

## Original Article

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ISSN: 1735-0344 Tanaffos 2012; 11(2): 27-33

TANAFFOS 

# Outcome of the Surgical Treatment of Bullous Lung Disease: A Prospective Study

Yasir Ahmad Lone, Abdul Majeed Dar,  
Mukand Lal Sharma, Irfan Robbani, Arif  
Hussain Sarmast, Enas Mushtaq,  
Mohammad Yousuf Kachroo, Omar  
Masood Khan

Sher-i-Kashmir Institute of Medical Sciences,  
Srinagar, India

Received: 29 December 2011

Accepted: 31 March 2012

Correspondence to: Yasir Ahmad Lone

Address: Yunis Manzil, Lalbazar, Srinagar (Pin:  
190011) J & K, India.

Email address: dr\_yalone@yahoo.co.in

**Background:** This study aimed at evaluating the outcome of surgery for bullous lung disease by comparing the preoperative and postoperative subjective dyspnea score, pulmonary function and clinical features.

**Materials and Methods:** This prospective study was conducted from May 2009 to October 2011, on 54 patients operated for bullous lung disease. Follow-up at 3-6 months consisted of taking a comprehensive history, physical examination, radiological work-up, and evaluation of changes in subjective dyspnea score, arterial blood gas analysis (ABG), and pulmonary function test (PFT). After comparison with preoperative values, the student's paired t-test was used to calculate the statistical significance.

**Results:** With approximately 21.6 cases per year, the most common underlying lung pathology was primary bullous lung disease, followed by COPD. The most common presenting complaint was spontaneous pneumothorax in tall young adults in their fourth decade of life with a history of smoking. Bullectomy, with or without decortication, was done for all cases. Improvement in mean PaO<sub>2</sub> (arterial partial pressure of oxygen), SaO<sub>2</sub> (arterial oxygen saturation) and PaCO<sub>2</sub> (arterial partial pressure of carbon dioxide) was seen in most cases but was statistically insignificant. Improvement in mean FEV<sub>1</sub> (forced expiratory volume in 1st second), FVC (forced vital capacity) and FEV<sub>1</sub> / FVC was statistically significant, with FEV<sub>1</sub> being the most reliable indicator of postoperative progress. Improvement in subjective dyspnea score was statistically significant and showed an inverse correlation with FEV<sub>1</sub>. Those with diffuse pulmonary parenchymal involvement had poorer baseline values and less significant postoperative improvement. Complications occurred more commonly in those with diffuse disease. Mortality was seen exclusively in those with diffuse disease.

**Conclusion:** We conclude that surgery is required for bullous lung disease more frequently in our community since we have a high number of young patients with primary bullous lung disease and localized parenchymal involvement and these patients have a good surgical outcome. Potentially fatal complications like pneumothorax and recurrent infections can therefore be prevented in them. Those with underlying diffuse disease and severely decreased FEV<sub>1</sub> (especially below 1 L) also benefit from surgery but require careful patient selection.

**Key words:** Bullous lung disease, Bulla, Bullectomy

## INTRODUCTION

Patients who have bullous lung disease in the presence of diffuse parenchymal involvement (emphysematous or non-emphysematous) should be evaluated on an individual basis and surgery should be performed for

patients in whom even a small increase in pulmonary function might be of major benefit (1). Computed tomography scan (CT-scan), bronchography and angiography can outline bullae that are not visible on a plain chest radiograph (2). Bullae that enlarge enough to

compress adjacent lung tissue are best diagnosed by CT scan of the chest which can identify potentially operable well defined bullae from inoperable generalized emphysema locally worsened in the area of suspected bulla (3). CT-can also measure the bulla volume and ventilation. Change in forced expiratory volume in 1st second (FEV1), forced vital capacity (FVC) and their ratio (FEV1 / FVC) after surgery, as measured by the pulmonary function tests (PFT) is the main outcome measure (4). Increase in arterial oxygen partial pressure (PaO<sub>2</sub>), oxygen saturation (SaO<sub>2</sub>) and arterial carbon dioxide partial pressure (PaCO<sub>2</sub>) as estimated from the arterial blood gas analysis (ABG) of an arterial blood sample is also among the commonly used outcome variables after surgery, besides changes in clinical and radiological features.

Bullectomy or resection of the entire bulla, either through a video assisted thoracoscopic surgery (VATS) or a standard open thoracotomy, is the most common surgical technique used for treatment (1).

