.

STATISTICAL METHODS

Categorical variables are expressed as number and percentage of patients and compared across the groups using chi square test for independence of Attributes. Continuous variables between subjects like FBS, creatinine, ejection fraction etc. have been expressed as mean value+-standard deviation and compared across two groups using logistic regression analysis and across more than two groups using analysis of variance (ANOVA) test. Continuous variables of ADHF patients like ejection fraction, number of hospitalizations and duration of stay in hospital has been expressed as mean value standard deviation. The statistical analysis software STATA 11.2 version has been used for the analysis.

ANALYSIS

65.2% of patients in hsTnT positive group are males whereas 34.8% patients were female. In troponin negative group, 55.9% were males and 44.1% were females.

Average age of patients in our study was (67.17 years 14.9, SD). In troponin positive patients minimum age was 29 years and 19 years in hsTnT negative patients whereas maximum age in troponin positive patients is 90yrs and troponin negative patient is 94 years. Mean age in cTnT positive group is (68.07SD 14.61) which is higher than mean age of negative group (65.35, SD15.59)

NYHA class of the enrolled patients showed that almost 88%(n=30) patients who are troponin negative and 86% in the negative group were in NYHA class IV .On discharge,73.8%(n=45) of cTnT +ve cases are in class IV whereas only 26.4%(n=9) of the –ve group. On follow up,8 patients(23.5%) of TnT negative(<50ng/l) group were in class IV in comparison to 38 patients (77.5%) in the troponin positive group.

Recurrent hospitalization(>= 2times) was a common problem in our study. 54.5 percent patients in the cTnT +ve group were hospitalized two times in comparison only 17.7% of patients in the negative group. Three times admission was also more in cTnT positive group (21.2%) than negative group(2.9%). 3.1% of patients in the positive group were admitted for 4 times and 2.9% in the negative group did so.

In hospital mortality was higher in the hsTnT positive group(34.8%,n=23) than in negative group(8.8%,n=3). Death outside hospital was nil in troponin T negative patients but it was 9.1% in troponin positive group.

Distribution Ejection Fraction (%) with hsTnT

Ejection fraction which is a measure of systolic function was 35.6%(mean, 4.3) at admission in hsTnT negative group whereas it was 30.2 (mean, Sd 6.7) for positive group. On discharge, EF was 28.1%(mean, SD7.5%) for cTnT positive group and 35.3(mean, SD5.2) in the negative group. At 3 months follow up EF was 28% (mean, SD) in the troponin positive group, in comparison it was 36.8% (mean, SD7.3) in the negative group.

Variation of hsTnT with Ejection Fraction

Mean systolic blood pressure was higher in Troponin negative patients on admission(109.114.1SD) than troponin positive patients (9110.5SD).At 3 months follow up SBP was much lower in hsTnT positive patients(91 10.3SD) than in hsTnT negative patients(108.810.5SD).

Distribution Fasting Blood Sugar with hsTnT

In hsTnT positive cases mean fasting blood sugar level on admission was 131.442.9 which was higher than that of troponin negative patients (98.933.2).

Distribution Left Ventricular Internal Diameter (Diastolic) with hsTnT LVIDD on admission in cTnT positive patients was63.48.5 and in negative patients it was 56.86.2.On follow up study, LVIDD increased to 658.4 in troponin positive patients but decreased into 55.58.0 in troponin negative patients.

Distribution Left Ventricular Internal Diameter (Systolic) with hsTnT Systolic internal diameter on echocardiography was 46.65.8 in troponin T negative patients and was 53.78.9 in troponin positive patients on admission. At discharge, it was 57.915.8 in hsTnT positive group and 49.320.2 in troponin negative patients.

Distribution duration of stay in hospital & number of hospitalization with hsTnT

Duration of stay in hospital was 11.95.3 days in cTnT positive patients whereas it was 5.93.6 in negative patients of troponin. Number of hospitalization was 2.10.74 times in troponin positive patients and 1.30.68 times for troponin negative patients.

Logistic Regression Analysis of SBP,FBS,LVID(d), LVID(s), EF, Duration of stay in hospital with hsTnT positivity

Variables	Odds Ratio	Std. Err	95% CI	P value
Systolic Blood Pressure (mm-Hg)				
Admission	0.99	0.03	0.94 - 1.05	0.838
Discharge	1.01	0.04	0.93 - 1.10	0.788
Follow up	0.86	0.04	0.79 - 0.93	<0.001
Fast Blood Sugar (mg/dl)				
Admission	1.02	0.01	1.00-1.04	0.049
LVIDD (Left Ventricular Internal Diameter-Diastole, mm)				
Admission	0.89	0.07	0.76 - 1.05	0.172
Discharge	0.99	0.13	0.77 - 1.28	0.972
Follow up	1.23	0.11	1.03 - 1.46	0.022
LVIDS (Left Ventricular Internal Diameter-Systole, mm)				
Admission	0.87	0.06	0.75 - 1.01	0.064
Discharge	1.27	0.09	1.09 - 1.48	0.002
Follow up	1.01	0.01	0.97 - 1.03	0.953
EF (Ejection Fraction %)				
Admission	0.98	0.07	0.85 - 1.14	0.862
Duration of Stay	1.38	0.09	1.20 to 1.59	<0.001
in Hospital Creatinine:				
	Coefficient	**Std. Err**	**95% CI**	**P value**
Admission	0.33	0.09	0.15 - 0.51	<0.001

Logistic regression analysis-

The predictor of main interest in my analysis was the measurement of quantitative troponin T and I consider adjusting this data with age, SBP, FBS, LVID(d), LVID(s),, EF, NYHA class one to one (univariate analysis).

The logistic regression analysis of datas collected has the following important findings.

