

Changes in Blood Gases and Hemodynamic Parameters in Patients Undergoing Lung Resection Surgery and Its Clinical Implications

Abid Saleem¹, Wahid Syed^{2*}, Akbar Bhat², Lone Ghulam Nabi², Zubair Ashraf², Haroon Naqshi², Farooq Ganie², Nadeem Kawoosa²

¹ Plastic Surgeon, Department of Cardiovascular and Thoracic Surgery, SKIMS, Soura, Srinagar, JK, India

² Cardiovascular and Thoracic Surgeon, Department of Cardiovascular and Thoracic Surgery, SKIMS, Soura, Srinagar, JK, India

ARTICLE INFO

Article type:
Original Article

Article history:
Received: 14 Nov 2018
Revised: 06 Jan 2019
Accepted: 19 Jan 2019

Keywords:
Blood Gasometry
Complications
Hemodynamic Changes
Lung Function
Lung Resection

ABSTRACT

Introduction: Lung resection surgery is a challenge to thoracic surgeons. The outcome of this surgery depends on patients' tolerance for reduced lung volume and hemodynamic alterations. The present study aimed to investigate the changes in blood gases and hemodynamic parameters in patients undergoing lung resection surgery and the associated clinical implications.

Material and Methods: This study included 25 candidates for lung resection surgery. After thoracotomy, the isolation of pulmonary artery (PA) and veins was performed as usual. Blood samples were taken from the PA and radial artery simultaneously before PA clamping, as well as 5 and 20 min after clamping the PA. The systemic and PA pressure was also measured. All patients were followed up, and arterial blood gas and pulmonary function tests were performed 3-6 months after the surgery.

Results: Cough (56%) and hemoptysis (56%) were the most common symptoms. Squamous cell carcinoma (56%) was identified as the most prevalent pathology. Lobectomy was the most common procedure performed on the patients. No change was observed in blood gases before and after the clamping of the PA. There was a significant increase in the mean PA pressure ($P < 0.001$), while the mean arterial pressure showed no significant change ($P = 0.457$). The pulmonary function tests showed a significant decrease in vital capacity, forced vital capacity, and forced expiratory volume in 1 sec at the postoperative follow-up. The patients with a pre-operative partial pressure of carbon dioxide (PCO_2) of > 45 mmHg had more postoperative complications than those with a PCO_2 of ≤ 45 mmHg ($P = 0.047$).

Conclusion: Given the lack of any significant changes in the PCO_2 and oxygen saturation following the lung resection surgery, it seems that this parameter is not a limiting factor for deciding on operability in patients with lung lesions having an acceptable preoperative partial pressure of oxygen. However, the patients with a PCO_2 of > 45 mmHg should be categorized as a high-risk group since they have significantly higher postoperative complications/morbidity.

► Please cite this paper as:

Saleem A, Syed W, Bhat A, Ghulam Nabi L, Ashraf Z, Naqshi H, Ganie F, Kawoosa N. Changes in Blood Gases and Hemodynamic Parameters in Patients Undergoing Lung Resection Surgery and Its Clinical Implications. J Cardiothorac Med. 2019; 7(1): 406-412.

Introduction

Patients undergoing lung resection surgery generally become easily fatigued and have

physical limitations due to decreased cardiopulmonary reserve and limited oxygen

*Corresponding author: Wahid Syed, Department of Cardiovascular and Thoracic Surgery, SKIMS, Soura, Srinagar, JK, India. Tel: 919596543823; Fax: 917006098089; Email: dr.wahidsyed@gmail.com

© 2019 mums.ac.ir All rights reserved.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

delivery to the body systems. After surgery, the capacity to accommodate the blood flow in the lungs is reduced due to the reduction of the pulmonary capillary vascular bed, which also raises the pulmonary arterial pressure (1) and results in pulmonary edema.

Pulmonary edema is a serious concern in the postoperative phase of pneumonectomy patients. However, this transudation of fluid from the pulmonary capillary bed to interstitium effectively decreases the circulatory volume and pulmonary arterial pressure, thereby lowering the strain on the right heart (1). Right heart failure is uniformly fatal and can occur as a result of volume and pressure overload in the pulmonary bed.

With this background in mind, the present study aimed to investigate the hemodynamic and blood gas changes during and after lung resection and the associated clinical implications.

