

SAFETY AND RISK FACTORS FOR THE MORBIDITY AND MORTALITY OF PNEUMONECTOMY: A RETROSPECTIVE 10-YEAR STUDY IN A SINGLE INSTITUTION

Joana Rei^{*1}, Susana Lareiro¹, Pedro Fernandes¹, Patrícia Castro¹, Sara S. Costa¹, José Miranda¹, Luís Vouga¹, Miguel Guerra^{1,2}

¹Cardiothoracic Surgery Department, Centro Hospitalar de Vila Nova de Gaia/Espinho-EPE, Vila Nova de Gaia, Portugal

²Faculty of Medicine of the University of Porto, Oporto, Portugal

*Contacto Autor: jcfrei93@gmail.com

Abstract

Objectives: Pneumonectomy is a procedure with high post-operative morbidity and mortality. This study aims to assess and identify possible risk factors that can affect post-operative outcome, therefore determining the safety of pneumonectomy in specific groups.

Methods: A total of 63 patients submitted to pneumonectomy at our centre, from February 2008 to February 2018, were included in our retrospective study. Age, gender, side of intervention, diagnosis, pre-operative symptoms, substance abuse and comorbidities were assessed. Early and late post-operative complications, as well as death were our major outcomes. We analysed the impact of preoperative variables on major outcomes using SPSS statistics.

Results: We found a 9,8% surgery-related mortality and 1-year survival rate of 76,2%. The incidence of early complications in our population was of 35% while eleven patients (17,4%) developed late post-operative complications. No statistical difference was found when comparing survival time between genders or age groups. Right sided pneumonectomies seem to be associated with an higher mortality risk. No other association between risk factors and outcomes reached statistical significance in both univariate and multivariate analysis.

Conclusions: Pneumonectomy is a viable option regardless of age whenever the patient has a good functional and cardiopulmonary status. Gender and diagnostic group do not seem to influence adverse event risk, although right-sided pneumonectomies show an increased risk for post-operative death. Care should be taken with patients submitted to neoadjuvant therapy. All patients should be encouraged to cease smoking as early as possible before surgery, given the increased risks for post-operative complications.

INTRODUCTION

The first pneumonectomy was performed in 1933 and was the procedure of choice during the 1950s, before surgery evolved to less invasive approaches.¹ It is often referred to as a disease itself, given the high incidence of post-operative complications, mortality and decrease in overall quality of life.²

Lung resection is often the best treatment modality for both malignant and several non-malignant conditions. The anatomical extension of the pulmonary pathology usually dictates the need for a pneumonectomy in detriment of less invasive techniques, as so, pneumonectomy is reserved for particular cases in which limited resections cannot be performed.^{3,4}

Many risks factors have been advocated to influence the risk of post-operative complications following a pneumonectomy, although consensus still lacks within the literature. Age per se has not proved to be a risk factor, despite the higher risks inherent to the population itself, and other proclaimed risk factors remain debatable. Besides the risk for early complications, one of the most feared complications of pneumonectomy is the development of a bronchopleural fistula, which increases morbidity and severely compromises quality of life. There is still relatively little published evidence on the role of bronchial stump reinforcement in the prevention of bronchopleural fistulae.⁵

This study focuses on analysing the safety of pneumonectomy, identifying risk factors within the population

that can help determine operative suitability and predict post-operative complications, in the intent to minimize both morbidity and mortality.

MATERIALS AND METHODS

Population and data

We have retrospectively reviewed all patients submitted to pneumonectomy at the Centro Hospitalar Vila Nova de Gaia/Espinho, Portugal, from February 2008 to February 2018. A total of 63 patients were included in our study, with ages ranging from 20 to 80 years old. Patients under 18 years of age and submitted to pneumonectomy due to trauma were excluded. Patients were considered candidates for surgery whenever the underlying pathology was not addressable through minor resections (central tumours, disease invading major fissures) and whenever the benefits overcame the risks of surgery. Malignant disease with distant metastases or oesophageal infiltration were absolute contra-indications for surgery. All patients submitted to pneumonectomy were adequately studied through pre-operative imaging (either chest x-ray, chest CT, bronchoscopy and/or PET scan when needed) and lung function studies. Patients with a predicted post-operative FEV1 over 60% were considered fit for surgery.