Systolic Blood Pressure is reduced significantly (p<0.001) on follow up study in hsTnT positive patients.

FBS(>126mg/dl)is significantly increased on admission in hsTnT positive patients (131.442.9) in compared to hsTnT negative patients.(meanSD=98.933.2). The data is statistically significant on admission(p=0.049).

LVID(d) is significantly increased at admission, discharge and at follow up study. The increase is statistically significant at 3month follow-up examination(p=0.022)

LVID(s) is raised in both the groups but the increase is more in hsTnt positive patients and it becomes statistically significant at discharge (p=0.002).

Reduction in EF(%) is statistically significant (p=0.03.CI=0.75to 0.94 and odds ratio0.84) in the three months follow-up study.

Duration of stay in hospital is more in hsTnT positive patients than in troponin negative patients as detailed in the descriptive study above. The value becomes statistically significant in our study(p<0.001).

DISCUSSION

The study was conducted amongst patients attending outpatient/MIPD/MOPD of the Darbhanga Medical College and Hospital The study was conducted amongst 100 patients admitted into indoor with diagnosis of decompensated heart failure. In GISSI HF trial 64% patients are positive for hsTnI at baseline and 47.1% at baselineTnT positive.Shakuja et al found that 46% had measureable troponin T>0.01 ng/ml and in two recent reports of Xue et al and Pasucal Fig et al reported that nearly all patients with acutely decompensated heart failure had a highly sensitive troponin I or T value above the 99th percentile.Miller et al (53%), Perna et al (32%), Latini et al (92% hsTnT), parenti et al (48%) and Howrich et al (49.1%) demonstrated increased incidence of detectable troponins in their studies. So our study which shows 66% positive patients for hsTnT is corroborating with findings of other studies.

In hospital mortlity was higher (23.88%) for troponin positive patients (n=23) in comparison to troponin negative patients (3.12%) (n=3). Out of hospital death was also higher in cTnT positive patients(n=6) (9.1%) when compared with patients of troponin negativity(n=0). These results corroborates with previous studies of Latini et al and Kocial et al (65,66) which showed higher incidence of troponin positivity in ADHF patients and prognosis worse than in cTnT negative patients.La Vacchia et al (2000), Howrich et al (2003), DeiCarlo et al, You et al (2007), Miller et al (2007), Peacock et al (2008), all the investigators in their studies found a clear cut association of increased incidence of death in troponin detectable and/or troponin positive patients of acutely decompensated heare failure patients. In ADHERE registry, mortality was 8% in troponin positve patiens versus 2.7% in negative patients for troponin.84% of patients had detectable troponin in their serum and 32% had abnormal levels. ADHERE investigators found that troponin positive patients had lower blood pressure values and inhospital mortality was also higher.In Val HeFT, 24 months of followup of ADHF patients showed 16.5% mortality in patients with non measurable troponin versus 43.3 % in patients who had measureable cTnT. Mortality was lower with lowest quartile (7.8%) vis a vis with highest quartile (35.6%). In FINN AKVA study in acute heart failure, 51.1% had cTnI and 29.7% had cTnT levels above the cut off and all cause mortality at 6 months was 18.7%. Pasucal figal et al found 83% of their patients had an hs TnT level above the 99th percentile value of 0.013 ng/ml. A total of 29 patients died (27.1%) died in their study and the patients who died had significantly higher concentration of hsTnT (0.028 to 0.124 ng/ml). A continuous slow release of troponins might reflect ongoing cardiac myocyte cell death and stretch of cardiac myocytes might lead to leakage of the cytosolic pool of troponin T by transient loss of cell membrane integrity. Recurrent hospitalisation was a problem, which was very much significant in troponin positive positive patients in comparison to troponin negative patients (Bar Diag). Which was in concordance with the earlier studies like that of Val He FT, EFFECT Study and ADHERE registry. Multiple investigators like Del Carlo et al and Hudson et al (RR2.7,CI 1.7 to 4.3) found significant association between detectable troponins and HF rehospitalisations.

Duration of stay in hospital was more in troponin T positive patients in our study (p<0.001). Latini et al and Val He FT investigators demonstrated that patients with heart failure who were positive for troponins required greater use of hospital resources including longer stay in hospitals and intensive care units. Ejection fraction which is an indication of cardiac systolic function is low in both troponin T positive and negative patients on admission but the deterioration of systolic function was noted to be significant during the followup period (p value0.003) in troponin positive patients. NYHA functional class which denotes clinical condition of the patient was mostly III or IV during admission in both troponin T positive or negative patients of ADHF,but with time symptoms and signs deteriorated more in the troponin positive patients and accordingly NYHA class changed on a higher direction (like III to IV)(bar diagram)

Thus the present study demonstrated that the patients who were positive for hs troponin has worse prognosis than troponin T negative patients and with time there was deterioration of symptoms or functioal class in these patients.

Similar observations had been met with studies of Latini et al and Val He FT which matche's with findings of present study.

In short the results of present study which is also in correlation with studies of Latini et al and Val He FT.

CONCLUSION

The present study titled prognostic correlation of cardiac troponin T estimation in acute decompensated heart failure patients admitted in a tertiary care hospital clearly depicts a higher troponin T concentration in patients of ADHF. The patients with troponin T positivity show higher mortality(both in hospital and outside) and recurrent hospitalization in comparison with troponin T negative patients. Duration of stay in hospital is higher for hsTnT positive patients when compared with troponin negative patients. NYHA class and ejection fraction changed in a negative direction in patients of ADHF who are troponin positive.

Though from the present study, we got some positive directions in making prognostic correlation of ADHF patients with troponin positivity, further large prospective randomized trials are necessary before coming to definite conclusion in making recommendation for doing quantitative troponin T in all patients of acute decompensated heart failure for prognosis and guiding therapy.

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