Pulmonary Complications following Major Lung Resection for Benign and Malignant Lung Diseases

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Key Words

Pulmonary complications · Pulmonary function test · Lobectomy

Abstract

Objective: To assess the incidence and to identify the possible associated risk factors for postoperative pulmonary complications after major lung resection. **Subjects and Methods:** One hundred and sixty-eight consecutive patients undergoing major lung resection for benign and malignant lung disease over a 3-year period were included in the study. Preoperative assessment clinical parameters, intraoperative and postoperative events were recorded. Pulmonary complications were noted according to a precise definition. The risk of complications associated with age, comorbidity, forced vital capacity (FVC), blood transfusion and extended operation was evaluated using logistic regression analysis. **Results:** The mean age of the patients was 47.1 years (range 16–80 years), 137 (77%) patients underwent lobectomy, 23 (14%) pneumonectomy, and 15 (9%) bilobectomy. Forty-six (27%) patients developed postoperative pulmonary complications and 2 (1.1%) died within 30 days following the operation. Age ≥ 65 years (OR 3.7, 95% CI: 1.5–8.6, $p = 0.002$), the presence of comorbid cardiopulmonary

disease (OR 0.2, 95% CI: 0.1–0.5, $p = 0.001$), FVC $< 50\%$ (OR 0.2, 95% CI: 0.1–0.8, $p = 0.02$), blood transfusion (OR 0.2, 95% CI: 0.1–0.4, $p = 0.0001$), and extended operation (OR 0.2, 95% CI: 0.07–0.6, $p = 0.005$) were the identified factors associated with the development of postoperative pulmonary complications, which necessitated an increased length of hospital stay. **Conclusion:** Postoperative pulmonary complications are more likely to develop in patients with age ≥ 65 years with comorbid cardiopulmonary disease, FVC $< 50\%$, blood transfusion, and extended operation.

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Introduction

Major lung resection belongs to the group of surgical procedures with significant morbidity. Despite advances in surgical techniques and perioperative care, mortality ranges from 2 to 12% [1, 2]. Significant respiratory impairment is caused by parenchymal resection and deterioration of ventilatory mechanics. In addition, a wide spectrum of postoperative pulmonary complications (PPCs) may occur in as much as 30–60% of patients [3]. Therefore, improvement of patients' survival and quality of life following major lung resection can be achieved

through identification of operative risk factors and high-quality perioperative medical care. However, there have been relatively few prospective studies accurately describing the PPCs that may occur following major lung resection.

The objectives of this study were to describe the PPCs after major pulmonary resection, and assess the preoperative or intraoperative factors that may predispose to the development of these PPCs.

Subjects and Methods

Selection of Patients

From January 2002 to December 2004, 168 patients (119 male and 49 female; mean age 47.1 years, range 16–80 years) who underwent major pulmonary resection, lobectomies, bilobectomies (removal of two lobes in the right side) or pneumonectomies (removal of whole lung) were included in this study. Patients who underwent wedge resections, exploratory or staging thoracotomy procedures, thoracoscopy with wedge excisions of the lung and emergency lung resections were excluded from the study. All patients were operated on by the same surgical team through either a standard posterolateral thoracotomy ($n = 110$) or muscle-sparing thoracotomy ($n = 58$). Extended resections were performed in 20 patients and that included 13 chest wall, 4 pericardial and 3 diaphragmatic resections. All surgical procedures were performed under general anaesthesia with a double-lumen endotracheal tube. Unless otherwise indicated, all patients were extubated in the operating room at the end of the operation and transferred to a monitored thoracic ward bed. Postoperative pain control was mainly achieved by epidural analgesia. All patients had an active program of chest physiotherapy and incentive spirometry during the postoperative period.

Data Collection

Preoperative assessment included the documentation of historic information (comorbid diseases) as well as preoperative haemoglobin, serum creatinine, and serum albumin. Associated comorbidity factors were defined as coronary artery disease (angina or myocardial infarction), congestive heart failure, peripheral vascular disease, chronic obstructive airway disease, chronic renal failure and diabetes mellitus. Preoperative pulmonary evaluation included arterial blood gas analysis (Pa CO_2 , Pa O_2) and spirometry, forced expiratory volume in 1 s (FEV_1) expressed in percent with regard to theoretical FEV_1 , and forced vital capacity (FVC) expressed in percent with regard to theoretical FVC.

Postoperative Evaluation

All patients were followed up after surgery and complications occurring during hospitalization were recorded. Complications were defined to include pulmonary complications: pneumonia (fever $>38^\circ\text{C}$, purulent sputum, new and persistent lung infiltrate on chest radiograph), atelectasis evidenced on chest radiograph requiring bronchoscopy, prolonged air leak (duration of chest tube drainage >7 days), postlobectomy space, bronchopleural fistula, empyema, adult respiratory distress syndrome, acute respiratory failure (postoperative ventilator dependence >24 h or reintubation for

controlled ventilation), pneumothorax evidenced on chest radiograph requiring chest tube placement and bleeding.

