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Original Article

Internal Medicine Section

Cardiac Troponin I Levels in Acute Exacerbation of COPD Patients: A Cross-sectional Study

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is associated with right ventricular overloading and pulmonary hypertension. In COPD patients co-morbidities determine the outcome and quality of life. Cardiac Troponins (cTn) are suspected to be elevated in right ventricular failure.

Aim: To find the incidence of cardiac Troponin I levels and association of elevated cTnI levels with clinical outcome in acute exacerbation of COPD.

Materials and Methods: The cross-sectional study comprised of 102 patients with acute exacerbation of COPD. These patients were admitted in medical wards and Intensive Care Unit (ICU) in the Department of General Medicine, Karnataka Institute of Medical Sciences Hospital, Hubli, Karnataka, India, from 2018-2020. Investigations included complete blood count, renal function tests, serum electrolytes, liver function tests, Electrocardiography (ECG), ECHO and chest X-ray. Association of cardiac troponin I and acute exacerbation of COPD was evaluated. The cTnI level ≥0.01 ng/mL was considered positive.

Results: The serum cTnI was found to be positive in 43 (42.2%) patients with acute exacerbation of COPD. The patients with cTnI levels ≥0.01 ng/mL had significantly higher need for Non Invasive Ventilation (NIV) 32 (74.4%), invasive ventilation support 5 (11.6%), prolonged duration of hospital stay 33 (76.7%), and higher mortality 15 (34.9%) rate as compared to patients having cTnI <0.01 ng/mL.

Conclusion: The cTnI is elevated in a significant subset of patients with acute exacerbation of COPD. cTnI elevation was associated with higher need for NIV and invasive ventilator support. Levels of cTnI ≥0.01 ng/mL may be considered as a biomarker to predict morbidity and mortality in acute exacerbation of COPD patients.

Keywords: Chronic obstructive pulmonary disease, Invasive ventilation support, Non invasive ventilation, Pulmonary hypertension

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is characterised by a poorly reversible limitation in airflow, and corresponds to the major cause of chronic respiratory insufficiency and cor pulmonale [1]. COPD as a systemic disease causes structural and functional changes in lung and in many organs [1]. It is a chronic inflammatory disease with extra pulmonary manifestations like cardiovascular diseases, osteoporosis, lung cancer, diabetes, metabolic syndrome, and depression. Acute Exacerbations of COPD (AECOPD) is defined as "an event in the natural course of the disease characterised by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD" [1].

The AECOPD accounts for substantial morbidity and mortality, attributed to COPD [2]. These impair quality of life and also cause permanent loss of lung function. Hospitalisations due to COPD exacerbations are a major economic burden [3,4]. Cardiovascular risk factors and cardiac co-morbidity are more in patients with COPD. It reflects the severity of the exacerbation. COPD patients with elevated troponins have reduced saturations, ABG showing more acidotic and more hypercapnoeic [5]. In AECOPD, damage to the cardiac myocyte and cardiac injury occurs. Right ventricular (RV) dysfunction and pulmonary vascular disease are common and progressing in nature [4]. Loss of cell membrane integrity releases of free cytoplasm troponin-I into the circulation followed by release of structurally bound troponin resulting in sustained elevation [6].

The cTnI elevation has been attributed to increased work of breathing, increased left ventricular afterload because of more negative intrathoracic pressure, worsening of pulmonary hypertension, hypoxaemia and hypercapnoea [7]. This study aimed to evaluate the prognostic value of Troponin I level, and its impact on the hospital outcome in patients with AECOPD.

MATERIALS AND METHODS

It was a single centre cross-sectional study, conducted on patients admitted in the Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India, from 1st November 2018 to 30th March 2020. Institutional ethical clearance was obtained vide letter number KIMS:ETHCS COMM: 108/2: 2018-19. The patients were enrolled into the study after obtaining written consent from them or their attendants.

Sample size calculation: The sample size was calculated using the following formula:

$n=(z)^2pq/d^2$ n=sample size, CI=95%, d=0.2, z=1.96, p=0.12, q (100-p)=0.88

$n=(1.96)^2\times0.12\times0.88/(0.2)^2\times10$

n=102

Inclusion criteria: All hospitalised AECOPD patients with worsening breathlessness along with increased purulence or quantity of sputum were included.

