

# Cardiac Troponin I Levels in Patients with Chronic Obstructive Pulmonary Disease and Cor Pulmonale

Ahmet Selim Yurdakul\*, Nevin Taci Hoca\*\*, Filiz Çimen\*\*, Ebru Ünsal\*\*  
Omaç Tüfekçioğlu\*\*\*, Türkan Eryılmaz\*\*, Tuğrul Şipit\*\*, Şükran Atıkcın\*\*

\*Department of Pulmonary Medicine, Gazi University Faculty of Medicine

\*\*Atatürk Chest Disease and Thoracic Surgery Education and Research Hospital

\*\*\*Türkiye Yüksek İhtisas Education and Research Hospital, Department of Cardiology

## Summary

The level of serum cardiac troponin I (cTnI) is an important biochemical marker that reflects myocardial cell damage. The damage caused by hypoxia seen in obstructive airways disease on myocardial fibers is controversial. Our purpose is to investigate the cTnI levels in patients with chronic obstructive pulmonary disease (COPD) and cor pulmonale due to COPD, and to evaluate whether there is myocardial damage or not. 35 patients with COPD, 30 patients with cor pulmonale due to COPD, and 20 patients with acute myocardial infarction (MI) were included in the study. Cardiac troponin I levels were determined by immunoenzymatic method. cTnI levels in COPD and COPD related cor pulmonale patients were in normal range where it was found as elevated in patients with MI and the mean value of cTnI level was found  $50.4 \pm 34.1$  ng/mL in patients with MI.

As a result, it was found that the hypoxia in patients with COPD and cor pulmonale did not cause damage in myocardial cells and significant increases in serum cTnI levels where it was found as elevated in patients with acute myocardial infarction.

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**Key Words:** Cardiac troponin I, COPD, Cor pulmonale, MI

## Özet

### KOAH ve Kor Pulmonaleli Hastalarda Kardiyak Troponin I Düzeyi

Serum kardiyak troponin I (cTnI) düzeyi miyokardiyal hücre hasarını yansıtan önemli bir biyokimyasal belirleyicidir. Obstrüktif hava yolu hastalığında görülen hipoksinin, miyokardiyal fibriller üzerinde oluşturduğu hasar tartışmalıdır. Çalışmanın amacı; KOAH'lı hastalar ile KOAH'a bağlı kor pulmonale gelişen hastalarda cTnI düzeyini incelemek ve hipoksik miyokardiyal hasar olup olmadığını değerlendirmektir. KOAH'ı olan 35 hasta, KOAH'a bağlı kor pulmonale gelişen 30 hasta ve akut miyokard infarktüsü 20 hasta çalışmaya dahil edilmiştir. cTnI düzeyi, immunoenzimatik method kullanılarak ölçülmüştür. KOAH ve KOAH'a bağlı kor pulmonalesi olan hastalarda cTnI düzeyi normal sınırlar içinde bulunmasına karşın akut miyokard infarktüsü olan hastalarda ise yüksek düzeyde tespit edilmiştir ve miyokard infarktüsü hastalarda ortalama cTnI düzeyi,  $50.4 \pm 34.1$  ng/mL bulunmuştur.

Sonuç olarak, akut miyokard infarktüsü olan tüm hastalarda cTnI düzeyinde belirgin bir artış saptanırken, KOAH'lı hastalar ile KOAH'a bağlı kor pulmonale gelişen hastalarda mevcut hipoksinin miyokardiyal hücrelerde hasara yol açmadığı ve serum cTnI düzeyinde anlamlı bir artışa neden olmadığı görülmüştür.

