The purpose of this study was to assess the mortality and risk factors of complications after pneumonectomy for lung cancer. Between 1996 and 2001, we reviewed and analysed the demographic, clinical, functional, and surgical variables of 168 patients to identify risk factors of postoperative complications by univariate and multivariate analyses with Medlog software system. The mean age was 60 ± 10 years, overall mortality and morbidity rates were 4.17% and 41.6%, respectively. All frequencies of respiratory complications were 1.2% for acute respiratory failure, 10.1% for pneumonia, 2.4% for acute pulmonary oedema, 4.17% for bronchopleural fistula, 2.4% for thoracic empyema and 18.5% for left recurrent nerve injuries. Postoperative arrhythmias developed in 46% of our patients. The risk factors for cardiopulmonary morbidity and mortality with univariate analysis were advanced age (P < 0.01), preoperative poor performance status (P < 0.015), and chronic artery disease (P < 0.008). Factors adversely affecting morbidity with multivariate analysis included age (P = 0.0001), associated cardiovascular disease (P = 0.001), and altered forced expiratory volume in 1 s (P = 0.0005). Complications after pneumonectomy are associated with high mortality. Careful attention must be paid to patients with advanced age and heart disease. Chest physiotherapy is paramount to have uneventful outcomes.

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Keywords: Lung cancer; Pneumonectomy; Complications
2.1. Statistical analysis

The primary endpoints of analysis were operative mortality and postoperative morbidity. The effects of risk factors on these endpoints were evaluated with both univariate and multivariate analysis. The χ²-test was only used if all expected frequencies were ≥5. Otherwise, Fisher’s exact test was used and a P-value of 0.05 or less was considered statistically significant. Those variables exhibiting \( P < 0.05 \) in the univariate analysis were considered for entry in a stepwise logistic regression analysis for multivariate analysis to simultaneously evaluate the effects of risk factors between patients with and without postoperative major complications. These models were reported using odds ratios with 95% confidence intervals (CI).

2.2. Postoperative complications and mortality

Those occurring within 30 days after pneumonectomy or before discharge from the hospital.

2.3. Respiratory complications were classified

Acute respiratory failure: postoperative mechanical ventilation for 24 h or reintubation for controlled ventilation or need of invasive ventilation.

Pneumonia: one of the following: fever (>38°C); leukopenia (<4000 mm³) or leukocytosis (>12,000 mm³), and at least two of the following: new onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements, new onset or worsening cough, or dyspnoea, or tachypnoea, or need of invasive ventilation.

Empyema: was defined as the presence of purulent material in the postpneumonectomy space.

 Bronchopleural fistula (BPF): communication between the bronchial air space and the pleural cavity and was confirmed by bronchoscopy, thoracotomy or both.

Acute lung injury (ALI): ALI requires all four of the following: acute onset, bilateral infiltrates (radiographically similar to pulmonary edema), no evidence of elevated left atrial pressure (the pulmonary capillary wedge pressure is \( \leq 18 \) mmHg if measured), a ratio of arterial oxygen tension to fraction of inspired oxygen (\( \text{PaO}_2/\text{FiO}_2 \)) of 201–300 mmHg.

Postpneumonectomy pulmonary oedema (PPO): early postoperative onset of dyspnoea, rales and diffuse chest X-ray opacities; infection and left ventricular dysfunction should be excluding factors.

2.4. Cardiovascular complications included

Arrhythmias, myocardial infarction, acute heart failure, pulmonary emboli, and strokes.

For the assessment of our outcomes, we distinguish between two types of complications, and we define:

Major complications: included reintubation, reoperation for bleeding or infection, BPF, empyema, pneumonia, pulmonary oedema or adult respiratory distress syndrome, and myocardial infarction.

Minor complications: including atrial dysrhythmias, wound infections, bronchoscopy for secretions, contralateral pneumothorax, or a urinary tract infection. Transient or permanent vocal cord paralysis was also included.

3. Results

There were 108 left and 60 right pneumonectomies. The average age was 60±10 years with 156 men and 12 women. One hundred and fifty-three patients (91.0%) were smokers. The comorbidity was as follows: anaemia in 41 cases (24.0%), COPD in 24 cases (14.2%), chronic coronary disease in 35 cases (20.8%), diabetes mellitus in 12 cases (7.0%), and tuberculosis in 13 cases (7.7%).

Induction chemotherapy was given in 26 cases (15.5%). Statistical analysis of the performance status ASA revealed a predominance of ASA 2 in 62.0%, ASA 1 in 25.5%, and ASA 3 in 12.5%.

The average value of FEV was 81.1%±9% and vital capacity was 79.5%±8%. All surgical procedures were performed by five surgeons (Table 1).

Squamous cell carcinoma occurred in 70.0% of cases, adenocarcinoma in 23.0%, large cell carcinoma in 5.0%, bronchioalveolar carcinoma (1.0%). Postoperative staging was as follows: stage I (2.4%), stage II (34.5%), stage IIIA (50%), stage IIIB (13.1%). Chest pain was treated through thoracic epidural analgesia in all cases.

Death occurred in seven cases (4.17%) of the 168 pneumonectomies related to pneumonia with acute respiratory failure in three patients, myocardial infarction in two patients, pulmonary emboli in one patient and operative haemorrhage in one patient.

BPF occurred in seven patients (4.17%). Four BPF developed after left pneumonectomy and three developed in the right side. Coverage of bronchial stumps had been performed with a pedicled well-vascularized flap in 55.0% of cases (intercostals flap, pericardial fat, azygos pleura).

Atrial fibrillation and supraventricular tachycardia occurred in 79 (47.0%) patients. Drug conversion to sinus rhythm was succeeded without disturbances.

Table 2 shows the frequency of the individual components of the major and minor complications. In univariate analysis, factors associated with major complications are given in Table 3.