Materials and Methods

This study was conducted on a cohort of 25 patients undergoing lung resection surgeries over a period of 2 years in the Department of Cardiovascular and Thoracic Surgery of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India, from June 2009 to October 2011. All 25 patients with indication for lung resection surgery (i.e., lobectomy or pneumonectomy) were evaluated with baseline investigations, including hemogram test and serum chemistry profile, chest X-ray, electrocardiogram, baseline arterial blood gas (ABG) test, pulmonary function tests, bronchoscopy, and a high-resolution computed tomography (CT) scan of the chest.

For the purpose of the study, 19 patients were subjected to bronchoscopic or CT-guided biopsy preoperatively. Furthermore, two patients underwent positron emission tomography scan. The exclusion criteria were: 1) age of <15 or >85 years, 2) hypertension, uncontrolled diabetes, and chronic renal failure, 3) evidence of systemic metastasis, 4) history of preoperative radiotherapy, and 5) forced expiratory volume in 1 sec (FEV1) of < 40% predicted (<800 ml) and vital capacity (VC) of < 40% predicted.

After obtaining informed consent, all patients were subjected to surgery under general anesthesia induced through using morphine, propofol, atracurium, oxygen, nitrous oxide, and halothane. Anesthesia was maintained by using intermittent positive pressure ventilation with oxygen, nitrous oxide, and halothane. Blood sampling was accomplished by the insertion of radial artery (RA) catheter. All patients were ventilated on 100% FiO₂ using one-lung ventilation technique in order to obtain uniform results of the perioperative blood samples.

Posterolateral thoracotomy and isolation of PA and pulmonary veins were performed in a routine manner. Blood samples were collected from the pulmonary artery (PA) and RA simultaneously at three different time intervals, namely before clamping, and 5 and 20 min after clamping. In this regard, at first, the blood samples were simultaneously taken from the PA and RA before clamping the PA. The PA pressure was also measured at this stage by placing a 23 G needle into the PA and connecting it to the transducer of the pressure monitor (Cardio cap II, Datex Engstrom, Finland). The systemic arterial pressure was also measured concurrently.

The second blood sampling was performed 5 min after clamping by collecting samples from the proximal PA and RA, followed by the measurement of the PA pressure. The same measurements were implemented 20 min after pneumonectomy or lobectomy. Based on the obtained data, the patients were examined for the partial pressure of oxygen (PO₂), partial pressure of carbon dioxide (PCO₂), bicarbonate, oxygen saturation (SO₂), mean PA pressure, and mean arterial pressure. All the patients were followed up, and ABG and pulmonary function tests were again performed 3-6 months postsurgery. The collected data were analyzed in SPSS software (2010).

Results

The study population consisted of 19 males and 6 females with the mean age of 48.5 years (age range: 21-67 years). Most of the patients (66.7%) were within the age group of > 45 years. The mean ages of the males and females were 49 [12.1] and 46.8 [11.39] years, respectively. Hemoptysis and cough (n=14, 56%) were the most common symptoms among the patients, followed by dyspnea (n=10, 40%). On the other hand, fever and weight loss (n=1, 4%) were the least common symptoms present in the study population. About 72% of the patients (n=18) were smokers, and 32% of them were hypertensive. Furthermore, 24% of the patients had a previous history of receiving anti-tubercular treatment.

Specific chest evaluation

Pulmonary nodule (n=8, 32%) was the most common X-ray and CT finding, followed by mass lesion (n=7, 28%) in the particular lobe. The other findings included cavitary lesion (n=4, 16%), bronchiectasis (n=2, 8%), consolidation (n=2, 8%), fibrosis (n=2, 8%), lymphadenopathy and irregular calcification (n=1, 4%). After workup, the final established diagnosis was most commonly squamous cell carcinoma (n=14,

Table 1. Surgical Procedures done in the 25 subjects of our study

Procedure	Number of Cases
Pneumonectomy	2
Left Upper Lobectomy	4
Lower Lobectomy	3
Pneumonectomy	1
Upper lobectomy	3
Middle lobectomy	5
Right Lower lobectomy	4
Upper and Middle lobectomies	2
Middle and Lower lobectomies	1

56%), followed by bronchiectasis (n=4, 16%), post-tuberculosis cavitory lesion (n=3, 12%), adenocarcinoma lung (n=2, 8%), and abscess (n=2, 8%).