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**Anahtar Kelimeler:** Kardiyak troponin I, KOAH, Kor pulmonale, MI

## Introduction

Troponin-I is a component of the contractile proteins in all muscles (1,2). Troponin-I has three iso-forms specific to slow skeletal, fast skeletal, and cardiac muscles (3,4). The amino acid sequence of cardiac troponin-I (cTnI) is found only in cardiac muscle (1). Serum cTnI level is a rather specific marker that reflects the cardiac muscle

damage. In myocardial damage, cTnI remains in serum for a long period, and it is important since it has a high sensitivity (1,2). Serum cTnI levels remain within the normal reference values in all other acute muscle damages without myocardial muscle damage (5). As a specific marker, cTnI is rather well defined in patients with acute myocardial infarction with ischemic or necrotic cardiac damage (6,7). Recent studies have shown that

**Address for Correspondence:** Ahmet Selim Yurdakul, Balkiraz mah, Bucak Sok., Yükselbaba apt., No: 31/7, Abidinpaşa, Ankara.

Tel: 90 312 202 41 43 , Fax: 90 312 212 90 19, E-Mail: ayurdakul@gazi.edu.tr

there are increases in serum cTnI levels in left heart failure without ischemia, myocarditis, infiltrative cardiomyopathy, and right heart failure related to pulmonary embolism (8-11). However, the effects of hypoxia due to COPD and right heart failure on cTnI are still controversial. Our purpose is to investigate cardiac troponin I levels in patients with COPD and cor pulmonale, and to evaluate whether there is hypoxic myocardial damage or not in patients with COPD and cor pulmonale.

## Patients and Methods

35 patients diagnosed as COPD according to Guidelines for Diagnosis and Treatment of COPD in Turkish Thoracic Society (12), 30 patients with cor pulmonale due to COPD, and 20 patients with acute myocardial infarction were included in this study. COPD related cor pulmonale was diagnosed with clinical, electrocardiography and systolic pulmonary artery pressure (sPAP) more than 30 mmHg in echocardiography. In addition, acute myocardial infarction was diagnosed with electrocardiography in patients who had chest pain and cardiac enzymes. COPD and/or cor pulmonale patients with atherosclerotic heart disease, cardiomyopathy, and/or acute coronary syndrome, cirrhosis, septic shock, renal failure, and arterial hypertension were excluded.

cTnI and creatine kinase MB band (CK-MB), which is specific for myocardium were tested in blood samples. After blood samples were centrifuged for 10 minutes in 3000 rpm to separate serum, cTnI levels were determined by Automated Enzyme Immunoassay Analyzer. Tosoh AIA-pack reagent was used in Eurogenetics-Tosoh AIA-ZI. The solid test reagent that consisted of a magnetic ball coated with antibody was incubated after adding serum. Balls were washed to separate the free antibody and bonded antibody. Cardiac troponin I levels were measured with fluorescent rate method using 4-methylumbelliferyl phosphate (4-MUP) as substrate. cTnI levels were accepted within normal range under 0.45 ng/ml. The levels over 0.45ng/ml were accepted over the normal limits. CK-MB levels were determined with immune-inhibition method by using ILAB 1800 chemistry analyzer with ILAB test reagent. CK-MB levels less than 24 IU/L were considered as normal.

The echocardiographic studies were performed with Hitachi EUB 6000 echocardiography device. The sPAP was calculated by obtaining a pressure gradient between right ventricle and right atrium with continuous-wa-

ve Doppler through tricuspid failure, and by adding 10 mmHg in patients with neck veins are prominent, and 5 mmHg in patients with neck veins are visually normal (13,14). The echocardiographic studies were performed to the patients with findings of cor pulmonale as clinical, electrocardiographic and radiological. All of the patients gave their written informed consent, having been informed about the details of the study and approved by local ethic committees.

**Statistical Evaluation:** Data processing and statistical analysis were performed using SPSS windows package program. All data are presented as mean  $\pm$  standard deviation. Student-t test was used for categorical variables. Correlations were determined using the spearman correlation test. A p value less than 0.05 was considered as statistically significant.

## Results

Totally 85 patients were involved in this study, 35 of these had COPD, 30 had cor pulmonale due to COPD, and 20 had acute myocardial infarction. The demographic features of the patients, and cTnI (ng/mL) and CK-MB (IU/L) results are given in Table 1.

cTnI levels of patients with COPD and COPD related cor pulmonale were in normal range. However, in all the patients with acute myocardial infarction, cTnI levels were over 0.45 ng/mL (Table 1).

