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## Arterial Blood Gas Analysis in Chronic Obstructive Pulmonary Disease Patients Undergoing Coronary Artery Bypass Surgery

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Abstract **OBJECTIVES:** We aimed to investigate the impact of arterial blood gas (ABG) on morbidity and mortality in chronic obstructive pulmonary disease (COPD) patients undergoing CABG surgery.

**MATERIAL AND METHODS:** The records for 75 COPD patients who underwent elective CABG surgery our institution clinic between November 2008 to 2011 and had a forced expiratory volume in 1 second (FEV<sub>1</sub>) /forced vital capacity (FVC)  $\leq$  70% value in the pulmonary function tests (PFT) performed prior to the surgery were evaluated retrospectively. COPD patients were divided into two groups; Group 1; FEV<sub>1</sub>  $\geq$  60% and Group 2; FEV<sub>1</sub>  $\leq$  59%. Groups were compared for mortality and adverse events after identification of other preoperative and postoperative factors that could affect mortality and adverse events. An ABG was obtained immediately before and 3 to 6 hours after surgery to study the predictive value of ABG in seperate COPD groups.

**RESULTS:** There were no significant differences in patients with high partial pressure carbondioxide ( $PaCO_2$ ) preoperative values compared to patients with normal values. Also there were no significant differences in patients with lower partial pressure of oxygen ( $PaO_2$ ) preoperative values compared to patients with normal values in terms of mortality. Postoperative myocardial infarction (MI) was significantly higher in patients with low  $PaO_2$  values (p<0.05).

**CONCLUSION:** In conclusion, in our study, there could not be found a relation between the degree of preoperative obstruction and mortality for COPD patients who underwent CABG surgery. ABG was not found useful for predicting mortality in COPD patients undergoing CABG surgery, but could be useful to predict postoperative MI in patients with COPD.

KEYWORDS: Coronary artery bypass graft surgery, chronic obstructive pulmonary disease, arterial blood gas analysis

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a partially reversible disease characterized with the limitation of airflow, which develops as a result of the inflammation of the respiratory tract. COPD is a substantial problem affecting pre and post-operative success in patients on whom adult coronary artery bypass grafting (CABG) is performed. It was first expressed in 1963 that COPD is a relative contraindication in terms of coronary artery surgery [1]. It has been known till then that the association of CABG (coronary artery bypass grafting) and COPD is a dangerous one. Mortality reaching up to 50% was found in studies carried out in the past years and the presence of COPD created unrest [2]. However, in recent years, preoperative intense therapies, use of more efficient medication and showing more sensitivity to patients with COPD have decreased mortality and morbidity [3].

Arterial blood gas (ABG) is a frequently used test before anesthesia induction in cardiovascular surgery and in the evaluation of postoperative patients. Therefore, ABG analysis may have the significance of predicting mortality and postoperative events in COPD patients undergoing CABG. Consequently, this study aimed to investigate the effects of ABG on postoperative morbidity and mortality after CABG in patients with COPD.

## MATERIALS AND METHODS

Seventy-five COPD patients, on whom elective CABG was performed and whose respiratory function test (RFT) values were as force expiratory volume ( $FEV_1$ ) / force vital capacity (FVC)  $\leq$  70%, were retrospectively included into the study. Patients with missing data or the ones that underwent additional procedures (heart valve surgery or aneurysmectomy)



were excluded from the study. Moreover, patients operated on for valvular diseases, patients with asthma, sleep-apnea syndrome and the ones with restrictive and combined respiratory function disorder were also excluded from the study. All clinical and demographic data of the patients present in the files and their postoperative mortality and complication data were recorded. Respiratory function tests were routinely carried out before surgery while the patient was seated by using a computer system (Jaeger, Master Screen, MS Pneumo; Erich Jaeger GmbH; Hoechberg, Germany). The best one out of the three test done consecutively is accepted for analysis. FEV, and FVC values of the pulmonary test results were measured as liters and the percentages of the expected values were obtained. COPD groups were divided into two as Group 1:  $FEV_1 \ge \%60$  and Group 2:  $FEV_1 \le \%59$  (Table 1). Belowmentioned preoperative variables that could affect the result of the surgery were recorded in both groups. Both groups were compared in terms of both mortality and morbidity-affecting events and with respect to the effect of arterial blood gas results on mortality and morbidity in these groups. In the blood samples obtained from the radial artery for arterial blood gas analysis, parameters of PH, partial oxygen pressure (PaO<sub>2</sub>) and partial carbondioxide pressure (PaCO<sub>2</sub>) were recorded. In addition, in the postoperative period, the same parameters were recorded from the blood gases routinely taken 3 and 6 hours after post-extubation and during 3 L/min oxygen intake. Medica Easystat (Medica Corp. Bedford, MA, USA) is used for blood gas analyses. In preoperative blood gas analysis, PaCO, 44 mmHg and higher was considered high; PaO, 70 mmHg and lower was considered low.