This study aimed at evaluating the epidemiological and clinical profile of bullous lung disease in patients admitted to our hospital over the study period. The main objective was to analyze the short term and long term outcome of surgery by comparing preoperative and postoperative subjective dyspnea score, clinical features, radiological features and pulmonary function.

## MATERIALS AND METHODS

The present study was conducted in the Department of Cardiovascular and Thoracic Surgery (CVTS), Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar from May 2009 to October 2011. Out of 65 cases admitted to this department for bullous lung disease, 60 were eventually operated and 56 out of these 60 met the inclusion criteria for the present study. With 2 cases lost in the follow-up, the present prospective study finally consisted of 54 cases who are still continuing follow-up.

All patients operated on in the Department of CVTS for bullous lung disease and met the inclusion criteria were enrolled in the study. Patients were evaluated and

managed according to the set protocol and followed up accordingly.

The patients were analyzed in terms of:

- 1) History taking
- 2) General physical examination
- 3) Systemic examination
- 4) Investigations (baseline investigations and specific investigations, especially chest radiography, computed tomography scan of the chest (chest CT-scan), arterial blood gas analysis (ABG) and pulmonary function tests)
- 5) Operative findings
- 6) Histopathological examination of resected specimen
- 7) Postoperative stay in the hospital (First week monitoring for immediate outcome and complications)
- 8) Appropriate follow up plan to monitor early (<1 month) and late (>1 month) complications and long term outcome. OPD follow up 1 week and 1 month after discharge and at 3-6 months post-operatively was done. Follow up at 3-6 months was done for all patients. Further follow ups were planned at 9-15 months (completed for 26 patients as of date), 21-27 months (completed for 3 patients as of date), 33-39 months, 45-51 months and 57-63 months to complete a full five-year follow up.

The inclusion criteria were as follows:

- 1) Presence of bulla(e) occupying at least one third or more of hemithorax
- 2) Bulla(e) in the presence of symptoms or complications known to be attributable to them, like pneumothorax or recurrent respiratory infections.

The exclusion criteria were as follows:

- Surgery done primarily for some other lung disease during which bullectomy was also performed (e.g. patients undergoing lobectomy for bronchiectasis and having associated bulla (e) that were also excised were excluded from the study)

For comparing the postoperative dyspnea score based on Medical Research Council guidelines (5) and the ABG and PFT values with the preoperative ones, the student's paired t-test was used to evaluate the statistical significance of this quantitative data.

## RESULTS

The mean overall age was  $41.07 \pm 14.92$  years (range 11 to 65 years). There were 43 males and 11 females with a male to female ratio of 3.9 / 1. Spontaneous pneumothorax was the predominant presenting complaint (28 out of 54 patients, 52 %). Breathlessness (without spontaneous pneumothorax) in 23 out of 54 patients (42%) was the second most common presenting complaint. Traumatic hemopneumothorax bringing the bullous lung disease to attention was observed in only 2 patients (i.e. 4 %) while one patient with a history of IV and inhalation drug abuse presented with spontaneous hemopneumothorax. The most common underlying lung pathology was idiopathic / primary bullous lung disease (19 out of 54 cases, 35.19 %) (Figure 1). COPD was the second most common underlying lung pathology (17 out of 54 cases, 31.48 %). Those with underlying idiopathic/primary bullous lung disease presented more commonly with spontaneous pneumothorax (13 out of 19 patients, 68.42%). Those with underlying COPD presented more commonly with breathlessness in the absence of spontaneous pneumothorax (9 out of 17 patients, 52.94%). The mean overall age of patients was  $41.07 \pm 14.92$  years. Those with idiopathic / primary bullous lung disease were found to develop the disease at a younger age (mean age of 31 yrs) (Figure 2). The mean age of those with underlying collagen vascular disease was also younger (mean age of 26 yrs). Those with underlying COPD developed the disease at an older age (mean age of 56.53 years). The mean overall height was  $67.91 \pm 4.19$  inches. Chest CT-scan confirmed the diagnosis in all patients. Bullae were more common in the upper lobes (40 out of 54 cases, 74.07 %). Open thoracotomy and bullectomy were done in 54% of cases while 46% needed bullectomy along with decortications. Mean chest tube drainage in the 1st 24 hours post operatively was  $450 \pm 220$  ml with a range of 250 – 900 ml. Chest tubes were removed 9 – 14 days postoperatively (average day 5) excluding the 2 patients who developed empyema. Minor complications were seen distributed among 15 patients. Major complications were seen in only 5 patients in the form of air leak > 1 week in 3 and