CK-MB levels in patients with COPD and cor pulmonale due to COPD were in normal range, and no statistically significant difference was found between the two patient groups in terms of CK-MB values ( $p < 0.05$ ). However, in patients with acute myocardial infarction, CK-MB levels were over the normal limits and significantly elevated as compared to patients with COPD and cor pulmonale ( $161.3 \pm 128.5$  IU/L,  $19.1 \pm 14.2$  IU/L,  $16.4 \pm 9.9$  IU/L, respectively).

We found no correlation between cTnI levels and PaO<sub>2</sub>, PaCO<sub>2</sub>, hematocrite, FEV<sub>1</sub>, sPAP. The values of arterial blood gases, hematocrite, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC and sPAP in patients with COPD and cor pulmonale due to COPD are given in Table 2.

## Discussion

It is known that troponin increases in serum because of the myocardial cell damage in acute myocardial infarction as a result of the ischemia and necrosis (5,8,15). Ho-

**Table 1: Clinical characteristics of patients and the levels of cTnI (ng/mL) and CK-MB (IU/L)**

	COPD	COPD+Cor Pulmonale	Acute myocardial infarction
Number of patients	35	30	20
Age, years	61.5 $\pm$ 11.6	62.4 $\pm$ 8.5	59.9 $\pm$ 12.4
Gender (M/F)	32/3	27/3	19/1
cTnI (ng/mL)	<0.45	<0.45	50.4 $\pm$ 34.1
CK-MB (IU/L)	19.1 $\pm$ 14.2	16.4 $\pm$ 9.9	161.3 $\pm$ 128.5

wever, in patients with COPD and right heart failure due to COPD, existence of hypoxic myocardial damage, and its effect on cTnI levels has not been defined.

We found that the existing hypoxia in patients with COPD and cor pulmonale did not cause a significant increase in serum cTnI, which is an important marker of myocardial cell damage. Myocyte injury results in damage to contractile proteins and is a key mechanism responsible for the release of the structurally bound cTnI (8,16). Recent studies have shown that the increase in serum troponin in patients with MI is accurate and early indices of infarct size (2,17). Harvey et al stated that serum troponin was commonly raised in acute exacerbations of COPD and appear to reflect the severity of the exacerbations. Patients with raised troponin had no evidence to support the diagnosis of an acute coronary syndrome (18). In the study of Billard et al, in patients with serious COPD acute attacks, they found that serum cTnI levels were over 0.5ng/mL (mean 1.00 ng/mL) in 13/71 (18%) patients. They stated that the reason for cTnI elevation is difficult to determine in patients with COPD, because the cardiovascular alterations are complex. During episodes of exacerbation, the increased work and oxygen cost of breathing, the increase in left ventricular afterload related to the more negative intrathoracic pressure, the worsening of pulmonary hypertension and the presence of hypoxaemia and hypercapnia may all contribute to the development of cardiac injury. They concluded that high level of cTnI was an independent and powerful marker of the deaths in patients of intensive care units with serious COPD acute attacks (19). However, the patient group consisted of patients with serious COPD attacks followed in intensive care units. Our patient group consisted of either outpatient or hospitalized groups who have not an indication for intensive care follow up. Nobel et al found that increased serum cTnI concentrations occur frequently in the ICU suggesting that there is a high incidence of cardiac injury in these patients. They stated that increases in cTnI might be a consequence of membrane leakage and not a result of damage to the myofibrillar structure or cell death. Much of tissue injury in the critically ill patient is mediated via the action of oxygen