In order to investigate risk factors for post-pneumonectomy complications, categories such as age, gender, side, underlying disease, pre-operative symptoms, (such as cough, dyspnoea, haemoptysis, loss of weight), tobacco and alcohol abuse and history of respiratory and cardiovascular disease were assessed and registered. We defined an age cut-off at 70 years old, dividing our population into two comparable groups. Patients were divided in two groups in terms of underlying disease: malignancy (including all histological subtypes) and benign disease, including both infectious disease (such as tuberculosis or aspergillosis) and structural lung disease (such as bronchiectasis). In cases in which pneumonectomy was performed due to malignancy, histological type and additional therapy (both adjuvant or neoadjuvant chemotherapy and radiotherapy) were assessed.

Post-operative complications were divided into two categories: early complications, defined as those occurring during in-hospital stay (including haemorrhage, acute lung injury, surgical site infection, atrial arrhythmias) and late complications, such as empyema and bronchopleural fistula. Both early and late complications contributed to patient's post-operative morbidity. The cut off for a prolonged in-hospital stay was set at 10 days after surgery.

Total length of stay and ICU days were also documented.

Early mortality was defined as death within the in-hospital stay or during first 30 days post-discharge. Early and total mortality, as well as 1-year survival rate, were also calculated.

All data used in our study were obtained through the patient's personal medical records.

The mean follow-up time was 1458 days.

Outcome

The primary end points of analysis were morbidity, regarding early and late complications, and mortality. Age, gender, side of the procedure, diagnostic group, tobacco abuse, previous history of tuberculosis and pre-operative therapies (such as chemo and radiotherapy in cases of lung malignancy) were considered as potential risk factors. Survival curves were analysed through the Kaplan-Meier method and compared through log-rank tests. The effects of risk factors on these end points were evaluated with both univariate and multivariate analysis, through chi-square tests and logistic regression models.

Surgical technique

All procedures were performed by cardiothoracic surgeons from the Department of Cardiothoracic Surgery of the Centro Hospitalar Vila Nova de Gaia/Espinho, Porto, Portugal. Patients were submitted to either standard, extended or completion pneumonectomy, depending on the underlying pathology. Bronchial stump reinforcement with intercostal muscle flap or U sutures was performed in cases of patients submitted to neoadjuvant therapy and whenever intra-operative findings were suggestive of bronchial stump dehiscence.

RESULTS

Population and clinical setting

A total of 63 patients were submitted to pneumonectomy over the course of this study, 46 of them were male and 17 were female, with a ratio male:female of almost 3:1. Age at time of surgery ranged from 20 years old to 80, with a mean age of 59.98 and a median of 61 years of age.

Patients were divided into two categories according to age, with 16 patients within the age of 70 or older and 47 younger than 70 years of age. The majority of patients (56 patients) submitted to pneumonectomy were diagnosed with malignant disease involving the lung, either primary or secondary, as we can see in Table 1. Twenty-one patients (37.5% of those with malignant disease) received neoadjuvant therapy, while 23 were submitted to either chemo or radiotherapy after surgery. Of those receiving neoadjuvant therapy, 16 patients were aged under 70 years old while only 5 were over 70. The histological characteristics of all diagnosed malignant lung tumours are listed in Table 1. Four patients presented with structural lung disease manifesting as bronchiectasis and 3 with infectious disease (2 of them with aspergillosis and 1 with empyema). Eighteen patients were asymptomatic at presentation.

The most frequently reported symptoms were cough (24 patients) and haemoptysis (23 patients). In terms of previous medical history, a total of 66.7% of patients had a history of tobacco abuse and 12 patients (19%) had a previous diagnosis of tuberculosis during their lifetime.