Procedure

Out of 25 patients, pneumonectomy was performed on only 3 cases, and the remaining 22 patients underwent lobectomy or bilobectomy (Table 1).

Arterial blood gas

The ABGs of the PA showed no significant difference after clamping the PA, compared to that obtained before clamping (Table 2). Similarly, no change was observed in peripheral ABG before and after clamping the PA. However, there was a significant change in certain parameters of intraoperative peripheral ABGs when compared with postoperative ABGs 1 month after the surgery. The PO₂ and SO₂ showed a significant increase, while PCO₂ decreased; however, the change was not statistically significant (Table 3).

Hemodynamic parameters

The results indicated a significant increase in systolic, diastolic, and mean PA pressures upon the completion of the procedure. However, there was no significant change in the mean peripheral arterial pressure 20 min after clamping the PA (Table 4).

Table 2. Pulmonary Artery ABG before, and 5 and 20 minutes after PA clamping

	Before Clamping Mean ± SD (Min.-Max.)	After 5 minutes Mean ± SD (Min.-Max.)	After 20 minutes Mean ± SD (Min.-Max.)	p value
PO ₂	48.8 ± 8.8 (33.0 - 65.2)	48.8 ± 7.1 (36.5 - 60.6)	48.8 ± 7.1 (37.0 - 61.0)	0.221 (NS)
PCO ₂	62.8 ± 10.8 (42.6 - 85.2)	62.8 ± 8.8 (44.9 - 78.6)	63.9 ± 10.9 (44.2 - 87.4)	0.170 (NS)
HCO ₃	22.5 ± 2.9 (17.5 - 29.2)	22.0 ± 2.5 (19.1 - 30.0)	22.6 ± 2.9 (17.7 - 29.3)	0.036 (NS)
Saturation	64.4 ± 13.5 (45.5 - 84.0)	67.7 ± 11.1 (48.2 - 85.6)	67.9 ± 12.3 (45.5 - 84.0)	0.221 (NS)

Statistical test used: Paired t-test. NS(not significant)

Table 3. Intra-op (at different intervals) and Post-Op Peripheral Artery ABG

	Before clamping Mean ± SD (Min.-Max.)	After 5 minutes Mean ± SD (Min.-Max.)	After 20 minutes Mean ± SD (Min.-Max.)	1 month after surgery Mean ± SD (Min.-Max.)	p value
PO ₂	77.9 ± 15.3 (61 - 125)	77.9 ± 14.8 (46 - 112)	77.1 ± 14.4 (46 - 112)	78.9 ± 8.2 (50.2 - 90.4)	0.048 (Sig)
PCO ₂	48.0 ± 6.7 (32.9 - 63.6)	50.7 ± 7.0 (33.7 - 64.0)	53.5 ± 12.5 (30.2 - 82.0)	48.7 ± 7.6 (27.2 - 62.3)	0.234 (NS)
HCO ₃	21.7 ± 2.3 (17.0 - 26.1)	20.9 ± 2.0 (17.0 - 25.2)	21.9 ± 2.5 (15.3 - 26.5)	21.7 ± 2.4 (18.6 - 25.4)	0.208 (NS)
Saturation	93.4 ± 3.4 (85.1 - 98.7)	93.3 ± 3.1 (89 - 102)	92.9 ± 5.0 (75.0 - 98.9)	93.3 ± 2.6 (88.6 - 98.7)	0.016 (Sig)

Statistical test used: Paired t-test. NS: not significant, Sig: significant, SD: Standard deviation

Table 4. Pulmonary and systemic hemodynamic changes before and after clamping of Pulmonary artery

	Pulmonary Artery			Peripheral Artery		
	SBP Mean±SD (Min-Max)	DBP Mean±SD (Min-Max)	MPAP Mean±SD (Min-Max)	SBP Mean±SD (Min-Max)	DBP Mean±SD (Min-Max)	MAP Mean±SD (Min-Max)
Before clamping	23.8 ± 5.8 (18 - 46)	12.6 ± 3.0 (9 - 25)	16.2 ± 4.4 (12 - 32)	124.0 ± 11.6 (106 - 155)	77.4 ± 7.4 (58 - 84)	94.8 ± 4.6 (83 - 103)
After 5 minutes	25.1 ± 5.0 (20 - 43)	12.5 ± 1.6 (10 - 17)	16.0 ± 3.5 (13 - 28)	126.3 ± 8.6 (114 - 148)	79.0 ± 5.5 (64 - 86)	92.9 ± 5.6 (78.7 - 101.3)
After 20 minutes	26.3 ± 6.2 (22 - 48)	13.2 ± 2.1 (8 - 19)	16.7 ± 2.9 (13 - 24)	123.7 ± 8.5 (110 - 140)	78.4 ± 9.4 (52 - 88)	93.4 ± 7.1 (72.7 - 102.0)
p value	<0.001 (Sig)	<0.001 (Sig)	<0.001 (Sig)	0.018 (Sig)	0.311 (NS)	0.457 (NS)

