Original Article

Prognostic value of cardiac troponin I during acute exacerbation of chronic obstructive pulmonary disease: A prospective study

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a major cause of mortality and morbidity. It is the fourth leading cause of death worldwide. Acute exacerbations of COPD are common and are associated with worsening lung function and mortality. **Objectives:** To evaluate the prevalence of elevation of cTnI in patients admitted with acute exacerbation of COPD and to study its association with the need for ventilator support, duration of hospital stay, and in-hospital mortality. **Methods:** In a prospective design, 50 patients admitted to our hospital with acute exacerbation of COPD were included. cTnI was assayed in a blood sample obtained at admission and 24 h later. Levels above 0.017 μg/L were taken as positive. The following data were also recorded–demographic data, pattern of tobacco use, clinical symptoms and signs, comorbidities, Glasgow Coma Scale, arterial blood gas, electrocardiogram/two-dimensional echocardiography, chest X-ray, and peak expiratory flow rate. **Results:** Among the 50 patients, 4 were females, and 46 were males. cTnI was positive in 32% of patients with a mean value of 0.272. Patients with cTnI positive were taken as Group I and those with negative were included in Group II. Prevalence of comorbidities was higher in cTnI positive group, so was the duration of COPD. cTnI elevation correlated significantly with the need for ICU admission and ventilator support. No significant difference was found in the duration of ventilator support, hospital stay, and in-hospital mortality. **Conclusion:** cTnI is elevated in a significant subset of patients with acute exacerbation of COPD. Duration of their illness was longer, higher incidence of ischemic heart disease was also found in these patients. Patients with cTnI elevation are more likely to require ICU care and ventilator support. However, it did not predict in-hospital mortality. Thus, it can be used as a marker to identify high-risk patients during acute exacerbation of COPD.

KEY WORDS: Chronic obstructive pulmonary disease, mortality, troponin I, ventilator support

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. Currently ranked as the 4th leading cause of death worldwide, it represents an important public health challenge that is both preventable and treatable. The burden of COPD is projected to increase in coming decades due to continued exposure to COPD risk factors and the aging of the world's population.[1] World Health Organization (WHO) predicts that it will become the third leading cause of mortality by 2030[2] COPD often coexists with other comorbidities which may have a significant impact on its prognosis. Cardiovascular diseases, osteoporosis, lung cancer, diabetes, metabolic syndrome, and depression are among a few of them.[3]

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Cardiovascular disease is a major comorbidity in COPD patients and probably the most frequent and most important coexisting illness as these conditions have many common risk factors such as age, male sex, cigarette smoking although its actual prevalence is unknown

COPD exacerbations are defined as, "An event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute on onset, and may warrant a change in regular medication in a patient with underlying COPD"[1,4]

Many factors lead to acute exacerbation, of which bacterial or viral infections are most common; however, in many patients, the underlying cause remains unrecognized, of which acute left ventricular (LV) dysfunction may be one. Its vice versa also holds true that acute exacerbation, whether or not with a history of cor pulmonale, has an increased cardiac burden, but prompt identification remains difficult because of nonspecific symptoms and signs, and echocardiography is not always feasible to recognize it. However, identifying these patients may influence treatment and outcome for many of them. Thus, biomarkers such as cardiac troponins which can be measured by a simple test and are widely available can help us identify these patients. This study was aimed to see if cardiac troponin I (cTnI) has prognostic significance during an acute exacerbation of COPD.

METHODS

This was a prospective study**.** Fifty patients admitted to our hospital with signs and symptoms of acute exacerbation of COPD between November 2012 and October 2013 were included in the study. The patients with marked renal failure, persistent hemodynamic instability requiring inotropic or vasoactive support, pulmonary embolism, myocardial infarction, sepsis, and cardiac arrest before admission were excluded. Written informed consent was taken from each patient.

Basic demographic data, history, and symptoms were recorded from each patient.

