

Research Article

Pneumonectomies for Infectious Diseases: Predictors of Morbidity and Mortality in a Multicenter Study

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Abstract

Objectives: Pneumonectomy is associated with a higher risk of adverse outcomes compared with other types of pulmonary resections. The objective of this study is to identify the risk factors for post-operative complications in patients who undergo a pneumonectomy for infectious lung diseases.

Methods: This is a multicenter cross-sectional study that includes 61 patients who were operated on by the Thoracic Surgeons from Ibn Rochd University Hospital in Casablanca, Morocco and Marmara University Hospital in Istanbul, Turkey.

Results: The patients' mean age was 38.6 years old. The sex ratio was 1.18. The most frequent indications for pneumonectomy were tuberculosis (62.3%), aspergillosis (24.6%), bronchiectasis (36.1%) and empyema (13.1%). Complications occurred in 45.9% of the cases and the mortality rate was 6.6%. Post-operative transfusion, more than 3 comorbidities and bronchiectasis were the factors associated with a higher morbidity rate. Mortality was significantly higher with extrapleural dissection, intra-operative complications, and post-operative hemodynamic instability.

Conclusion: Pneumonectomy is associated with higher postoperative morbidity and mortality rates. Even though it is rarely indicated for infectious diseases, should be performed when there are no alternative treatment options. It is important to know predictors for intraoperative and postoperative complications for better outcomes.

Keywords: Pneumonectomy, Pulmonary infectious diseases, benign lung diseases, outcomes

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Everts A. Graham performed the first successful pneumonectomy at Barnes Hospital in St. Louis, MO on April 5, 1933.^[1] Pneumonectomy is primarily indicated for the surgical treatment of non-small cell lung cancers when parenchymal-sparing resections are not feasible due to tumor anatomy and extension.^[2] It is associated with higher mortality and morbidity rates compared to other pulmonary anatomical resections.^[3] Complication and mortality rates showed a diverse pattern in the literature with a rate between 38–59%

and 3–12%, respectively.^[4–6] Older age, cardiopulmonary diseases, right pneumonectomy, limited pulmonary functions and smoking status are the major risk factors for postoperative complications. Occasionally, a pneumonectomy is indicated to treat patients with infectious lung disease.^[7,8] Classical indications for pneumonectomy of the infectious diseases can be listed as; tuberculosis, cystic bronchiectasis, suppurative lung diseases and opportunistic infections in immunosuppressed patients.^[9] Pneumonectomy for infec-

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tious diseases is also challenging from surgical technique standpoint due to infectious thick adhesions and significant changes in the anatomy. Despite advances in surgical techniques, pneumectomy for infectious lung disease represents one of the highest-risk procedures because of its associated morbidity and mortality.^[10] Although there are few studies exist in the literature, predictors of unfavorable outcome are still not clear yet. Here, we designed a multi-center study to identify the risk factors associated with increased morbidity and mortality for this specific group of patients.

Methods

We conducted a multicenter, retrospective cohort study by collecting data on patients who underwent pneumonectomy or completion pneumonectomy for infectious lung diseases from January 2005 to May 2019 in the Thoracic Surgery Departments in the University Hospital Ibn Rochd in Morocco and the Marmara University Hospital in Turkey. The ethical application was approved by the research board of University Hospital Ibn Rochd in Morocco. Data collection and analysis were performed with Microsoft excel and SPSS software. Student's t and χ^2 tests were used for inter-group comparisons. Logistic regression analysis was used for univariate and multivariate analyses.

Results

Characteristics of the Patients

Of all the pneumectomies conducted during this period, 61 were performed for infectious lung diseases. The patients' average age was 38 years old with a range from 6 to 79 years old. The sex ratio was 1.18 with a slight male predominance (33 males vs 28 females). Comorbidities are shown in Table 1. Symptoms were mainly productive cough, hemoptysis, chronic empyema, and recurrent chest infection. Chest X-ray and pulmonary function test were

Table 1. Comorbidities of the patients^a (n=61)

Comorbidity	n	Percentage %
Tuberculosis	46	75.4
Smoking	14	23
Respiratory Infection	10	16.4
Hypertension	1	1.6
Diabetes Mellitus	1	1.6
CAD	1	1.6
CKD	1	1.16
Immunosuppression	1	1.16
Hematologic Diseases	1	1.16