#### **Preoperative Variables**

Patient characteristics and comorbid diseases having an effect on the operation including age, gender, body mass index (BMI), history of smoking, creatinine, blood urea nitrogen (BUN), diabetes mellitus (DM), history of COPD, re-done CABG, previous myocardial infarction (MI), cerebrovascular disease (CVO), arterial hypertension (HT), and ejection fraction (EF) in COPD groups were compared with regard to Euroscore, and a statistically significant difference was not found except for history of COPD (Table 2).

#### Definitions

History and physical examination records, chest radiography records, blood gas analyses and spirometric measurements of

all the patients included into the study were retrospectively reviewed, and COPD diagnosis was confirmed by a chest diseases specialist in line with these records. Having FEV1/  $FVC \le 70\%$  on spirometer and SFT were accepted as airway obstruction. Hospitalization duration of eight and more than eight days was considered prolonged hospitalization. Intubation of more than 24 hours was considered prolonged intubation. On PA chest radiography, closure in costophrenic sinus and homogenous density images whose gap faced upwards following obscured diaphragmatic contour were evaluated as pleural effusion. Respiratory distress was accepted present in patients with dyspnea, discomfort, tachycardia, tachypnea (respiratory rate more than 20), and elevated wheezing on postoperative records. For the diagnosis of pneumonia, in addition to the occurrence of new and progressive infiltrations on chest radiography, at least two of the criteria of elevated body temperature (> 38°C), purulent tracheobronchial secretion and leukocytosis should have been present. Renal failure was defined as a creatinine level over 2 mg/dL postoperatively or as the need for hemodialysis, stroke was defined as regional neurologic dysfunction that could ameliorate without sequela, and mortality was defined as death due to any reason before discharge.

## **Operative Technique**

Following median sternotomy, moderate (28°C) systemic hypothermia was established with venous cannulation from the ascending aorta and right atrium. Myocardium protection was provided by intermittent cold K+ blood cardioplegia. Left internal mammary artery and saphena were used as bypass graft. Principally, distal anastomoses were made. Proximal anastomoses were made to the aorta under lateral clamp. When it was necessary, mechanical and pharmacological support were given to disconnect from cardiopulmonary bypass (CPB). All patients were taken to the intensive care unit in the postoperative period.

#### **Statistical Analysis**

Descriptive values for the obtained data were given as mean  $\pm$  standard deviation (SD) and number (percentage) frequencies in charts. Preoperative categorical measurements between the groups and morbidity and mortality parameters were analyzed with  $\chi^2$  test. For continuous variables, normal

Table 1. COPD groups					
	Group 1 (n= 37)	Group 2 (n= 38)	р		
FVC (L)	$3.21 \pm 0.64$	$2.38 \pm 0.64$	0.0001		
FVC%	81.56 ± 11.17	$61.73 \pm 12.60$	0.0001		
$FEV_1$ (L)	$2.17 \pm 0.44$	$1.49 \pm 0.37$	0.0001		
FEV <sub>1</sub> %	$71.34 \pm 9.32$	$48.18 \pm 9.26$	0.0001		
FEV <sub>1</sub> /FVC	$66.90 \pm 2.80$	$62.70 \pm 5.81$	0.005		
PEF (%)	61.95 ± 12.79	45.77 ± 12.75	0.0001		
FEF 25-75	$45.55 \pm 8.69$	$29.43 \pm 7.62$	0.0001		

COPD: Chronic Obstructive Pulmonary Disease, FEF 25-75: Force expiratory flow in 25-75% of the expiration phase, FEV<sub>1</sub>: First second force expiratory volume, FEV<sub>1</sub> %: The percentage of first second force expiratory volume, FVC: Force vital capacity, FVC %: The percentage of force vital capacity, FEV<sub>1</sub>/FVC: The rate of first second force expiratory volume to force vital capacity, PEF: Force expiration peak flow rate.