Depending on tobacco use patients were categorized as current, former (>1-year abstinence), or nonsmokers. Glasgow Coma Score was also calculated for each case.

Probability of pulmonary embolism was assessed using Wells score

Each patient was subjected to arterial blood gas analysis, chest X-ray, electrocardiogram (ECG), echocardiography, spirometry in patients who were able to perform it, and other routine blood/biochemical investigations.

The following were also recorded:

- Duration of hospital stay, including stay in ICU and duration of ventilator support if any and in-hospital mortality and not mortality rate, was noted for each patient.

Blood samples for cTnI taken on admission and 24 h later were analyzed using quantitative assay by immunofluorescence method. Levels above 0.017 μg/l were taken as positive.

RESULTS

Fifty patients who met the inclusion and exclusion criteria were included in the study.

Among them, 46 were males, and 4 were females. Fifty-eight percent of the patients were current smokers, 34% were former smokers, and only 4% were nonsmokers.

cTnI was found to be positive in 19 patients and negative in 31 patients. Accordingly, they were divided into two groups, Group I included patients with cTnI positive and Group II with cTnI negative. Mean age did not significantly differ between the two groups; it was 64.1 years in Group I and 66.72 years in Group II. The time between onset of symptoms to presentation to the hospital in majority of patients was 1–3 days in Group I, whereas it was >7 days in Group II.

Mean duration of COPD in Group I was 6.42 years, whereas in Group II, it was 3.97 years. Comorbidities such as hypertension, diabetes, ischemic heart disease (IHD), and atrial fibrillation were more prevalent in patients in Group I compared to Group II. Further, this difference was statistically significant for IHD. Mean SpO_2 in cTnI positive group was 75%, and in cTnI negative group, it was 82.29%, which was significantly lower.

There was no significant difference in findings on systemic examination and Glasgow Coma Scale among the patients in both groups. These baseline characteristics of patients in both groups are compared and shown in Table 1.

Comparing the cardiovascular characteristics of patients between the two groups, atrial fibrillation (AF) was found in one patient in Group I. IHD was prevalent in 36.8% of patients in Group I and only in 6.45% of patients in Group II.

Sinus tachycardia was the most common finding on ECG in both the groups, followed by P pulmonale which was seen on ECG in 31.5% of patients with elevated cTnI and 45.2% with cTnI negative. AF was found in 1 patient. Other findings on ECG included atrial premature contractions, ventricular premature contractions, multifocal atrial tachycardia, and evidence of old myocardial infarction as depicted in Table 2.

On two-dimensional echocardiography, the pulmonary artery systolic pressure (PASP) at rest was high in about 90% patients in both groups. However, severe pulmonary hypertension was found in 31.5% of patients with cTnI elevated as compared to 19.5% of patients without elevated cTnI. Dilated right heart chambers were found in 63.15% patients in Group I versus 32.25% patients in Group II.

LV dysfunction was also significantly higher in patients belonging to Group I [Table 3].

About 94.7% needed admission to ICU in the group with elevated cTnI, whereas only 51.6% required admission to ICU in those without cTnI elevation.

About 78.9% and 38.7% patients required ventilator support, including both noninvasive and invasive ventilation, among the two groups, respectively. However, no significant difference was found in the duration of ventilator support required.

No significant difference was found in the length of ICU stay or hospital stay among both groups [Table 4].

Mortality

Mortality was 15.8% in Group I and 6.5% in Group II.

Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean ± standard deviation (min-max), and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

Student's *t*-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

DISCUSSION

Among the 50 patients included in this study, cTnI was found to be elevated in 19 patients, which corresponds to

Table 1: Baseline characteristics of patients on admission according to level of cTnI

Variables	cTnI positive (>0.017 μg/dL) (*n*=19) (%)	cTnI negative (<0.017 μg/dL) (*n*=31) (%)	*P*
Troponin I (μg/L)	0.272	<0.017	-
Age	64.15±7.75	66.72±8.62	0.286
Males	17 (89.5)	29 (93.5)	0.606
Females	2 (10.5)	2 (6.5)	0.606
Current smokers	9 (47.4)	20 (64.5)	0.232
Disease duration (years)	6.42±3.34	3.97±1.94	0.002**
Comorbidity	10 (52.6)	8 (25.8)	0.055+
HTN	6 (31.6)	5 (16.1)	0.201
DM	5 (26.3)	5 (16.1)	0.382
IHD	7 (36.8)	2 (6.5)	0.018*
AF	1 (5.3)	0 (0)	0.204
Clinical features			
RR	31.79±4.61	30.32±4.90	0.299
HR	108.32±12.42	103.94±11.76	0.217
SBP	123.47±22.91	128.13±16.99	0.415
SpO_2	75.00±11.44	82.29±4.86	0.003**
Rhonchi	17 (89.5)	30 (96.8)	0.291
Crackles	13 (68.4)	18 (58.1)	0.464
Silent chest	6 (31.6)	4 (12.9)	0.109
GCS			
<6.0	1 (5.3)	0	0.388
6-9	2 (10.5)	1 (3.2)	0.549
>9	16 (84.2)	30 (96.7)	0.147
PaO_2 mmHg	78.07±46.05	76.77±32.69	0.907
$PaCO_2$ mmHg	54.76±24.19	47.77±23.29	0.315

** *P* value <0.05 is significant. cTnI: Cardiac troponin I, DM: Diabetes mellitus, HTN: Hypertension, IHD: Ischaemic heart disease, AF: Atrial fibrillation, RR: Respiratory rate, HR: Heart rate, SBP: Systolic blood pressure, GCS: Glasgow Coma Scale

Table 2: Cardiovascular characteristics of patients according to level of cTnI

Variables	cTnI positive (>0.017 μg/dL) (*n*=19) (%)	cTnI negative (<0.017 μg/dL) (*n*=31) (%)	*P*
Cardiovascular disease			
AF	1 (5.26)	Nil	0.380
IHD	7 (36.8)	2 (6.45)	0.018*
ECG			
ST	14 (73.7)	24 (77.42)	0.764
P pulmonale	6 (31.5)	14 (45.16)	0.341
AF	1 (5.26)	Nil	0.380
Others	Old MI=4 APC's=2	APC=1 VPC=1 MAT=1	-

* *P* value <0.05 is significant. cTnI: Cardiac troponin I, IHD: Ischemic heart disease, AF: Atrial fibrillation, ECG: Electrocardiography, MI: Myocardial infarction, APC: Atrial premature contraction, VPC: Ventricular premature contraction, MAT: Multifocal atrial tachycardia

Table 3: Comparing echocardiography characteristics of patients in both groups

Variables	Troponin I positive (>0.017 μg/dL) (*n*=19) (%)	Troponin I negative (<0.017 μg/dL) (*n*=31) (%)	*P*
PASP mmHg			
Normal <30	2 (10.5)	3 (9.6)	0.914
Mild 31-45	7 (36.8)	15 (48.4)	0.218
Moderate 45-59	4 (21.05)	7 (22.5)	0.859
Severe >60	6 (31.59)	6 (19.5)	0.326
Chambers			
Dilated RA/RV	12 (63.15)	10 (32.25)	0.033*
LVD	6 (31.59)	1 (3.22)	0.009*

* *P* value <0.05 is significant. PASP: Pulmonary artery systolic pressure, LVD: Left ventricular dysfunction, RV: Right ventricle, RA: Right atrium

Table 4: Admission to ICU, need for ventilation, length of stay, and mortality of patients according to level of cTnI