Regarding laterality, 23 patients were submitted to a right pneumonectomy, while the remaining 40 were submitted to surgery on the left. Only five procedures were

Table 1

Population demographic and clinical pre-operative data

	(n)
Age at time of surgery (years; $\mu \pm SD$)	59.98 (± 12.21)
Gender	
• Male	46
• Female	17
Diagnosis	
• Lung malignancy	56
○ Adenocarcinoma	20
○ Squamous cell carcinoma	17
○ Carcinoid	6
○ Sarcomatoid carcinoma	6
○ Bronchioloalveolar carcinoma	2
○ Small cell carcinoma	1
○ Mesothelioma	1
○ Metastasis	1
○ Unknown	2
• Bronchiectasis	3
• Aspergillosis	2
• Empyema	1
Pre-operative symptoms	
• Cough	24
• Haemoptysis	23
• Chest pain	9
• Weight loss	8
• Asymptomatic	12
Pre-operative symptoms	
• Tobacco abuse	42
• Diabetes	7
Tuberculosis	12
Side of pneumonectomy	
• Left	40
• Right	23

completion pneumonectomies. Overall, 90.5% of surgeries were standard pneumonectomies. Only one patient was submitted to an extra-pleural pneumonectomy due to mesothelioma. Of the remaining, in 3 the procedure was extended to the pleura and 2 to the pericardium.

The median length of stay was of 8 days (min.: 5 – max.: 123 days). All patients were admitted to our ICU ward on the operative day. The majority of patients were transferred to the general cardiothoracic ward in the first post-operative day, only 7 stayed in the ICU ward for over 48 hours (11.1%) due to early post-operative complications.

Outcome

We found an overall mortality of 36.5% during the study's 10-year time span. The calculated mean survival time was of 8.4 years. Meanwhile, early mortality was 9.8% (6 patients) and the 1-year survival rate was 82.5%. Survival curves are shown in Figure 1.

Median overall survival time in patients over 70 years of age was of 101.1 months, while those younger than 70

showed a median survival time of 81.9 months. No difference in survival curves was found between patients younger and older than 70 years of age (log rank: $p=0.673$).

Early mortality rate according to diagnostic group was of 8.9% in lung malignancy cases and of 14.3% for benign conditions.

Regarding side of the intervention, the mortality rate for right-sided interventions was of 26% and for left-sided ones, of 0%. All 6 cases of peri-operative death occurred in right-sided interventions (chi square=0.001)

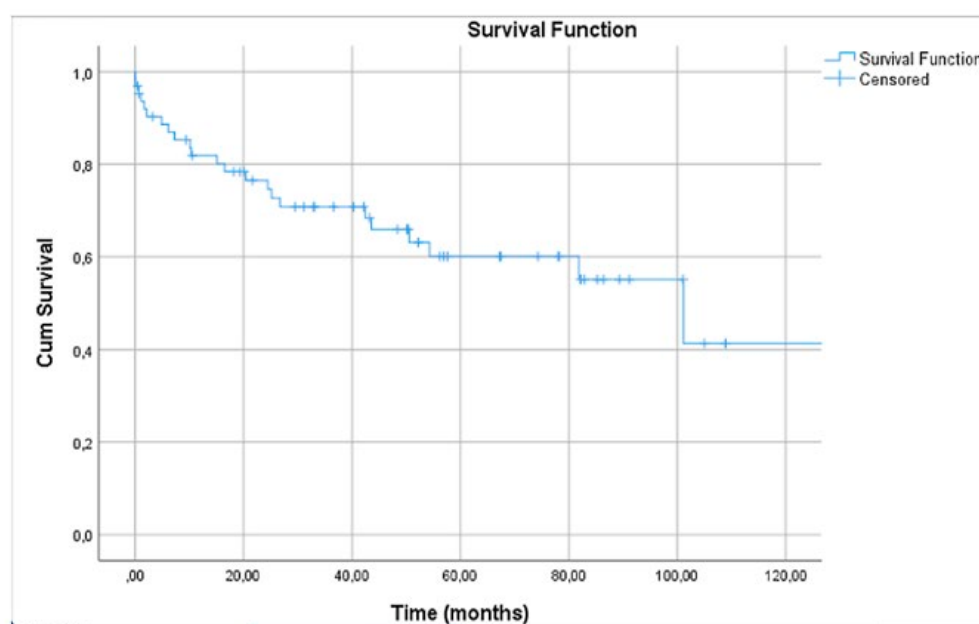
No statistical difference was found when comparing survival time between genders (log rank $p>0.05$). Mortality among women was 5.9% and among men 10.9% (chi square = 0.549). 66.7% of early deaths occurred in patients with a history of tobacco abuse, none of which had a previous diagnosis of tuberculosis.