SBP: systolic blood pressure, DBP: diastolic blood pressure, MPAP: mean pulmonary artery pressure, MAP: mean (systemic) arterial pressure, SD: Standard deviation, NS: not significant, Sig: significant

Statistical test used: Paired t-test

Table 5. Spirometry in patients undergone lung resection surgery before and after the surgical procedure

	Predicted Mean ± SD (Min.-Max.)	Preoperative Mean ± SD (Min.-Max.)	1 month FU Mean ± SD (Min.-Max.)	3 month FU Mean ± SD (Min.-Max.)	6 month FU Mean ± SD (Min.-Max.)	p value
VC	3.7 ± 0.5 (3.0 - 4.4)	2.7 ± 0.9 (1.2 - 3.9)	2.5 ± 0.7 (1.0 - 3.4)	2.3 ± 0.7 (1.0 - 3.3)	2.0 ± 0.7 (0.95 - 2.88)	<0.001 (Sig)
FVC	3.8 ± 0.7 (3.0 - 5.3)	2.8 ± 0.9 (1.5 - 3.9)	2.5 ± 0.8 (1.3 - 3.5)	2.2 ± 0.9 (1.0 - 3.3)	1.9 ± 0.8 (0.67 - 2.96)	<0.001 (Sig)
FEV1	3.0 ± 0.5 (2.2 - 3.6)	1.9 ± 0.7 (0.9 - 2.8)	1.6 ± 0.7 (0.7 - 2.6)	1.4 ± 0.7 (0.6 - 2.7)	1.2 ± 0.6 (0.45 - 2.03)	<0.001 (Sig)
FEV1 /FVC	75.2 ± 4.9 (65.7 - 2.3)	65.5 ± 5.4 (60.5-87.5)	63.8 ± 5.0 (58.8-85.4)	62.9 ± 6.0 (54.6 - 6.2)	59.5 ± 8.2 (50.1 - 82.4)	<0.001 (Sig)

Statistical test used: Paired t-test

Sig (Significant), FU (Follow Up), SD (Standard deviation), VC(Vital capacity), FVC(Forced Vital capacity), FEV1(Forced expiratory volume in one second)

Table 6. Complications in post operative period in relation to pre op PCO₂

Complications	Yes No	≤ 45mmHg	> 45mmHg	p value
		n=12	n=13	
		7	12	
		5	1	
Type of Complication	Breathlessness Grade I	2	6	0.047 (Sig)
	Breathlessness Grade II	2	1	
	Pneumonia	1	1	
	Died	1	1	
	Fistula	0	1	
	Prolonged Air Leak	1	2	

Statistical test used: Fisher’s exact test Sig(Significant)