Statistical Analysis

Data were expressed as mean, number or percentages. Data analyses were made using SPSS software for Windows® version 8 packages (SPSS, Chicago, Ill., USA). The cutoff level for statistical significance was $p < 0.05$. The unpaired Student t test was used to assess the significance between means of continuous variables in two groups. The Pearson χ^2 test was used to ascertain the significance of association between the two categorical variables. The χ^2 test was replaced by Fisher's exact test if the cell frequencies of the 2×2 contingency table dropped below 5. Multivariate analysis was used to identify predictors for the development of postoperative respiratory complications.

Results

Study Population

Of the 168 patients, pulmonary resection was indicated for non-small cell lung cancer in 94 (56%) cases and benign lung disease in 74 (44%) cases. The aetiology of benign lung disease included bronchiectasis in 40 patients, tuberculosis sequelae in 11, lung abscess in 9, fungus ball in 7 and organizing pneumonia in 7. Lobectomy, the most common operation, was performed in 130 (77%) cases, while 23 (14%) patients underwent pneumonectomy and 15 (9%) bilobectomy. Eighty-two (48.8%) patients had a comorbid disease, such as hypertension, diabetes mellitus and chronic obstructive airway disease. The clinical data of patients with benign and malignant lung diseases are shown in table 1.

Postoperative Pulmonary Complications

Forty-six (27%) patients developed a total of 53 PPCs (table 2). There was no significant difference between the pulmonary complication rate and the operative procedure. Six (26%) PPCs occurred after pneumonectomies, 35 (27%) after lobectomies, and 5 (33%) after bilobectomies ($p = 0.8$). Prolonged air leak (15%) and atelectasis (4%) were the most prevalent complications, followed by bronchopleural fistula (3%), and bacterial pneumonia (2.4%). Air leak occurred in 13 of 74 (17.5%) patients in whom pulmonary resection was done for benign disease, and in 12 of 94 (12.7%) patients with malignant disease. The difference was statistically not significant ($p = 0.2$). Prolonged air leak occurred in 20 (15.4%) and 5 (33.3%) patients for whom lobectomy and bilobectomy were done, respectively. The difference was statistically significant ($p = 0.01$).

Thirteen (8%) patients experienced 15 complications other than respiratory ones, including 8 cardiovascular

Table 1. Characteristics of patients with benign and malignant lung diseases

	Benign lung disease (n = 74)	Malignant lung disease (n = 94)	OR	95% CI	p value
Age ^a , years	40.24 (14)	52.6 (12.9)	–	8.2–16.5	0.0001
Sex (M:F)	40:34	79:15	4.4	2.1–9.1	0.0001
Smoking (Y:N)	25:49	81:13	12.2	5.7–26	0.0001
Comorbid cardiopulmonary disease (Y:N)	31:43	51:43	1.6	0.8–3	0.07
FVC (<50%: ≥ 50%)	8:66	9:85	0.8	0.3–2.3	0.7
FEV1 (<1.3litres: ≥ 1.3 litres)	8:66	8:86	0.7	0.2–2.1	0.6
Haemoglobin (≤ 10 g/dl: >10 g/dl)	18:56	11:83	0.4	0.1–0.9	0.02
Serum albumin ^a , g/dl	34 (8.2)	33.5 (6.6)	–	–2.7 to 1.7	0.6
Side (right:left)	40:34	53:41	0.7	0.5–2	0.6
Transfusion (Y:N)	35:39	25:69	0.4	0.2–0.7	0.004
Hypertension (Y:N)	8:66	7:87	0.6	0.2–1.9	0.4
Diabetes mellitus (Y:N)	3:71	13:81	3.7	1–13	0.03
Ischaemic heart disease (Y:N)	2:72	9:85	3.8	0.7–18	0.07
Respiratory disease (Y:N)	12:62	15:79	0.9	0.4–2.2	0.9
Lobectomy, bilobectomy vs. pneumonectomy	72:2	73:21	0.09	0.02–0.4	0.0001
Muscle sparing vs. standard thoracotomy	31:43	27:67	0.5	0.2–1	0.07
Postoperative complications (Y:N)	29:45	30:64	0.7	0.3–1.3	0.2
Operating time ^a , h	3.5 (0.8)	2.9 (0.6)	–	–0.7 to 0.3	0.02
Intraoperative blood loss ^a , ml	492.4 (348.3)	329.1 (271.4)	–	–25 to 68.8	0.001
Extended operation (Y:N)	3:71	17:77	5.2	1.4–18	0.005

OR = Odds ratio; CI = confidence interval; Y = yes; N = no.