Exclusion criteria: Present or previous case of Ischaemic Heart Disease (IHD), acute myocardial infarction and renal failure were excluded.

Study Procedure

Patients' demographic details, history, duration of COPD, co-morbid condition like Type 2 Diabetes mellitus and systemic hypertension, history of smoking and alcohol consumption were noted. Investigations included complete blood count, renal function tests,

serum electrolytes, C-reactive Protein (CRP), liver function tests, ECG, ECHO and chest X-ray. Association of cardiac troponin I and acute exacerbation of COPD was evaluated. Normal range of cTnI was considered to be between 0 and 0.01 ng/mL. A positive cTnI test was 0.01 ng/mL or higher.

STATISTICAL ANALYSIS

Data was analysed using Statistical Package for Social Sciences (SPSS) version 22.0 software. A p-value of <0.05 was considered as statistically significant. Chi-square test was used as test of significance for qualitative data. Pearson correlation was done to find the correlation between quantitative and qualitative variables.

RESULTS

The study group comprised of 102 AECOPD patients. These patients were admitted in medical wards, and ICU. Mean age of the study population was 64.22±10.611 years. Majority of the study population were in the age group 61-70 years (33.3%). Total 71 (69.6%) patients were males, and 31 (30.4%) were females.

The cTnI was positive in 43 (42.2%) patients and negative in 59 (57.8%) patients. There was a non-significant difference in cTnI level in relation to (age, sex, smoking habits and causes of exacerbation p>0.05), but a significant difference with severity of exacerbation (p<0.05) [Table/Fig-1].

Parameters	Troponin I		p-value
	Normal ≤0.01 count (%) 59 (57.8%)	Increased >0.01 count (%) 43 (42.2%)	
Age (Mean±SD)	60.5±7.2	59±7.5	>0.05
Sex			
Males (71)	40 (67.7)	31 (72)	>0.05
Females (31)	19 (32.2)	12 (27.9)	
Smoking status			
None (56)	36 (61.0)	20 (46.5)	>0.05
Ex (6)	1 (1.6)	5 (11.6)	
Current (40)	22 (37.2)	18 (41.8)	
Severity of exacerbation			
Mild (23)	19 (32.2)	4 (9.3)	<0.05
Moderate (27)	16 (27.1)	11 (25.5)	
Severe (52)	24 (40.6)	28 (65.1)	

[Table/Fig-1]: Baseline characteristics and clinical data of patients in relation to cardiac Troponin I level (ng/mL).

There was a significant positive correlation between duration of COPD, and Troponin I. i.e. with increase in duration of COPD, there was increase in Troponin I levels [Table/Fig-2].

Variables		Troponin I		Significant
		Increased (>0.01) Count (%) 43 (42.2%)	Normal (<0.01) Count (%) 59 (57.8%)	
COPD duration	≤5 years (32)	6 (13.9)	26 (44.0)	χ^2=14.966, df=2, p=0.001
	6 to 10 years (59)	28 (65.1)	31 (52.5)	
	>10 years (11)	9 (20.9)	2 (10.9)	
Mean duration of COPD	7.02±2.41	Pearson correlation (r)=0.500		
Mean Troponin level (ng/mL)	0.606±1.0125	p-value <0.001		

[Table/Fig-2]: Duration of COPD and troponin I correlation.

There was a significant difference in Troponin elevation in relation to sinus tachycardia and P-pulmonale, Mean Pulmonary Artery Pressure (mPAP) but a non significant difference as regards Atrial Fibrillation (AF) among the AECOPD patients [Table/Fig-3]. There was a significant difference in Troponin elevation with regards to CRP and White Blood Cells (WBC) count among the studied AECOPD patients [Table/Fig-4].