free radicals on cell membranes (1). In addition, some conditions in the ICU, such as hypotension, arrhythmia and the use of inotropic drugs promote myocardial ischemia. Furthermore, it has been shown that the level of the hypoxia required for the development of myocardial damage is more higher than the clinical levels of hypoxia, and it is probably associated with the marked catecholamine release (20). Myocardial damage didn't develop in our patients since they did not have serious hypoxia. Cardiac troponin I remains within the normal range in the absence of myocardial injury. An increase of cardiac troponin I in the circulation may reflect minor amounts of myocardial necrosis (8). In the study of Chan et al, in patient with an increased troponin level without evidence of ischaemic cardiac injury, troponin I became undetectable after the serum was treated with polyethylene glycol, which removed any interfering antibodies. They stated that clinicians should be ready to perform additional laboratory tests in patients with raised troponin, because of the possibility of false-positive results due to immunoassay interference (21).

In patients with COPD, pulmonary vascular resistance increases because of reasons like the direct pulmonary arteriolar vasoconstriction, and responses to hypoxia like releasing of some mediators and polistemia, and increases in pulmonary artery pressures. The augmentation in pulmonary arterial pressure increases the afterload of the right ventricle, this causes hypertrophy in the right ventricle at first, and then right ventricle failure (13,20). We found right heart failure and increase in pulmonary arterial pressure in patients with cor pulmonale related COPD by using echocardiography. However, there was no increase in serum cTnI levels. It has not been clearly defined that whether the increase in pulmonary artery pressure causes damage in myocardial fibers or not, and its effects on cTnI levels. In case of acute myocardial cell damage, for example in myocardial infarction, acute right heart failure due to massive pulmonary thromboembolism, or non-ischemic acute left heart failure, recent studies have shown that troponin I is released from contractile proteins (3,5,8,11). Chen et al showed that in patients with an improving profile of heart failure, serum cTnI concentrations lowered. Ho-

**Table II: The values of arterial blood gases, hematocrite, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC and sPAP in patients with COPD and cor pulmonale.**

	COPD	COPD+Cor Pulmonale
PaCO <sub>2</sub> (mmHg)	42.4±7.6	50.1±8.9
PaO <sub>2</sub> (mmHg)	60.1±7.1	54.5±11.9
SaO <sub>2</sub> (%)	91.3±3.7	85.2±8.6
Hematocrite	45.9±6.3	49±7.4
FEV <sub>1</sub> (% , predicted)	56±18.4	34.1±14.5
FEV <sub>1</sub> /FVC	65.1±14.9	66.5±28.7
sPAP (mmHg)	-	45.5±11.5

wever, when heart failure was decompensated, serum cTnI levels increased (22). Missow et al stated that the levels of cTnI in heart failure patients reflect cellular injury and ongoing degradative processes of the contractile apparatus, and severe congestive heart failure is associated with noncontiguous areas of myocardial cell death and progressive interstitial fibrosis (3). Davilla-Roman et al found right ventricle dysfunction and increased pulmonary artery pressures in the echocardiographic studies of the subjects trained athletes exercising on high altitudes with a program that requires exertion of power. However, they found no increases in cTnI levels in these athletes (23). Hypoxic myocardial damage is not determined in individuals living in high altitudes and in patients with congenital cyanotic heart diseases (20). cTnI levels were significantly higher in patients with ischemic and non-ischemic heart failure when compared to the healthy control group. However, in patients with cor pulmonale related COPD, there was no statistically significant difference in serum cTnI levels from the healthy control group. Left heart failure patients with an elevated troponin I may be experiencing a lower degree of myocardial injury of the left ventricle, but not the right ventricle (8). Because it is known that in heart failure altered coronary flow reserve and structural remodeling may be responsible for impaired oxygen supply and thus may account for ischemia (24). In patients with cor pulmonale, physiological adaptation mechanisms like O<sub>2</sub> consumption decrease in the myocardium of the right ventricle and inhibition of ischemia become active. Therefore, in right heart failure, no significant damage in myocardial cells occurs.

As a result, we found that the existing hypoxia in patients with COPD and cor pulmonale related COPD do not cause damage in myocardial cells and significant increases in serum cTnI levels, while significant increases in cTnI levels of patients with acute myocardial infarction.

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