Stepwise multiple logistic regression analysis showed that advanced age, high ASA physical status, COPD and CAD were statistically significant associates of major complications at \( P < 0.05 \).

<table>
<thead>
<tr>
<th>Surgeon</th>
<th>Years of experience</th>
<th>Pneumonectomy</th>
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<tbody>
<tr>
<td>Surgeon 1</td>
<td>20</td>
<td>29</td>
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<td>Surgeon 2</td>
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4. Discussion

The mortality rate in our series of 4.17% included any death that occurred within the hospital stay or 30 days following surgery actual mortality rates being from 5 to 10% [4]. A review of the literature and a recently published case control study revealed a postoperative mortality rate of 16–20% [5] and 11% after pneumonectomy in patients >70 years. Mortality related to respiratory failure after extensive pneumonia was found in three elderly patients with prolonged mechanical ventilation. Myocardial ischaemia or infarction was directly implicated in operative death in two patients related to pre-existing CAD. We believe that application of a strict selective screening approach should be done to identify patients who require more intensive preoperative care with myocardial revascularization if possible before surgery [6].

In our series, 132 patients (78.5%) have FEV$_1$ above 2 l/s. The underlying pulmonary disease particularly COPD has been advocated as a major risk factor for postoperative complications in a previous report [7]. In our series, only 24 (14.2%) patients had COPD. A decrease in FEV$_1$ was associated on logistic regression analysis to major complications in our series.

In our study, the incidence of nosocomial pneumonia of 10.1% was similar to previously reported rates of 3.3–21.8% [8]. Respiratory insufficiency after pneumonia occurred at 3.3–17.4% [9, 10]. Chest physiotherapy is highly recommended to prevent atelectasis and secondary infections. Because pneumonia after pneumonectomy is a very dangerous complication, careful preoperative evaluation, better preservation of the functional residual volume by preoperative and postoperative physiotherapy, optimal pain control and early mobilization were needed for better outcomes.

In our study, BPF was occurred in seven (4.17%) patients, in three cases with empyema; we performed Eloesser procedure for chest cavity drainage with thoracoplasty by omental flap or extrathoracic chest wall muscle transposition the last time. We performed early surgical suture and transposition of vascularized pedicle flaps in three others cases. In one patient, we successfully closed the fistula by direct application of silver nitrate which was used through a rigid scope to seal stump leaks.

There were no significant differences in our study of BPF and the side effects of operation. Many authors have reported higher operative risks after right pneumonectomies [11, 12]. Controversy exists regarding the merits of manual vs. stapled bronchial sutures. Many authors advocate the superiority of staplers sutures [13]. We are unable to confirm this proposition, because in our institution, manual bronchial suture is the preferred technique. Failure of stump healing has many explanations: radical lymphadenectomy favours the devitalization of bronchial tissue, the quality of the flap used to cover the bronchus, neoadjuvant therapy and nutritional status. Our study did not demonstrate reduced incidence of BPF with tissue reinforcement. However, our data must be interpreted with caution, it does not prove that the bronchial stump should not be covered. In addition, chemotherapy and radiotherapy can directly interfere with bronchial healing. Fowler et al. [14] also reported a high frequency of bronchial fistula when a preoperative radiotherapy of 60 Gray was used. In our experience, only one patient received such radiotherapy. Induction chemotherapy was given in 26 cases (15.5%) and the rate of BPF was not affected by this factor.

The experience of surgeons helps to pay attention to the details (bronchial blood supply, length of bronchial stump) to prevent subsequent stump breakdown. Empyema occurred in 2.4% of our patients and 2–16% in the literature [15]. This complication is often associated with BPF leading to aspiration pneumonia; thoracostomy should be done as it has shown good results.

Postpneumonectomy oedema (PPO) is an uncommon complication, which has been observed in 1–5% of patients in a previous study [7]. In our experience, four patients 2.4% developed PPO without operative mortality. Perioperative crystalloid and blood transfusion had the adverse affect of increasing the incidence of this complication.

4.1. Cardiovascular complications

In two cases myocardial infarction occurred in the operating theatre with fatal outcomes. Myocardial revascularization needed time before surgery in patients with poor ventricular function and/or severe CAD. Pulmonary embolism occurred in three patients with one mortality 13 days
after operation. Correction of risk factors, hypercholesterolaemia, obesity, poor vein function, prophylaxis with low weigh molecular heparin and early mobilization helped to decrease the incidence of this complication. Supraventricular arrhythmia was the most frequent complication which varied from 12.3 to 34%. In our experience, arrhythmias occurred in 79 (47.0%) patients. Fortunately, many authors consider it not to have an influence on either postoperative mortality or morbidity. Rapid drug therapy (amiodarone, calcium entry blockers, digitalis) proved sufficient to prevent further severe complications.

However, we have noted a high frequency of vocal cord palsy after left pneumonectomy (46.0%) and extensive lymphadenectomy. Many factors contributed to the increase of this (N2 disease, induction therapy, excessive electro coagulation, surgeon experience) [8, 9].

This study showed an association between some preoperative variables and complications after pneumonectomy. We observed a statistically significant relationship between advanced age, performance status, low FEV1, CAD and major complications with high mortality.

Although our study is limited by its retrospection. The patients who received the neoadjuvant treatment, therefore, represented a select subgroup and must be considered different to the patients who were treated solely with surgical intervention. Although recent studies have endeavoured to identify patients at high-risk for postoperative mortality and morbidity survival at 90 days after pneumonectomy is considered a good outcome, we have no accurate information about this and it is possible that the outcome is not as favourable as has been shown in our results.

Based on previous reports and the present series, careful attention must be given to patients with significant risk factors, such as ageing and CAD who are undergoing pneumonectomy.

References