Parameters	cTnI >0.01 43 (42.2%)	cTnI <0.01 59 (57.8%)	p-value
P-pulmonale			
Positive (88)	43 (100%)	45 (76.2)	<0.05
Negative (14)	0 (0)	14 (23.7)	
Sinus tachycardia			
Positive (56)	38 (88.3)	18 (30.5)	<0.05
Negative (46)	5 (11.6)	41 (69.4)	
AF			
Positive (4)	4 (9.3)	0 (0)	>0.05
Negative (98)	39 (90.6)	59 (100)	
PASP mmHg			
Normal	22 (51.2)	39 (66.1)	<0.05
Mild	4 (9.3)	9 (15.3)	
Moderate	2 (4.7)	2 (3.4)	
Severe	15 (34.9)	9 (15.3)	

[Table/Fig-3]: Cardiac changes by ECG and ECHO and its relation to troponin.
PASP: Pulmonary artery systoloc presure; AF: Atrial fibrillation

Variables		Troponin I			p-value
		Increased (>0.01) Count (%) 43 (42.2%)	Normal (<0.01) Count (%) 59 (57.8%)	Total Count (%)	
WBC (cells/uL)	<4000	1 (2.3)	1 (1.7)	2 (2.0)	<0.001
	4000 to 11000	8 (18.6)	41 (69.5)	49 (48.0)	
	>11000	34 (79.1)	17 (28.8)	51 (50.0)	
	Total	43 (100.0)	59 (100.0)	102 (100.0)	
CRP (mg/dL)	≤25	1 (2.3)	37 (62.7)	38 (37.3)	<0.001
	>25	42 (97.7)	22 (37.)	64 (62.7)	
	Total	43 (100.0)	59 (100.0)	102 (100.0)	

[Table/Fig-4]: Association between Troponin I levels and CRP, WBC count among studied AECOPD patients and Troponin I levels.

[Table/Fig-5,6] shows a significant difference in Troponin level in relation to the time since admission, need for mechanical ventilation, and outcome (p<0.05), as cTnI positivity was more prominent among patients with AECOPD. Cases which had elevated cTnI levels had increased need of NIV (74.4%), and invasive mechanical ventilation (11.6%) and increased duration of hospital stay. In the group with increased troponin I, higher mortality (34.9%) was observed because of cardiorespiratory arrest. Serum cTnI level showed a weak but positive significant correlation with the duration of hospitalisation, PASP, WBC and CRP [Table/Fig-7].

Variables		Troponin I			p-value
		Increased (>0.01) Count (%) 43 (42.2)	Normal (<0.01) Count (%) 59 (57.8)	Total Count (%)	
Hospital stay	≤10 days	10 (23.3)	51 (86.4)	61 (59.8)	<0.001
	>10 days	33 (76.7)	8 (13.6)	41 (40.2)	
Outcome	Death	15 (34.9)	5 (8.5)	20 (19.6)	0.001
	Discharged	28 (65.1)	54 (91.5)	82 (80.4)	
	Total	43 (100.0)	59	102 (100.0)	

[Table/Fig-5]: Duration of hospital stay and outcome of patients in present study population comparison with respect to Troponin I levels.

Variables		Troponin I			p-value
		Increased (>0.01)	Normal (<0.01)	Total	
		Count (%) 43 (42.2%)	Count (%) 59 (57.8%)	Count (%)	
NIV	No	11 (25.6)	42 (71.2)	53 (52.0)	0.001
	Yes	32 (74.4)	17 (28.8)	49 (48.0)	
IMV	No	38 (88.4)	58 (98.3)	96 (94.1)	0.035
	Yes	5 (11.6)	1 (1.7)	6 (5.9)	
Total		43 (100.0)	59 (100.0)	102 (100.0)	

[Table/Fig-6]: NIV and IMV requirement comparison with respect to Troponin I levels among AECOPD subjects.