Table 2. Preoperative data of COPD group			
	Group 1 (n= 37)	Group 2 (n= 38)	р
Age	$61.91 \pm 8.71$	$59.81 \pm 7.32$	0.261
Gender (M/F)	35/2 (94.6%/5.4%)	37/1 (97.4%/2.6%)	0.537
BMI kg/m <sup>2</sup>	$25.38 \pm 4.29$	$26.82 \pm 3.11$	0.103
Cigarette (package/year)	37 (100)	34 (89.5)	0.017
Creatinine (mg/dL)	$0.93 \pm 0.18$	$1.00 \pm 0.21$	0.107
BUN (mg/dL)	$18.62 \pm 4.86$	$18.94 \pm 5.07$	0.777
DM (existent/non-existent)	10/27	13/15	0.499
COPD history (existent/non-existent)	6/31	22/16	0.001
Redo ACBG done/not done)	2/35	3/35	0.665
MI (postoperative) (existent/nonexistent)	16/21	23/15	0.133
CVO (existent/non-existent)	1/36	0/0	0.232
HT history (existent/non-existent)	18/19	26/11	0.082
EF (%)	53.18 ± 10.97	49.15 ± 11.55	0.126
Euroscore	$3.72 \pm 2.20$	$3.73 \pm 2.12$	0.989
Euroscore %	$4.15 \pm 3.97$	$3.93 \pm 2.74$	0.781

BMI: Body mass index, BUN: Blood urea nitrogen, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, Redo ACBG; MI: Myocardium infarction, CVO: Cerebrovascular disease, HT: Hypertension, EF: Ejection fraction.

distribution and assumptions of equality of the variances were respectively evaluated with Kolmogorogv-Smirnov and Levene tests. Inter-group differences for continuous variables were analyzed by Student's t test. SPPS for Windows (version 18) was used for calculations and p< 0.05 was considered statistically significant.

The ethics committee and human research committee of the center where the study was conducted gave approval before the commencement of the study.

## RESULTS

Data belonging to the COPD groups are given in Table 1. Demographic characteristics except for smoking and COPD history and the distribution of comorbid diseases were equal. Preoperative data of the COPD groups are given in Table 2.

#### **Perioperative Results**

When the operative data, including cardiopulmonary bypass time, cross clamp time, rate of patients on whom LIMA was

used, intubation duration, intensive care unit stay, and hospitalization duration of the COPD groups were compared between each other, no statistically significant difference was found (Table 3). Moreover, coronary artery bypass grafting on beating heart was performed in three patients each in both groups.

## The Effect of COPD Groups on Morbidity and Mortality

Mortality was found significantly high in Group 1 (p< 0.037). When the effect of COPD groups on morbidity was compared, arrhythmia was found significantly high in Group 1 (p= 0.024). Regression analysis could not be done since the number of mortality was low. When cause of death of the three patients who died were explored, each patient was extubated on time after the operation. One of the patients died due to arrhythmia non-responsive to treatment, the other died due to having undergone revision surgery for bleeding twice and having developed pneumonia afterwards, and the third one died because of pneumonia (Table 4).

Table 3. Operative data of the COPD groups					
	Group 1 (n= 37)	Group 2 (n= 38)	р		
CPB (d)	$102.97 \pm 34.82 \ (n=34)$	$115.31 \pm 59.63 \ (n=35)$	0.299		
CC (d)	$69.97 \pm 28.82 \ (n=34)$	$73.05 \pm 40.86 \ (n=35)$	0.719		
Lima	29 (80.6)	32 (86.5)	0.494		
Intubation (s)	18.13 ± 17.90	$16.23 \pm 10.06$	0.572		
Intensive care (g)	$1.40 \pm 0.76$	$1.78 \pm 2.00$	0.278		
Hospitalization (g)	$7.54 \pm 4.03$	$7.02 \pm 2.62$	0.514		
CPB: Cardiopulmonary bypa	ass, CC: Cross clamp time.				