^a Mean (SD).

ones (6 arrhythmias and 2 myocardial infarctions), 4 genitourinary (2 acute renal failures and 2 urinary retentions), and 3 miscellaneous (2 wound infections and 1 hypernatraemia).

Risk Factors for PPCs

Perioperative data for patients with or without pulmonary complications are presented in table 3. In univariate analysis, age, associated comorbid cardiopulmonary conditions, FEV1, FVC, haemoglobin ≤ 10 mg/dl, operation side, preoperative/intraoperative blood transfusion, extended resection and intraoperative blood loss were associated significantly with postoperative pulmonary complications. Preoperative FEV1 and FVC were predictive of pulmonary complications. Pulmonary complications occurred in 10 of 16 (62.5%) patients with FEV1 <1.3 litres versus 36 of 152 (24%) patients with FEV1 >1.3 litres (p = 0.002). Stepwise logistic regression analysis of perioperative variables independently associated with PPCs is given in table 4. Five risk factors were associated with the development of PPCs: age ≥ 65 years, presence of comorbid cardiopulmonary disease, FVC

Table 2. Pulmonary complications in 168 patients

Complications	Number	%
Prolonged air leak	25	15
Atelectasis	7	4.2
Bronchopleural fistula	5	3
Bacterial pneumonia	4	2.4
Mechanical ventilation	3	1.8
Respiratory insufficiency	3	1.8
Haemothorax	2	1.2
Pneumothorax	2	1.2
Residual pleural space	2	1.2
Total	53	31.8

<50%, blood transfusion and extended operation. Two independent risk factors were associated with the development of prolonged air leak: extended operation (OR 8.8, 95% CI: 3.1–24.7, p = 0.0001) and patients with chronic obstructive airway disease (OR 3.8, 95% CI: 1.3–11.2, p = 0.01).

Table 3. Characteristics of patients with or without pulmonary complications, univariate analysis

	With pulmonary complications (n = 46)	Without pulmonary complications (n = 122)	OR	95% CI	p value
Age (<65 years: ≥65 years)	20:26	98:24	0.3	0.15–0.66	0.002
Sex (M:F)	36:10	83:39	1.6	0.76–3.7	0.1
Smoking (Y:N)	30:16	76:46	1.1	0.5–2.3	0.4
Comorbid cardiopulmonary disease (Y:N)	33:13	49:73	3.7	1.8–7.9	<0.0001
FVC (<50%: ≥50%)	11:35	6:116	6.1	2.1–17.6	0.001
FEV1 (<1.3 litres: ≥1.3 litres)	10:36	6:116	5.3	1.8–15.7	0.002
Haemoglobin (≤10 g/dl:>10 g/dl)	17:29	12:110	5.3	2.3–12.5	<0.0001
Serum albumin ^a , g/dl	28.7 (5.2)	36.4 (6.9)	–	5.7–9.8	0.2
Side (right:left)	32:14	61:61	2.2	1.1–4.7	0.01
Transfusion (Y:N)	28:18	32:90	4.3	2.1–8.9	<0.0001
Hypertension (Y:N)	7:39	8:114	2.5	0.8–7.5	0.07
Diabetes mellitus (Y:N)	7:39	9:113	2.5	0.7–6.4	0.1
Ischaemic heart disease (Y:N)	1:45	10:112	0.2	0.03–2	0.1
Respiratory disease (Y:N)	14:32	13:109	3.6	1.5–8.5	0.003
Lobectomy, bilobectomy vs. pneumonectomy	40:6	105:17	1.1	0.39–2.9	0.5
Muscle sparing vs. standard thoracotomy	19:27	39:83	1.4	0.7–3	0.1
Benign vs. malignant	22:24	72:50	0.6	0.3–1.2	0.1
Operating time ^a , h	3.5 (0.7)	3.08 (0.7)	–	0.2–0.7	0.6
Intraoperative blood loss ^a , ml	547.8 (364.3)	345.7 (279.8)	–	97.8–306.3	0.001
Extended operation (Y:N)	12:34	8:114	5	1.9–13.3	0.001

OR = Odds ratio; CI = confidence interval; Y = yes; N = no.

^a Mean (SD).

Outcome

Two deaths (mortality rate 1.1%) occurred within 30 days after operation. Both patients had lung resection for malignancy. One patient died on day 7 due to massive pulmonary embolism and the other on day 21 due to respiratory failure. The mean duration of postoperative hospital stay was 9 days (7.8–12.6 days) and 12 days (10–22 days) for patients without and with PPCs, respectively ($p < 0.004$).