^aThe values are presented as number and the percentage of variables; CAD: Coronary Artery Disease; CKD: Chronic Kidney Disease.

the primary investigations. Computed tomography (CT) scan was used to determine the disease severity of the affected lung as well as its extent in the contralateral lung. Complete lung destruction was seen in 78.7% (48/61) of the cases. Bronchoscopy was performed on 26% of the patients and the only finding was an inflammatory state with no other visible abnormalities. The bronchoalveolar lavage fluid analysis and bronchial biopsies were negative. Seventeen patients (28%) had an aspergillus serology which was positive for 7 of them and nearly half of the patients (44.3%) had a sputum analysis, but no microorganisms were isolated. 49.2% of patients received preoperative preparation for the surgical procedure: 34.4% were treated with conservative antibiotic treatment while 7 patients required thoracic drainage prior to the surgery. At the end of the pre-operative assessment, primary indications for pneumonectomy were bronchiectasis (32.8%), tuberculosis (24.6%), empyema (23%) and aspergillosis (19.7%) (Table 2).

Operative Management

The surgical approach was a standard posterolateral thoracotomy in the 5th intercostal space in 93.4% (57/61) of the cases. 4 patients underwent a multiport video-assisted thoracoscopic surgery (VATS). The resection was extra-pleural (41%) if an intrapleural space could not be developed due to the extent of local adhesions. Overall, we performed 22 (36%) right and 39 (64%) left pneumectomies. 3 patients underwent a completion pneumonectomy; two of the three patients had a previous lobectomy for bronchiectasis and the remaining patient had a lobectomy for hydatidosis. Hilar dissection was very challenging for all the patients but only one of them required an intrapericardial dissection. Three vascular injuries occurred (1 left pulmonary artery and 2 right internal mammary arteries) but were easily controlled. The bronchial stump was oversewn in 57 (93.4%) patients and with stapled for 4 (6.6%). The bronchial stump closure was buttressed with an intercostal flap for all right pneumectomies. The intraoperative morbidity of this study was 44.3%. Seven percent of the patients had intraoperative hemodynamic instability, 15% lost a significant blood volume and 19% required intraoperative transfusion. At the end of the procedure, the chest was routinely drained with a 28F chest tube connected to a balanced drainage system.

Table 2. Surgical Indications^a (n=61)

Indication	n	Percentage %
Bronchiectasis	20	32.8
Tuberculosis	15	24.6
Empyema	14	23
Aspergillosis	12	19.7

^aThe values are presented as number and the percentage of variables.

Morbidity and Mortality

Complications occurred in 45.9% of patients (Table 3). Surgical site infection was the main adverse outcome (31.1%) and the rate of bronchopleural fistula (BPF) was 6.6%. In this study, 4 patients died during the perioperative period because of hemorrhagic shock, cardiopulmonary arrest and septic shock. The mortality rate was 6.6%.

Predictors of Morbidity and Mortality

Multivariate analysis indicated that 3 or more comorbidities ($p=0.039$), an important blood loss leading to a postoperative transfusion ($p=0.029$) and a post-operative diagnosis of bronchiectasis ($p=0.004$) were independent significant risk factors for complications post pneumonectomy. Risk factors for mortality are given in (Table 4). Additionally, extrapleural dissection ($p=0.049$), intra-operative morbidi-

ties ($p=0.049$) and postoperative hemodynamic instability ($p=0.001$) were the variables significantly impacting postoperative mortality.