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	Group 1 (n= 37)	Group 2 (n= 38)	р
Mortality	3 (8.1)	0 (0)	0.037
Prolonged hospitalization	6 (16.2)	7 (18.4)	0.801
Prolonged intubation	5 (13.5)	2 (5.3)	0.213
Pneumothorax	0 (0)	2 (5.3)	0.09
Pleural effusion	6 (16.2)	2 (5.3)	0.117
Pneumonia	2 (5.4)	1 (2.6)	0.537
Respiratory distress	7 (18.9)	5 (13.2)	0.496
Arrhythmia	13 (35.1)	5 (13.2)	0.024
Postoperative MI	0 (0)	1 (2.6)	0.241
Re-intubation	2 (5.4)	0 (0)	0.09
Revision	4 (10.8)	1 (2.6)	0.143
Hypotensive shock	1 (2.7)	0 (0)	0.232
Frenic nerve paralysis	2 (5.4)	0 (0)	0.09
Stroke	2 (5.4)	0 (0)	0.09
Acute renal failure	0 (0)	1 (2.6)	0.143

# The effect of the values of arterial blood gas analysis on morbidity and mortality

When patients with high preoperative  $PaCO_2$  (n: 10) were compared with the ones with normal  $PaCO_2$  (n: 65) in terms of mortality and morbidity parameters, a statistically significant difference was not found (p> 0.05). When patients with low preoperative (n: 13)  $PaO_2$  were compared with the ones with normal  $PaO_2$  in terms of morbidity and mortality parameters, prolonged hospitalization and arrhythmia rates were found high in patients with normal preoperative  $PaO_2$  (p< 0.05). Postoperative MI was found high in patients with low preoperative  $PaO_2$  (p= 0.05) (Table 5).

#### The effect of COPD groups on arterial blood gas analysis

When the parameters of preoperative, post-extubation and 3-6 h after extubation arterial blood gas analysis were compared, no significant difference was found. Interestingly, the number of patients with high preoperative  $PaCO_2$  was higher in Group 1 than in Group 2. The number of patients with low preoperative  $PaO_2$  was close to each other between the groups (Table 6).

#### DISCUSSION

Cardiopulmonary bypass (CPB) deteriorates alveolar stability by triggering complement cascade and changing neutrophil sequestration in the pulmonary microvascular bed, the formation of free oxygen radicals and the structure of alveolar surfactant. CPB is known to negatively affect respiratory functions. In patients undergoing CABG, the effect of COPD becomes a substantial problem due to the additional influence of CPB and sternotomy [4]. COPD has been defined as the most important preoperative risk factor for morbidity and mortality in patients on whom coronary artery surgery is performed [5,6]. Unwanted events of the respiratory system, such as respiratory failure and pneumonia, can cause postoperative complication in COPD patients on whom CABG is performed [7]. There are studies showing that as the stages of COPD increase so does morbidity and mortality in COPD patients on whom coronary artery surgery is performed [8,9]. It has been reported in many studies that postoperative complications are most frequently seen in the COPD patient group when compared to the control group [6-9].

It has been found in a study by Samuel et al. [6], where they have evaluated 191 patients undergoing CABG surgery, that intra-hospital mortality rates in patients with mild to moderate COPD were similar with the patients without COPD. Futer et al. [8] have evaluated mortality and morbidity according to obstruction severity in COPD patients and mortality has been found to be associated with the degree of obstruction. The patients whose FEV, value was under 60% was found to be specifically higher than those whose mortality was over 60% (24.6% vs. 1.4%) (p< 0.001). With the impact of this last study, the detection of moderate or advanced COPD in preoperative evaluation was accepted a risk for mortality. However, in recent years, it has been found in a study by Mangenes et al. that CABG surgery can be performed without increased mortality risk when severe COPD patients were compared with mild-to-moderate COPD patients and the ones with normal respiratory functions [3]. When postoperative results of severe COPD patients (FEV, less than 50% and FEV,/ FVC less than 0.7) were compared with that of the mild-to-moderate COPD patients (FEV, 50% and over, FEV<sub>1</sub>/FVC less than 0.7) and the ones with normal pulmonary functions, it was found that apart from increased pulmonary infection risk, inclination to postoperative atrial fibrillation and a bit increased hospitalization duration, the results were similar. Similar to the study of Mangenes et al., our study also established that moderate-advanced COPD did not carry a risk in terms of mortality and in fact, mortality was seen to be