empyema in 2 patients. All three patients who expired had diffuse disease in the surrounding lung parenchyma. Overall mortality rate at the end of study period was 5.56%. The change in ABG parameters was statistically insignificant while the improvement in PFT parameters and subjective dyspnea score was statistically significant (Table 1). FEV1 is the most reliable indicator of postoperative progress (correlation = 0.727) but improvement tends to decline over time (Figure 3). Patients with underlying diffuse lung disease had poorer baseline values and post operative outcome compared to those without underlying lung disease (Table 2). Two patients died post operatively without the opportunity for follow up PFT, thus the above values were computed for 17 patients instead of 19 who had diffuse disease; 25 patients did not have diffuse disease. All 3 patients who died post operatively also had underlying diffuse disease.

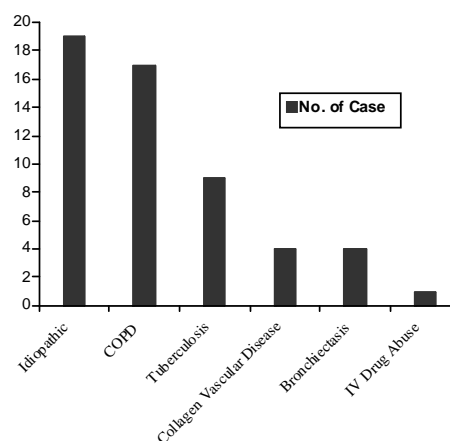


Figure 1. Underlying lung Pathology

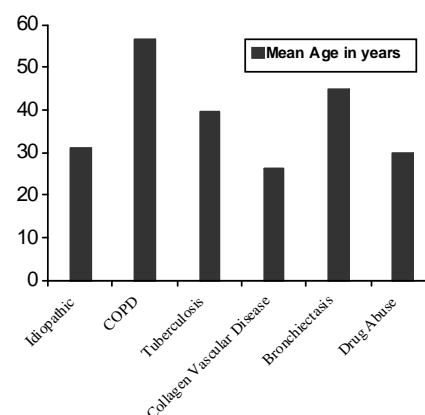


Figure 2. Mean age (in years) of various groups

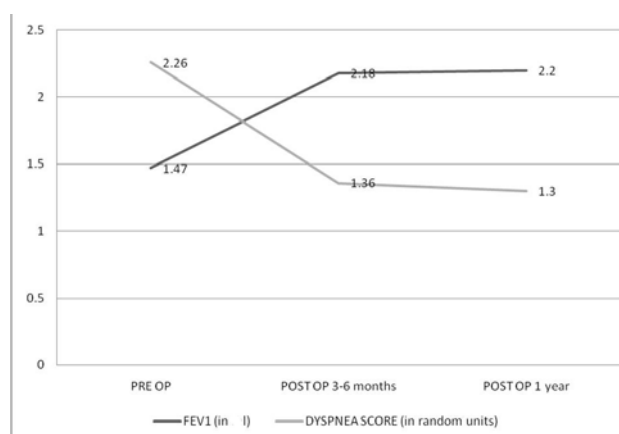
**Table 1.** Depicts mean values (with standard deviation) of ABG and PFT parameters at different time periods. P values of intraoperative and postoperative parameters are given in comparison with respective preoperative values. The change in ABG parameters was statistically insignificant while the improvement in PFT parameters and subjective dyspnea score was statistically significant. FEV1 is the most reliable indicator of postoperative progress (correlation = 0.727) but improvement tends to decline over time.

	PRE OP	INTRA OP	POST OP 1-3 DAYS	POST OP 4-7 DAYS	POST OP 3-6 MONTHS	POST OP 1 YEAR
PaO2 (mmHg)	74.06±7.08	73.29 ± 7.86	71.89 ± 11.28	75.88 ± 11.35	74.55 ± 8.08	73.92 ± 9.08
SaO2 (%)	92.45±4.44	91±6.55	90.69 ± 7.2	92.82 ± 6.18	93.23 ± 1.8	92.1 ± 7.5
PaCO2 (mmHg)	38.33±3.45	38.38 ± 3.96	38.99 ± 3.72	37.42 ± 3.55	37.43 ± 3.1	37.9 ± 4.08
FEV1 (Liters)	1.47±0.56				2.18 ± 0.49 *	2.2 ± 0.38*
FVC (Liters)	2.42±0.71				3.15 ± 0.65 *	3.3 ± 0.31*
FEV1/FVC (%)	60.56±14.9				69.47 ± 11.28*	66.67 ± 7.88*
Dyspnea Score	2.25±0.59				1.36 ± 0.9*	1.3 ± 0.45*

\* P<0.05 is statistically significant (sig.)