Discussion

Pneumonectomy is mostly performed for pulmonary malignancies, but preference and appliance are limited today due to the advances in the chemotherapy and immunotherapy agents used by medical oncologists. In addition to that, easy access, and widespread use of computerized tomography (CT) enable the physicians to diagnose patients at early stages which can be cured with lesser anatomical resections like lobectomies or segmentectomies.^[11] Even though pneumonectomy for malignant disease is associated with significant morbidity and mortality, it is more challenging in patients necessitating pneumonectomy for infectious lung disease.^[12-14] It is believed that chronic inflammation and fibrosis cause deterioration in the nature of the surrounding tissues which makes the surgery technically demanding. In addition to that, changes in the anatomy and neovascularization make the surgery more challenging by increasing proclivity to intraoperative complications, especially bleeding.^[15,16] Tuberculosis is considered as the most common indication for pneumonectomy in those with benign lung diseases followed by chronic empyema.^[7,9] Tuberculosis is still endemic in some areas of the world and unfortunately, its prevalence is increased as a co-infection after the Covid-19 pandemic.^[17] Although the most frequent indication was bronchiectasis, followed by pulmonary tuberculosis and chronic empyema in this study, this can change due to the this increase in prevalence of tuberculosis. There is some controversy about the complications and mortality rates of pneumonectomy in patients with benign lung disease. According to previous studies, postoperative mortality after pneumonectomy was between 0 and 25%.^[7,9] We found a mortality rate of 6.6%. This could be explained by the established preoperative workup for the patients and the experience of the surgeons that are accustomed to the challenging surgical inflammatory environment.^[2]

Also, some studies showed that right-sided pneumonectomy could increase complications and mortality rate.^[8,10] The risk factors associated with a right pneumonectomy include the loss of a larger lung, resulting in not only less remaining pulmonary, but also the entire cardiac output going through a smaller lung and relatively more right ventricular stress.^[18] In this study, the pneumonectomy was performed on the right side in 36% of the cases, but it was not a significant risk factor associated with complications ($p=0.629$). Moreover, BPF remains an important factor for

Table 3. Post-operative morbidities of the patients^a (n=61)

Morbidity	n	Percentage %
Surgical site infection	19	31.1
Cardiovascular complication	5	8.2
ARDS	4	6.6
BPF	4	6.6
PPE	4	6.6
Pneumonia	4	6.6

^aThe values are presented as number and the percentage of variables; ARDS: Acute Respiratory Distress Syndrome; BPF: Bronchopleural Fistula; PPE: Post-pneumonectomy Empyema.

Table 4. Predictors of morbidity and mortality (n=61)

Factor	Morbidity p	Mortality p
Age	0.329	0.515
Sex	0.895	0.483
Smoking	0.560	0.322
High BP	0.303	0.801
ICM	0.139	0.386
Comorbidities ≥ 3	0.039	0.878
Right-sided pneumonectomy	0.629	0.942
Completion pneumonectomy	0.303	0.801
Extra-pleural dissection	0.065	0.049
Recurrent Infection	0.692	1
Intraoperative complication	0.065	0.049
Postoperative transfusion	0.029	0.315
Postoperative hemodynamic instability	NA	0.001
Fungal Infection	0.103	0.349
Tuberculosis	0.811	0.092
Bronchiectasis	0.004	0.249

^aThe values are presented as p-values. P-value <0.05 was considered as statistically significant and written with bold font within the table. BP: Blood Pressure; ICM: Intercostal Muscle Flap.

morbidity and mortality after pneumonectomy and occurs more frequently on the right side.^[19] However, our results did not find that the side of the resection was a significant factor associated with BPF occurrence. This could be explained by the systematic consistent reinforcement (100%) of all right bronchial stumps with an intercostal muscle flap in the whole series.

Even though Massard and colleagues reported that pulmonary tuberculosis and chronic empyema were major risk factors for complications after pneumonectomy,^[14] the multivariate analysis indicated that underlying comorbidities, postoperative transfusion, and a post-operative diagnosis of bronchiectasis were significant risk factors (p respectively= 0.039, 0.029, 0.004) for major complications after pneumonectomy for benign lung disease.

As pleural adhesions and inflammation could be induced by chronic benign lung diseases, it was sometimes necessary to perform extra-pleural dissection which may increase blood loss during the surgery. In this study, extra-pleural dissection was performed in 41% of patients and significantly impacted the mortality after multivariate analysis ($p=0.049$).

Conclusion

Pneumonectomy for benign disease is rare but it is inevitable when there are no other treatment options. Even though it is believed to have a higher postoperative morbidity and mortality compared to pneumonectomy for malignancy, it should not be avoided when necessary. Experienced centers have an advantage in terms of dealing with the complications and it is important to know predictors for intraoperative and postoperative complications for better outcomes.

Disclosures

Ethics Committee Approval: The ethical application was approved by the research board of University Hospital Ibn Rochd in Morocco.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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