Table 5. Comparison of the effect of COPD groups on morbidity and mortality						
	Preop PaCO <sub>2</sub> Normal (n= 65)	Preop PaCO <sub>2</sub> High (n= 10)	р	Preop PaO <sub>2</sub> Normal (n= 62)	Preop PaO <sub>2</sub> Low (n= 13)	р
Mortality	3 (4.6)	0 (0)	0.349	3 (4.8)	0 (0)	0.280
Prolonged hospitalization	12 (18.5)	1 (10)	0.485	13 (21)	0 (0)	0.019
Prolonged intubation	6 (9.2)	1 (10)	0.938	5 (8.1)	2 (15.4)	0.438
Pneumonia	3 (4.6)	0 (0)	0.349	3 (4.8)	0 (0)	0.280
Pneumothorax	2 (3.1)	0 (0)	0.446	1 (1.6)	1 (7.7)	0.283
Pleural effusion	6 (9.2)	2 (20)	0.344	6 (9.7)	2 (15.4)	0.562
Respiratory distress	9 (13.8)	3 (30)	0.228	9 (14.5)	3 (23.1)	0.462
Re-intubation	2 (3.1)	0 (0)	0.446	2 (3.2)	0 (0)	0.379
Arrhythmia	16 (24.6)	1 (10)	0.668	18 (29)	0 (0)	0.005
Postoperative MI	1 (1.5)	0 (0)	0.591	0 (0)	1 (7.7)	0.05
Hypotensive shock	1 (1.5)	0 (0)	0.591	1 (1.6)	0 (0)	0.536
Revision	4 (6.2)	1 (10)	0.668	4 (6.5)	1 (7.7)	0.873
Frenic nerve damage	1 (1.5)	1 (10)	0.205	1 (1.6)	1 (7.7)	0.283
Stroke	2 (3.1)	0 (0)	0.446	2 (3.2)	0 (0)	0.379
Acute renal failure	1 (1.5)	0 (0)	0.591	1 (1.6)	0 (0)	0.536

	Group 1 (n= 37)	Group 2 (n= 38)	р
Preop Ph	$7.41 \pm 0.02$	$7.41 \pm 0.02$	0.723
Post-Ext. Ph	$7.38 \pm 0.05$	$7.38 \pm 0.03$	0.756
Ext. 3 h Ph	$7.38 \pm 0.03$	$7.39 \pm 0.03$	0.367
Preop PaCO <sub>2</sub>	$39.87 \pm 4.78$	$38.59 \pm 4.79$	0.249
Post-Ext. PaCO <sub>2</sub>	$38.42 \pm 6.09$	39.37 ± 5.10	0.462
Ext. 3 h PaCO <sub>2</sub>	$39.61 \pm 4.99$	$39.50 \pm 4.82$	0.928
Preop PaO <sub>2</sub>	82.17 ± 15.36	81.00 ± 11.11	0.705
Post-Ext. PaO <sub>2</sub>	$114.96 \pm 38.96$	$110.61 \pm 34.64$	0.611
Ext. 3 h PaO <sub>2</sub>	$117.91 \pm 40.08$	104.43 ± 23.97	0.080
Preop $O_2$ sat	$95.16 \pm 6.50$	$96.36 \pm 0.29$	0.269
Post-Ext O <sub>2</sub> sat	$97.47 \pm 2.18$	97.31 ± 2.82	0.788
Ext. 3 h O <sub>2</sub> sat	$97.39 \pm 2.05$	$97.55 \pm 1.74$	0.739
Preop PaCO <sub>2</sub>	7* (%18.9)	3* (%7.9)	0.156
Preop PaO <sub>2</sub>	6** (%16.2)	7** (%18.4)	0.801
Ext. 3 h PaCO <sub>2</sub>	5 (%13.5)	4 (%10.5)	0.690

\* The number of patients with high PaCO<sub>2</sub>.
\*\* The number of patients with low PaO<sub>2</sub>.

higher in the in mild-moderate COPD (Group 1) when compared with the moderate-advanced COPD (Group 2) [3]. These findings and results make us think that there are other factors affecting mortality independent of COPD stages in COPD patients on whom coronary artery surgery is performed. However, it is not possible to make a definite judgement due to total mortality count, limited size of the study sample and the retrospective nature of the study.