**Table 2:** Outcome in two groups with diffuse lung disease and without diffuse lung disease.

	WITH DIFFUSE DISEASE (n=17)		WITHOUT DIFFUSE DISEASE (n=25)	
	PRE OP	POST OP 3-6 MONTHS	PRE OP	POST OP 3-6 MONTHS
PaO2 (mmHg)	69.2 ± 10.6	72.43 ± 9.4	79.8 ± 8.02	80.45 ± 8.8
SaO2 (%)	90.0 ± 4.8	91.6 ± 5.22	93.1 ± 3.2	92.9 ± 2.91
PaCO2(mmHg)	39.9 ± 5.14	38.8 ± 3.92	37.5 ± 3.9	36.9 ± 3.63
FEV1 (Litres)	1.3 ± 0.45	1.82 ± 0.52	1.8 ± 0.6	2.62 ± 0.6
FVC (Litres)	2.3 ± 0.63	3.01 ± 0.59	2.5 ± 0.49	3.24 ± 0.6
FEV1/FVC (%)	56.5 ± 11.8	59.8 ± 12.8	72 ± 13.4	80.9 ± 12.1
Dyspnea Score	2.45 ± 0.62	1.66 ± 0.72	2.05 ± 0.5	1.05 ± 0.61



**Figure 3.** FEV1 and dyspnea score correlation. Line diagram showing time trends of FEV1 and subjective dyspnea score. Rise in FEV1 and fall in dyspnea score show a significant inverse correlation (the higher the rise in FEV1, the greater the improvement in subjective dyspnea score) with the improvement tending to plateau over time

## DISCUSSION

In our study, the incidence rate of bullous lung disease was approximately 21.6 cases per year.

Palla et al. (6), in one of the largest prospective studies of its kind, reported 193 cases who were operated for bullous lung disease, which would be an average of 12.87 cases per year. Although a hospital based study like ours has inherent limitations regarding calculation of the exact incidence rate, approximate number of cases per year can give us a rough estimate of the incidence of disease. Considering the rate of 21.6 cases per year, Kashmir has a high incidence of bullous lung disease. Since primary bullous lung disease and COPD constituted 35.2% (19 out of 54 cases) and 31.5% (17 out of 54 cases) of the cases respectively, both these entities can be said to have a high incidence in Kashmir. The high prevalence of tuberculosis

in our state may also account for the high number of cases (9 out of 54 cases in our study). Four out of 54 cases had an underlying collagen vascular disease / multisystem autoimmune disease. Two of these cases had Marfan syndrome, 1 had Kartagener syndrome and 1 had a multisystem autoimmune disease of unknown etiology, suspected to be a mild variant of Sjogren's syndrome. Underlying pulmonary bronchiectasis also accounted for 4 out of 54 cases and only 1 case out of 54 had a history of IV and inhalation drug abuse. Boushy et al. (5), Adeyemo et al. (2) and Palla et al. (6) reported COPD as the dominant underlying lung pathology in contrast to primary bullous lung disease in our study.

In this study, the mean age of patients was  $41.07 \pm 14.92$  years with a range of 11 to 65 years. A total of 51.9% (28 out of 54 cases) of patients in our study presented with a complication of bullous lung disease in the form of spontaneous pneumothorax; 42.6% (23 out of 54 cases) presented with progressively worsening dyspnea. Two patients presented with post traumatic hemo / pneumothorax with bullous lung disease as an incidental finding. One patient with a history of IV and inhalation drug abuse was the only one who presented with spontaneous hemothorax. Spontaneous pneumothorax was the more common presentation in those with primary bullous lung disease (13 out of 19 patients, 68.4%) while those with underlying COPD presented more commonly with progressively worsening dyspnea in the absence of spontaneous pneumothorax (9 out of 17 patients, 53%). Those with underlying parenchymal lung disease like tuberculosis or bronchiectasis also presented more commonly with dyspnea without pneumothorax (66.7% and 75%, respectively). 3 out of 4 patients (75%) with underlying collagen vascular disease/multisystem autoimmune disease presented with spontaneous pneumothorax.