Mortality in patients submitted to neoadjuvant therapy was 14.3% while in those who didn't receive pre-operative chemotherapy was 7.1%. In multivariate analysis, only laterality reached statistical significance.

Regarding early complications, there was a 20.6% incidence of atrial fibrillation in the immediate post-operative period. 4.8% of cases suffered from acute post-operative haemorrhage, with a need for reintervention for haemostasis revision. Only 1.6% of patients developed a surgical site infection. Overall, the incidence of early complications in our population was 35%. Through the chi-square test, no risk factors showed direct statistically significant impact on early complications. One of the only risk factors that approached statistically significant influence on early complication rate was male sex ($p=0.082$). Although not reaching statistical significance through the chi square test (OR=1; 95%CI [0.085-11.70]; $p=1.0$), smoking seemed to increase the risk of over ten days in-hospital stays ($p=0.039$).

Eleven patients (17.4%) developed late post-operative complications, 8 of whom were smokers, although the association between smoking and late complications was not confirmed by statistical analysis. All patients with bronchopleural fistula were smokers and the majority of them were from the male gender and suffered from a lung malignancy (4 out of 6). Four of the patients who developed a bronchopleural fistula had been submitted to a left pneumonectomy, while the remaining two were submitted to a right pneumonectomy. Four of the patients who developed a bronchopleural fistula had been submitted to a left pneumonectomy, while the remaining two were submitted to a right pneumonectomy. Previous history of pre-operative chemotherapy did not show any influence in the development of bronchopleural fistulae. Nineteen patients were submitted to bronchial stump reinforcement, 15 through the use of an intercostal muscle flap and 4 through direct U-suture. Bronchial stump reinforcement did not show to protect from bronchopleural fistula development, instead, this complication showed to be more frequent in patients who performed bronchial stump coverage (OR=5.6; CI95%=[0.93-33.8]).

Of the 8 patients with a previous history of tuberculosis, 4 presented late complications. This outcome showed to be more frequent in younger patients, as 9

**Figure 1***Kaplan-Meier 10 year survival curve.*

out 11 were aged under 70 years old. Although neoadjuvant therapy showed to impact early complications, it failed to do so for late complications. Regarding the body side intervened, 45.5% of complications occurred in right pneumonectomies, while the remaining 54.5% occurred in left ones. The majority of patients with late complications were male (72.7%). No association was found between risk factors and the incidence of late complications in multivariate analysis. No cases of post-pneumonectomy syndrome were found during the timespan of this study.

DISCUSSION

Despite the risks and the current trend for minimally invasive procedures, there are still cases where a pneumonectomy needs to be performed. Current indications for pneumonectomy include: centrally located tumours, locally advanced tumours irresectable by lobectomy or lesser lung resections, post-infectious lung destruction, multi-drug resistant extensive tuberculosis, congenital pathologies affecting lung parenchyma and trauma incidents.⁶⁻⁸ Given the extensive nature of the resection, only patients with acceptable cardiac and lung function are candidates for the procedure. Despite the advances in anaesthetic management and peri-operative care, overall morbidity and mortality related to pneumonectomy has remained stable throughout the years.^{2,6}

Many risk factors have been advocated in different studies as influencing post-pneumonectomy morbidity and mortality, but, in many, no consensus was yet found. Among them, old age, male sex, cardiac failure, benign disease, neoadjuvant therapy, decreased lung function, right sided pneumonectomy, acute blood loss during surgery and

tobacco abuse have been proposed to influence post-operative course.⁹⁻¹⁴ In our study we have investigated the role of age, sex, diagnosis, laterality, history of tuberculosis or tobacco abuse and neoadjuvant chemotherapy in post-operative complications and overall mortality, in order to access which factors must be taken into account when selecting patients for surgery.