Discussion

The finding of 27% PPCs is within the reported range of 7–49% of published studies [1–3]. The variability between different series could be explained by the methodology used and type of surgery. Most published studies in the literature were retrospective and hence data collection might not have been as complete as in prospective studies. This prospective study can be considered as population-based because we included all consecutive patients undergoing major lung resection from 2002 to 2004 in the Chest Diseases Hospital, the only centre for the surgi-

Table 4. Multivariate analysis forward logistic regression

Variable	OR	95% CI	p value
Comorbid cardiopulmonary disease	0.2	0.1–0.5	0.001
Age (<65 years: ≥65 years)	3.7	1.5–8.6	0.002
FVC (<50%: ≥50%)	0.2	0.1–0.8	0.02
Blood transfusion (Y:N)	0.2	0.11–0.46	0.0001
Extended operation	0.2	0.07–0.6	0.005

OR = Odds ratio; CI = confidence interval; Y = yes; N = no.

cal treatment of chest diseases in Kuwait. However, the drawback of this study is that the number is small and the population heterogeneous. The most frequent postoperative complication of this study (15%) which was prolonged air leak lasting more than 7 days is consistent with previous studies [2, 4, 5]. This unavoidable complication, though not life-threatening, is a major factor in increasing the hospital stay and corresponding costs, as well as increasing the rate of postoperative morbidity such as empyema, pneumonia and fever [6]. Brunelli et al. [6] re-

ported that for patients with reduced predicted postoperative FEV1, the presence of pleural adhesions and upper lobectomies is a predictive factor for prolonged air leak, whereas Abolhoda et al. [4] showed that FEV1/FVC of less than 50% was associated with prolonged air leak. In our study, two predictive independent risk factors for prolonged air leak were extended operation (OR 8.8, 95% CI: 3.1–24.7, $p = 0.0001$) and patients with chronic obstructive airway disease (OR 3.8, 95% CI: 1.3–11.2, $p = 0.01$). The prevention of air leak begins in the operating room by meticulous surgical techniques and complete expansion of the remaining lung. Postoperatively, ensuring full expansion and pleural apposition are essential if prolonged air leak is to be avoided.

The rate of 3% of bronchopleural fistula after pneumonectomy compares with the rates of 4–9% reported by other investigators [2, 7]. It is the most serious postoperative complication, especially after pneumonectomy, and is usually associated with poor quality of life and a high mortality rate (29–79%), as reported by Bernard et al. [7]. The preoperative predisposing factors for developing bronchopleural fistula are preoperative chemo- and/or radiotherapy, benign infected disease, immunosuppressant, diabetes mellitus, and low FEV1 or DLCO [8]. Surgical risk factors include long residual stump, residual tumour at the bronchial margins, right pneumonectomy, devascularization of the bronchial stump, prolonged ventilation and reintubation [8].

Numerous risk factors have been reported for poor outcome after pulmonary resection such as age, type and extent of surgery, abnormal spirometry, male sex and comorbidity [1, 7]. Age greater than 65–70 years has been associated with an increased incidence of major complications but Abolhoda et al. [4] did not report any significant difference. The difference in these results may be due to the fact that different criteria were used to select patients undergoing lung resection or the extent of surgical resection varied in different series. In this study using univariate and multivariate analysis, an age older than 65 years was associated significantly with PPCs ($p = 0.002$). The incidence of postoperative complications and the mortality rates in patients who undergo lobectomies and bilobectomies are clearly lower than those associated with more extensive resection that include pneumonectomy, chest wall resection, pericardial and diaphragmatic resection [7, 9, 10]. In our series, extended resection was a risk factor for developing PPCs, while others have reported reduced FEV1 as a predictive risk factor for increased PPCs and death [1, 9–12]. Myrdal et al. [1] showed that low respiratory capacity assessed as FEV1 appears to be

the most important predictor of a high risk of complications after lung resection. They showed that respiratory complications were closely related to impaired preoperative pulmonary function (FEV1 <70%) and were associated with approximately 50% of all deaths. In the present study, patients with FEV1 <1.3 litres had 62.5% PPCs as compared to 24% for those with FEV1 ≥ 1.3 litres. This result was statistically significant ($p = 0.002$).

The association of pulmonary complications with the increased incidence of other morbidity factors in surgical procedures is well established particularly in relation to cardiac complications. Whether the cardiac event predisposes to the pulmonary event or vice versa is probably difficult to determine since the two frequently occur simultaneously [13, 14].

Conclusion

Pulmonary complications are mainly responsible for morbidity of patients undergoing major lung resection. These are likely to develop in patients with age ≥ 65 years with comorbid cardiopulmonary disease, FVC <50%, blood transfusion, and extended operation. Great care must be taken to identify the patients who are at increased risk and determine methods to reduce morbidity and mortality.

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