Potgieter et al, (7) and Adeyemo et al. (2) mentioned progressively incapacitating dyspnea as the dominating presenting complaint in their respective series of bullous lung disease patients with spontaneous pneumothorax

affecting a much smaller number of patients. Many other studies tried to confirm this finding. The much more common late presentation of bullous lung disease with the complication of spontaneous pneumothorax in our study can be attributed to a number of factors. Due to the lack of awareness regarding this disease in the general population, people do not seek proper medical treatment for progressive dyspnea until it becomes incapacitating. Even if they do seek proper medical treatment, primary bullous lung disease is probably not thought of as commonly as it should be. Dyspnea in the elderly is taken more seriously and is promptly evaluated. Consequently a much higher percentage of older patients with underlying COPD were detected with bullous lung disease only with dyspnea before spontaneous pneumothorax complicated it (53%), even though this dyspnea may be attributed to diffuse disease in the surrounding lung parenchyma.

The mean preoperative  $\text{PaO}_2$ ,  $\text{SaO}_2$  and  $\text{PaCO}_2$  in our study was  $74.06 \pm 7.08$  mm Hg,  $92.45 \pm 4.44$  % and  $38.33 \pm 3.45$  mm Hg respectively. The minimum  $\text{SaO}_2$  was 89% and no patient with a saturation rate below this was operated.

The mean rate of preoperative  $\text{PaO}_2$ ,  $\text{SaO}_2$  and  $\text{PaCO}_2$  in our study among those who had diffuse disease (19 patients) was  $69.2 \pm 10.6$  mm Hg,  $90.0 \pm 4.8$  % and  $39.9 \pm 5.14$  mm Hg, respectively. These parameters among those without diffuse disease (25 patients) were  $79.83 \pm 8.02$  mm Hg,  $93.1 \pm 3.2$  % and  $37.5 \pm 3.9$  mm Hg, respectively.

The mean  $\text{PaO}_2$ ,  $\text{SaO}_2$  and  $\text{PaCO}_2$  3-6 months postoperatively in our study was  $74.55 \pm 8.08$  mm Hg,  $93.23 \pm 1.8$  % and  $37.43 \pm 3.1$  mm Hg, respectively. Even though the  $\text{PaO}_2$  usually improved, the changes in the mean  $\text{PaO}_2$ ,  $\text{SaO}_2$  and  $\text{PaCO}_2$  at 3-6 months postoperatively compared to the preoperative values were found to be statistically insignificant.

The mean preoperative  $\text{FEV}_1$ , FVC and  $\text{FEV}_1 / \text{FVC}$  in our study was  $1.47 \pm 0.56$  L,  $2.42 \pm 0.71$  L and  $60.56 \pm 14.88$  % respectively.

The mean preoperative  $\text{FEV}_1$ , FVC and  $\text{FEV}_1 / \text{FVC}$  in our study among those who had diffuse disease (19 patients) was  $1.3 \pm 0.45$  L,  $2.3 \pm 0.63$  L and  $56.5 \pm 11.8$  %, respectively.

respectively. The same parameters among those without diffuse disease (25 patients) were  $1.8 \pm 0.6$  L,  $2.5 \pm 0.49$  L and  $72.0 \pm 13.4$  %, respectively.

The mean FEV<sub>1</sub>, FVC and FEV<sub>1</sub> / FVC 3-6 months postoperatively in our study was  $2.18 \pm 0.49$  L,  $3.15 \pm 0.65$  L and  $69.47 \pm 11.28$  %, respectively. The improvement in mean FEV<sub>1</sub>, FVC and FEV<sub>1</sub> / FVC 3-6 months postoperatively compared to the preoperative values was found to be statistically significant with the strongest correlation for FEV<sub>1</sub> values.

The mean FEV<sub>1</sub>, FVC and FEV<sub>1</sub> / FVC values 3-6 months postoperatively in a study by Pearson et al. (8) was  $1.77 \pm 0.33$  L,  $2.84 \pm 0.37$  L and 62.3%, respectively. The improvement in mean FEV<sub>1</sub>, FVC and FEV<sub>1</sub> / FVC values 3-6 months postoperatively compared to the preoperative values was found to be statistically significant with the strongest correlation for FEV<sub>1</sub> values. Palla et al. (6) also observed a statistically significant improvement in the FEV<sub>1</sub>, FVC and FEV<sub>1</sub> / FVC values 3-6 months postoperatively.