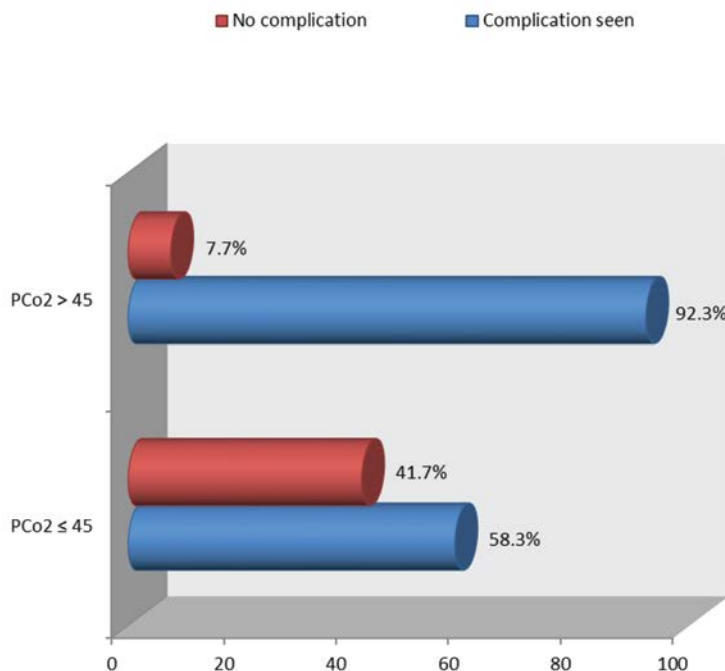


Figure 1. Postoperative complications Vs. Preoperative PCO₂

Pulmonary function parameters

The results of the pulmonary function tests showed a significant decrease in all parameters, namely VC, forced vital capacity (FVC), and FEV1, 1, 3, and 6 months after the surgery (Table 5).

Postoperative complications

The patients with a preoperative PCO₂ of > 45 mmHg showed more postoperative complications (Table 6). In this regard, out of the 13 patients

with a preoperative PCO₂ of > 45 mmHg, 12 cases developed complications, and some required postoperative ventilator support (Figure 1).

Discussion

Arterial blood gas level has not been extensively studied as a predictor of postoperative complications (2). Generally, thoracic surgeons are reluctant to operate patients with hypercapnia. Accordingly, PCO₂

level of > 45 mmHg in arterial blood is a relative contraindication to lung resection as it indicates chronic respiratory insufficiency. Nonetheless, Morice et al. (3) showed that patients with a PCO₂ of > 45 mmHg did well postoperatively. Similarly, the PCO₂ of > 45 mmHg (4, 5) was not indicated as predictive of postoperative complications in a few other studies. A great number of these patients are candidates for lung volume reduction surgery (LVRS) that results in the improvement of hypercapnia and postoperative status.

Lung malignancies are the most common indications for lung resection surgery worldwide. Similar to our study, in the literature, the indications and type of lung resection surgery remain relatively uniform. In a cohort study performed by Zeiher et al. (6), lung resection was conducted in the majority of cases (56%) for the management of neoplastic conditions, with other indications, including lung abscess, tuberculosis, and carcinoid. Similar to the present study, they performed lobectomy in the majority of cases.

Blood gas analysis

The ABG analysis was performed intraoperatively in the PA and peripheral artery at three stages, namely before clamping, as well as 5 and 20 min after clamping. The results revealed no statistically significant change in ABGs in any of the two vessels before and after clamping the PA (tables 2 and 3). However, when the intraoperative ABGs of peripheral artery were correlated with the postoperative ABG analysis, a statistically significant increase was observed in the level of PO₂ and SO₂. Additionally, there was a decrease in PCO₂; nonetheless, it was insignificant (Table 3).

To the best of our knowledge, there is no study directly investigating the changes in blood gases in patients undergoing lobectomy or pneumonectomy. However, a few studies have indicated the incidence of significant changes in blood gas parameters in LVRS. Albert et al. (7) studied the variation of blood gases after LVRS in 46 patients and reported that some patients showed a significant improvement in ABGs after surgery, while almost an equal number showed deterioration in ABGs. In the mentioned study, only minimal effects were observed.

However, in another study performed by Oswald-Mammosser et al. (8), investigating the effect of LVRS on gas exchange, PaO₂ and PaCO₂ showed a significant change after surgery. Since LVRS procedures are performed in patients with entirely different indications with deranged ABGs, correlating their results with our study would not be prudent.

In the current study, blood gas levels

remained constant during the lung resection surgery, whereas blood pressure in the PA and peripheral artery showed different changes. The mean PA pressure showed a statistically significant increase in the immediate postoperative period following lobectomy or pneumonectomy (Table 4).

These findings are in line with those reported by Hideki Nishimura et al. (9), who examined the effects of pulmonary lobectomy on cardiopulmonary function in nine patients with lung cancer. They observed a significant increase in the heart rate, PA pressure, and pulmonary vascular resistance index and a significant decrease in stroke volume index.

In another study conducted by Jesus Ribas et al. (10) on pulmonary hemodynamics in lung resection surgeries, PA pressure showed a significant increase from 18±5 to 23±5 mmHg (P<0.05). This rise in the mean PA pressure can be attributed to the fact that the reduction of pulmonary vascular bed restrains the accommodation of the entire right ventricular output and results in a rise in the pulmonary pressure. The increase in the mean PA pressure would correspond to the number of resected bronchopulmonary segments; accordingly, pneumonectomy is accompanied by a higher mean PA pressure than lobectomy.