Variables	Troponin I positive (>0.017 μg/dl) (*n*=19) (%)	Troponin I negative (<0.017 μg/dl) (*n*=31) (%)	*P*
Admitted to ICU	18 (94.7)	16 (51.6)	0.002**
NIV/invasive	15 (78.9)	12 (38.7)	0.006**
Duration of ventilatory support (median)	4.0	4.0	1.000
Length of stay (in days)			
In ICU	5.56±1.95	5.56±5.49	0.996
In hospital	8.94±4.46	8.61±4.25	0.792
Mortality	3 (15.8)	2 (6.5)	0.285

** *P* value <0.05 is significant.NIV: Noninvasive ventilation, cTnI: Cardiac troponin I, ICU: Intensive Care Unit

38% of the study population. This suggests that cardiac injury exists in patients with acute exacerbation of COPD. Cardiovascular mortality is a leading, but under-recognized cause of death in patients with COPD.

Beyond cor pulmonale and pulmonary hypertension, other cardiac abnormalities may be present in patients with COPD. Sin *et al*. estimated the percentage of patients with COPD who die of cardiovascular disease to be in the range of 12–37%.[5]

The most evident explanation for this high prevalence is the elevated occurrence among COPD patients of smoking and other known risk factors for cardiovascular diseases such as sedentary lifestyle and poor diet.[6] However, several studies have shown that impaired lung function is associated with cardiovascular risk even after adjusting for known cardiovascular risk factors.[7] Systemic inflammation, oxidative stress, hypoxia, and activation of the sympathetic nervous system that is seen in patients with COPD contribute to this.[8]

Our finding that cTnI is elevated during acute exacerbation of COPD is in accordance with studies reported previously. Baillard *et al*. showed that cTnI was elevated in 18% of patients studied.[9] Other cardiac biomarkers including cTnT and NTpro-BNP have also been studied and found to be elevated.[10]

The incidence of cTnI elevation also correlated with duration of COPD in this study, a finding not reported previously. These patients were also found to have a greater tendency toward severe pulmonary hypertension and cor pulmonale.

In agreement to other studies, this study showed a strong correlation with elevated cTnI and need for admission to ICU and ventilator support. However, the duration of ventilator and hospital stay was not statistically significant. While Baillard *et al*. reported elevated cTnI to be a strong predictor of mortality; this was not seen in this study. Martins *et al*. and Høiseth *et al*. have reported elevated cTnI and cTnT to be associated with higher mortality during follow-up period following exacerbation of COPD.[11,12] However, this was not within the scope of this study as death/discharge from hospital was taken as the end point.

The exact mechanism for elevation of cTnI in acute exacerbation of COPD is not known. This being an enzyme specific for cardiac muscle injury, the reasons for its elevation that could be proposed are increased work of breathing, increased LV afterload due to more negative intrathoracic pressure, worsening of pulmonary hypertension, hypoxemia, and hypercapnia.[13]

Given that, the above data suggests that cardiac injury during acute exacerbation of COPD may influence the prognosis of these patients. Thus, assessing the level of cTnI during admission helps us to identify a subset of patients at higher risk. This is an interesting observation because as reported by few studies mentioned above, mortality tends to be higher not only during acute exacerbation but also in the subsequent weeks to months. Therefore, by identifying patients at higher risk at an early stage gives enough time intervals for appropriate intervention and treatment which may alter the outcome of these patients. Future clinical trials are required to study this aspect.

Limitations

Relatively small number of patients was a limitation of this study. Second, due to severe dyspnea and low SpO_2 in some of the patients, ABG could not be assessed at room air in these patients. Furthermore, this study did not include follow-up. Hence, the long-term outcome associated with cTnI elevation could not be evaluated.

CONCLUSION

cTnI is elevated in a significant subset of patients with acute exacerbation of COPD. These patients had significantly longer duration of COPD, higher incidence of IHD, and lower SpO_2. It was associated with significantly higher need for ICU admission and ventilator support though it was not an independent predictor of stay in ICU or hospital. It did not predict in-hospital mortality. Thus, it can be used as a marker to identify patients with higher risk at the time of admission.

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Conflicts of interest

There are no conflicts of interest.

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