There are two studies involving the analysis of extra-thoracic arterial blood gas analysis, defending two different views. Fuso et al. have indicated that the presence of preoperative hypoxemia with moderate and advanced obstruction plays an important role in the development of postoperative respiratory complication [10]. On the other hand, it has been expressed in another study that preoperative PaO2 and PaCO<sub>2</sub> values are not beneficial in designating postoperative

respiratory complication [11]. Changes in ABG after CABG surgery may be related to circulatory failure, pulmonary disease or mechanic ventilation change [12]. In our study, the effect of PaO<sub>2</sub> and PaCO<sub>2</sub> on mortality was not detected among COPD stages. The effect of preoperative PaO<sub>2</sub> values on morbidity was found varying. While postoperative MI was found significantly high in patients with low PaO<sub>a</sub>, prolonged hospitalization and arrhythmia rate were found significantly high in patients with normal PaO<sub>2</sub>. When myocardial ischemia is considered to be related to the imbalance between oxygen transport and necessity, it can be thought that elevated myocardial oxygen need caused by surgical stress in patients with low preoperative PaO<sub>2</sub> values increases postoperative MI rate by deteriorating this balance. As a result, sustaining normal preoperative PaO<sub>2</sub> limits to decrease postoperative MI in COPD patients is vital. In patients that have normal values of PaO<sub>2</sub>, it is not clear to what prolonged hospitalization or elevated arrhythmia rate is related and most probably, they are related to other factors.

In a study involving patients on whom coronary artery surgery is performed, postoperative atrial fibrillation (AF) has developed in 1503 patients (32.3%), and it has been emphasized that many factors including chronic pulmonary diseases play a role in the development of AF [11]. Supraventricular arrhythmia has been observed to be the most frequently encountered reason of morbidity after CABG in patients with COPD when compared to the control group [13]. In our study, arrhythmia rate was observed to be significantly higher in Group 1. Moreover, in the comparison of the group with normal preoperative arterial blood gas analysis and the one with low preoperative arterial blood gas analysis, arrhythmia was found significantly higher in the group with normal PO<sub>2</sub> value. This situation makes us think that the effect of the degree of obstruction in COPD patients and the presence of preoperative hypoxemia on the development of postoperative arrhythmia is limited.

Although some authors object the implementation of SFT in the preoperative period, some studies also make us think that it can be important in confirming and designating the degree of COPD diagnosis and deciding on surgical risk [14,15-18]. Spirometric evaluation carried out before the surgery can reform surgical results in high-risk patients. Quitting smoking, bronchodilator treatment and steroid treatments, which are postoperative morbidity-decreasing strategies in patients with confirmed COPD diagnosis, have been indicated to provide success in the postoperative period [6]. We are of the opinion that respiratory function tests be routinely performed in patients undergoing major cardiac surgery due to the fact that a part of the COPD patients are not aware of the disease and that it may help designating postoperative COPD attack. It has been reported in a study by Öz et al. that postoperative parameters of moderate COPD patients on whom they administered treatment in the preoperative period were better when compared to the ones that did not receive any treatment [19].

In our results, a statistical change was not detected in postoperative  $PaCO_2$  values in cases with mild and advanced COPD.

#### Limitations to the Study

The most important limitations to the study are as follows: it is a single-center, retrospective study with a limited number of patients and the number of patients in whom mortality was seen is low. As the number of patients that died in the postoperative period (n= 3) is low, it is not possible to definitely specify the predictor values of ABG parameters on mortality or if the severity of COPD has an effect on mortality. Regression analysis could not be performed in this study because of the same reason, and therefore, it is not possible to designate factors affecting mortality with the data of this study. These questions will be clarified with a prospective study with a larger cohort.

In conclusion, an association was not found between the degree of preoperative obstruction and mortality in COPD patients on whom CABG is planned. ABG parameters taken from COPD patients in the preoperative period do not have any mortalityprediction value in COPD patients and COPD subgroups (mild or moderate-advanced). However, preoperative low PaO<sub>2</sub> levels may be predictive of postoperative MI. Yet, since the number of patients included into the study and who died is low, we are of the opinion that this study should be repeated with larger patient groups.

Written consent was not obtained from the patients since this is a retrospective study.

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