This postoperative issue is an important aspect of lung resection because a rise in mean PA pressure and volume overload would lead to right ventricular failure, which is fatal (1). In a study carried out by Lewis et al. (11), 53.8% of patients had no change or a mean drop of 8 mmHg in pressure at PA clamping, while the others had a mean rise of 12 mmHg. They also demonstrated that patients with normal PA pressures before intubation had an average rise of only 4 mmHg upon PA clamping. In the immediate postoperative period, only 10.0% of the entire group had normal PA pressure.

Lung function parameters

The measurement of spirometric indices, namely FEV₁ and FVC, was performed preoperatively and postoperatively (i.e., 1, 3, and 6 months after the surgery). The mean preoperative FEV₁ was obtained as 1.9 L. Furthermore, this parameter had the mean values of 1.6, 1.4, and 1.2 L 1, 3, and 6 months after the surgery, respectively. The decrease in FEV₁ was more in pneumonectomy than in lobectomy (Table 5).

The mean FVCs were estimated at 2.8, 2.5, 2.2, and 1.9 L before the operation, and 1, 3, and 6 months postsurgery, respectively. These findings are consistent with the results of the studies performed by Wintheda et al. (12), Bolliger et al.

(13), and Beccaria et al. (14), in which postoperative FEV1 and FVC measurements were performed 6 months after the surgery.

The aforementioned studies also demonstrated a significant decrease in FEV1 and FVC in postoperative period in the patients who had undergone lung resection surgery. There are scarce data regarding the change in spirometric parameters long after surgery when the patients resume to a normal condition. It is likely that some incremental changes happen as the compensatory hypertrophy of the remaining lung ensues.

Postoperative complications

The majority of the patients in our study developed dyspnea postoperatively. Additionally, 1, 2, and 3 patients had bronchopleural fistula, pneumonia, and prolonged air leak, respectively, and two patients passed away due to respiratory failure. Complications were correlated with respect to preoperative PCO₂. It was found that the patients having preoperative PCO₂ of > 45 mmHg had more complications as compared to those with a PCO₂ of ≤ 45 mmHg (92.3% vs. 58.3%). The incidence of complications among the patients with a PCO₂ of > 45 mmHg was 8.6 times more likely than that in the subjects that had a PCO₂ of ≤ 45 mmHg, and the difference was significant (Table 6).

Our findings are in congruence with those obtained by Zibrak et al. (15) and Tisi (16) who found that the persistently elevated PaCO₂ values of > 45 mm Hg predict a high risk for pulmonary complications or mortality. In other studies, conducted by Stein et al. (17), Tisi (16), and Milledge et al. (18), hypercapnia was reported to be associated with the increased incidence of postoperative complications.

The major limitation of our study is its small sample size. Large sample size is required to decrease the heterogeneity of the samples and substantiate the findings. Besides, the PCO₂ level of > 45 mmHg cannot be the only predictor of the risk of developing complications in the postoperative period. A study with a large sample size entailing the regression analysis of other factors, including age, gender, weight, PO₂ level, SO₂, FEV1, carbon monoxide lung diffusion capacity, and cardiac risk factors, will establish a strong cornerstone for predicting the risk of complications in lung resection surgery.

Conclusion

The findings of the study demonstrated no significant changes in blood gas parameters during lung resection surgery. However, PO₂ and SO₂ marginally increased after the surgery. The patients with a preoperative PCO₂ of > 45 mmHg

experienced more complications following the lung resection surgeries than those with a PCO₂ of ≤ 45 mmHg. Given the lack of observing any significant changes in the PO₂ and SO₂ with the lung resection surgery, this parameter cannot be a limiting factor for deciding on operability in a patient with lung lesion having an acceptable preoperative PO₂.

However, if PCO₂ is > 45 mmHg, the patient should be considered as a high-risk group by the surgeon since they are more significantly prone to postoperative complications/morbidity. Furthermore, thoracic surgeons should also pay attention to the significant elevation of mean PA pressure in the immediate postoperative period to avoid the right ventricular failure. Preoperative lung function parameters are of vital importance to determine the physiological operability in patients undergoing lung resection given the postoperative significant drop in VC and FEV1.