The mean postoperative dyspnea score significantly improved from a preoperative value of  $2.25 \pm 0.59$  to  $1.36 \pm 0.9$  and showed an inverse correlation with the change in FEV<sub>1</sub>. Palla et al. (6) in his study on 41 patients observed that the dyspnea score improved from  $1.8 \pm 0.9$  to  $1.4 \pm 0.8$  and showed a significant inverse correlation with the FEV<sub>1</sub> trend. Our observations are consistent with this study to a fair extent.

The mean postoperative dyspnea score in those with underlying diffuse disease (19 patients) improved from a preoperative value of  $2.45 \pm 0.62$  to  $1.66 \pm 0.72$ . The mean postoperative dyspnea score in those without underlying diffuse disease (25 patients) improved from a preoperative value of  $2.05 \pm 0.5$  to  $1.05 \pm 0.61$ .

The most common postoperative complication was air leak which occurred in a total of 13 patients (25.9%) but persisted for more than one week in only 3 patients, excluding the 2 patients with empyema. It sealed spontaneously with conservative management alone in all patients. Empyema with persistent drainage occurred in 2

patients. It healed with IV antibiotics and the chest tube was removed after 2 months in one patient but the other one never recovered and succumbed to infection after 4 months. Both air leak and empyema occurred more commonly in those with underlying COPD and diffuse disease (9 out of 16 patients had COPD and 10 out of 16 had diffuse disease).

Within two and a half years after the first case, 3 of our understudy patients died out of 54 with a mortality rate of about 5.56% (at the end of 2 ½ years). One patient with Kartagener syndrome died within one week postoperatively and was the only one who needed ventilatory support during the immediate postoperative period. The other one had empyema with persistent drainage and air leak from which he never recovered and succumbed to infection after 4 months. The third patient died one year after surgery due to superimposed pneumonia on a lung that had not shown significant postoperative improvement. All three patients had diffuse emphysematous changes in their lung parenchyma, and 2 had bronchiectatic changes.

The mortality rate was reported by Gunstensen et al, to be 9.5%. This rate was reported by Fitzgerald as 2.1% and by Potgeiter et al, as 9.5%. (7) Antonio Palla et al (6) reported a mortality rate of zero after 3-6 months, 7.3% after 1 year, 4.9% after 2 years with an overall mortality rate of 12.2% after 5 years (5 of 41 patients). All 5 patients had underlying diffuse emphysematous changes. The mortality rate in our study was quite comparable with that observed in the above studies and consistent with the fact that deaths occur almost exclusively in those with underlying diffuse disease in their surrounding lung parenchyma.

We draw the following conclusions from our study:

- The most common underlying lung pathology was primary bullous lung disease followed by COPD.
- The most common presenting complaint was spontaneous pneumothorax.
- The presented patients were usually tall young adults in their fourth decade of life (31 – 40 years) with a history of smoking.

- Improvement in mean  $\text{PaO}_2$ ,  $\text{SaO}_2$  and  $\text{PaCO}_2$  values was seen in most cases after surgery but was statistically insignificant.
- Improvement in mean  $\text{FEV}_1$ , FVC and  $\text{FEV}_1 / \text{FVC}$  was statistically significant, with  $\text{FEV}_1$  being the most reliable indicator of postoperative progress.
- Improvement in subjective dyspnea score was statistically significant and showed an inverse correlation with  $\text{FEV}_1$ .
- The above ABG and PFT parameters as well as the dyspnea score showed similar improvement when considered separately among those with diffuse disease and those without diffuse disease, though the former had poorer baseline values and postoperative improvement.
- Complications occurred more commonly in those with diffuse disease.
- Mortality was seen exclusively in those with diffuse disease.

We conclude that surgery for bullous lung disease is needed more frequently in our community since we have a high number of patients with primary bullous lung disease and localized disease and these patients usually have a good surgical outcome. Therefore, late diagnosis and potentially fatal complications like pneumothorax and recurrent infections would be prevented in them. Those with underlying diffuse disease and severely decreased  $\text{FEV}_1$  (especially below 1 L) also benefit from surgery but careful patient selection is necessary.

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