Parameters	r-value	p-value
PASP mmHg	0.5	<0.05
WBC cells/uL	0.3	<0.001
CRP mg/dL	0.5	<0.001
Hospital stay in days	0.4	<0.001

[Table/Fig-7]: Correlation between Troponin level and (PASP,WBC, CRP and duration of hospitalisation) among studied AECOPD patients.
PASP: Pulmonary artery systolic pressure; WBC: White blood cells; CRP: C-reactive protein

DISCUSSION

Cardiac troponin I (cTnI) assay measures cardio-specific components and is a marker for cardiac muscle cell injury. It has no cross reactivity with the two skeletal muscle isoforms. In cardiac injury, CTnI is a highly sensitive and long-lasting marker [7,8]. In the present study, cTnI was elevated (above 0.01 ng/mL) in 42.2% of AECOPD patients, the mean age of patient with positive cTnI was 59±7.5 years, and the mean age of patients with negative cTnI was 60.5±7.2 years [Table/Fig-1]. This is similar to the findings by Baillard C et al., [3], who found no difference between positive and negative cTnI in relation to age. The effect of smoking on cardiac troponin I in the published studies [3,9] and the present study showed no significant statistical difference. Contrarily, Antonelli Incalzi R et al., demonstrated that history of smoking, age, hypertension, and diabetes are common and led to a high prevalence of cardiac co-morbidity [10].

There was a significant statistical difference between patients with P-pulmonale and those without P-pulmonale. But there was no significant statistical difference between cTnI positive and negative patients with AF. This is in agreement with Baillard C et al., [3], who found no significant effect of AF on cTnI positivity. Sinus tachycardia showed a significant statistical difference between cTnI positive and negative patients. This is in agreement with the findings by Noble JS et al., who reported a significant cTnI elevation in patients with tachycardia [7]. There was a significant statistical difference between patients with high PAP in cTnI positivity. These findings are in agreement with those of Youssef et al., [11] and Aksay E et al., [12], who reported a significant effect of right ventricular dysfunction on cTnI elevation. Harvey MG and Hancox RJ [13] suggested that acute exacerbation causes cardiac damage and Troponin release.

In AECOPD, there occurs hypoxia and acidosis due to sepsis and/or metabolic stress which in turn causes acute elevation of PAP and cardiac damage. Hasaneen N et al., and Sokucu SN et al., found a strong correlation between right ventricular dysfunction and cTnI in a group of AECOPD patients [14,15]. CRP level was raised in cTnI positive patients (97.7%). There was a positive correlation between elevated CRP and longer hospital stay with greater need for non invasive ventilation.

As regards the need for MV, cTnI positivity was more prominent among patients who were on NIV support (74.4%) and invasive mechanical ventilator support (11.6%) [Table/Fig-6]. This is in agreement with the findings by Baillard C et al., [3] and Martins CS et al., [16]. Patients with respiratory failure or shock needs supportive care as mechanical ventilation. It worsen the right ventricular function and limitis diastolic filling of the right ventricule [17]. In this study, serum cTnI level showed significant correlation with the duration of hospitalisation [Table/Fig-5,7], where cTnI positivity was more prominent in patients with longer duration. This could be attributed to the more severity of the disease and exacerbation. Martin CS et al., and King DA et al., found that patients with more days in the hospital has high cTnI level than those with shorter duration [16,18].

As regards survival, patients with higher cTnI had a higher mortality. These findings are in agreement with few other studies that [3,11,19] reported high mortality and the positive predictive value of having a high cTnI level. In-ICU and in-hospital mortality were higher in patients who reported an elevated cTnI at admission. The above findings suggest that cardiac injury exists in patients with exacerbation of COPD. Cardiac muscle injury the due to increased work of breathing, increased left ventricular afterload, worsening of pulmonary hypertension, hypoxemia and hypercapnia [13]. The patients with elevated cTnI levels in AECOPD cases were identified as a group with high risk for complications and mortality. It is important to identify these subgroups early and undertake appropriate treatment helps in good outcome.

Limitation(s)

The present study was limited by the fact that the long-term outcome associated with cTnI elevation could not be known.

CONCLUSION(S)

The study reported an elevated cTnI in acute exacerbation of COPD patients. Need for ICU admission and ventilator support was significantly more in cTnI positive patients. In AECOPD patients cTnI ≥0.01 ng/mL may be considered as a biomarker to predict morbidity, longer hospital stay, and higher mortality. Thus, cTnI levels at admission can be used to triage patients who are at a higher risk.

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