Acknowledgments

Contribution of all authors and the patients is acknowledged.

Conflict of Interest

The author(s) declare no potential conflicts of interest with respect to the research, authorship, and publication of this article.

References

1. Kopec SE, Irwin RS, Umali-Torres CB, Balikian JP, Conlan AA. The postpneumonectomy state. *Chest*. 1998; 114:1158-84.
2. Debapriya D, Lahiri B. Preoperative evaluation of patients undergoing lung resection surgery. *Chest*. 2003; 123:2096-103.
3. Morice RC, Ryan MB, Putnam JB, Ali MK, Roth JA. Exercise testing in the evaluation of patients at high risk for complications from lung resection. *Chest*. 1992; 101:356-61.
4. Steéphan F, Boucheseiche S, Hollande J, Flahault A, Cheffi A, Bazelly B, et al. Pulmonary complication following lung resection: a comprehensive analysis of incidence and possible risk factors. *Chest*. 2000; 118:1263-70.
5. Kearney DJ, Lee TH, Reilly JJ, DeCamp MM, Sugarbaker DJ. Assessment of operative risk in patients undergoing lung resection. *Chest*. 1994; 105:753-9.
6. Zeiher BG, Gross TJ, Keru JA, Lanza LA, Peterson MW. Predicting postoperative pulmonary functions in patients undergoing lung resection. *Chest*. 1995; 108:68-72.
7. Hamed-Akbari Tousi S, Saberi MR, Chamani J. Comparing the Interaction of cyclophosphamide monohydrate to human serum albumin as opposed to holo-transferrin by spectroscopic and molecular modeling methods: evidence for allocating the binding site. *Protein Pept Lett*. 2010; 17:1524-35.
8. Oswald-Mammosser M, Kessler R, Massard G,

- Wihlm JM, Weitzenblum E, Lonsdorfer J. Effect of lung volume reduction surgery on gas exchange and pulmonary hemodynamics at rest and during exercise. *Am J Respir Crit Care Med.* 1998; 158:1020-5.
9. Nishimura H, Haniuda M, Morimoto M, Kubo K. Cardiopulmonary function after pulmonary lobectomy in patients with lung cancer. *Ann Thorac Surg.* 1993; 55:1477-84.
 10. Ribas J, Jiménez MJ, Barberà JA, Roca J, Gomar C, Canalís E, et al. Gas exchange and pulmonary hemodynamics during lung resection in patients at increased risk. *Chest.* 120:852-9.
 11. Lewis JW Jr, Bastanfar M, Gabriel F, Mascha E. Right heart function and prediction of respiratory morbidity in patients undergoing pneumonectomy with moderately severe cardiopulmonary dysfunction. *J Thorac Cardiovasc Surg.* 1994; 108:169-75.
 12. Housaindokht MR, Chamani J, Saboury AA, Moosavi-Movahedi AA, Bahrololoom M. Three binding sets analysis of alpha-Lactalbumin by interaction of tetradecyl trimethyl ammonium bromide. *Bull Korean Chem Soc.* 2001; 22:145-8.
 13. Bolliger CT, Guckel C, Eugel H, Stöhr S, Wyser CP, Schoetzau A, et al. Prediction of function reserve after lung resection; comparison between quantitative, computed tomography, scintigraphy and anatomy. *Respiration.* 2002; 69:482-9.
 14. Beccaria M, Corisco A, Fulgoni P, Zoia MC, Casali L, Orlandoni G, et al. Lung cancer resection: the prediction of postsurgical outcomes should include long term functional results. *Chest.* 2001; 120:37-42.
 15. Zibrak JD, O'Donnell CR. Indications for preoperative pulmonary function testing. *Clin Chest Med.* 1993; 14:227-36.
 16. Zolfagharzadeh M, Pirouzi M, Asoodeh A, Saberi MR, Chamani J. A comparison investigation of DNP-binding effects to HSA and HTF by spectroscopic and molecular modeling techniques. *J Biomol Struct Dyn.* 2014; 32:1936-52.
 17. Stein M, Cassara EL. Preoperative pulmonary evaluation and therapy for surgery patients. *JAMA.* 1970; 211:787-90.
 18. Milledge JS, Nunn JF. Criteria of fitness for anesthesia in patients with chronic obstructive lung disease. *Br Med J.* 1975; 3:670-3.