The overall mortality during the 10-year time in our study was of 36.5%, seemingly higher than most studies which report a 0-25% mortality.^{10,11,15-17} This may be mostly related to the fact that studies rarely report 10-year survival rates, opting for 30-day to 5-year data presentation. Also, this overall mortality does not exclude non-pneumonectomy related causes of death. Our peri-operative mortality was 11.1%, in line with most of the current literature which proclaims overall peri-operative mortalities of 3-12%.^{9,18,19} In concordance with other studies, 1-year survival rate in our study was of 76.2%, higher than that reported by Annessi et al, of about 66%.²⁰

Many groups have investigated the role of age in post-pneumonectomy prognosis in an attempt to evaluate whether the procedure is safe enough to be performed in elders. It has been consistently shown that, despite the comorbidities associated with old age, pneumonectomy is safe enough to be performed in elder with adequate lung and cardiovascular function.^{12,13,20-23} In our study, we have chosen to compare outcomes between 2 groups with a cut-off for age set at 70 years old, the classic definition for old age. Given the current extension in global average life expectancy, accompanied by a stable lung cancer incidence that affects mostly those in the 60-70s age group, the number of septuagenarians submitted to lung surgery has been increasing throughout the years.^{11,22} Through analysis of the Kaplan-Meier survival curve, early post-operative

mortality seems to be slightly higher in older patients, but overall survival doesn't show significant differences among both groups. The Lung Cancer Group has previously shown a perioperative mortality for pneumonectomy of about 5.9%, similar to our finding of a 6.5% perioperative mortality in patients aged over 70.²⁴ Age also did not show impact in the incidence of post-operative complications in our study, either early or late ones. Although one might predict higher morbidity in older patients, given their frequent comorbidities, studies are consistent in considering that pneumonectomy should be attempted in cases in which the patient is considered fit for surgery, especially in cases of lung cancer, regardless of age.^{12,13,23}

While in the past, tuberculosis was one of the major indications for pneumonectomy,¹⁰ currently, with the development of multi-drug treatment for tuberculosis, patients with lung malignancy represent the main objects of pneumonectomy. In our study, although the majority of patients suffered from a lung neoplastic disorder, precluding us from a faithful analysis, those with benign diseases seemed to experience an increased risk for early death. "Benign" diseases, in this study, included both structural and infectious diseases, probably affecting both lungs. An unhealthy contralateral lung renders it more difficult for patients to recover after pneumonectomy. Other studies have corroborated this finding, showing a worse prognosis in patients with benign disease submitted to pneumonectomy, especially in terms of early peri-operative risk.⁷ The reported higher surgical and peri-operative risk in benign diseases seems to be related to the amount of scar tissue and adhesions around major vascular structures that can difficult surgical dissection and increase the risk for bleeding.¹⁰ Regardless, pneumonectomy is safe in cases of lung cancer, with an estimate mean survival time of 8.4 years, compared with the disappointing results of palliative non-surgical therapies alone, with reported mean survivals of 10-12 months in the study of Bolukbas et al, along with the predicted 5-year survival rate of only 10% in those with Stage I lung cancer reported by Van Meerbeeck et al.^{12,13,22} Although tuberculosis was not the major indication for pneumonectomy in our patients, 19% had a previous history of Mycobacterium tuberculosis infection, which did not prove to influence neither post-operative morbidity nor mortality.

Right-sided pneumonectomies seem to be inherently associated with higher post-operative risks in other studies, attributable to the increased tension in the right ventricle resulting from delivering the whole cardiac output to the smaller left lung.^{13,25} Accordingly, we have found in our study that all post-operative deaths occurred in right sided pneumonectomies. Regarding complications in the remaining patients, only the development of Acute Respiratory Distress Syndrome (ARDS) occurred predominantly in right sided pneumonectomies, probably due to acute stress to an unprepared right ventricle ($p < 0.05$).

In the report from Shapiro using the STS Database⁹, male sex showed to impact the risk of post-operative events. In our study, we have also found both a higher mortality rate and a higher incidence of early complications, such as

haemorrhage and surgical site infection. The reason for that remains to be understood, although the higher number of male patients in our study may be a confounding factor in the extraction of conclusions.

There was a high prevalence of smokers in our population, with an overall mortality of 35.7%. Smoking showed to increase the incidence of early post-operative complications and was associated with longer in-hospital length of stay, findings in strict correlation with one another, since complications inherently augment the mean in-hospital time.

In those with a lung malignancy, neoadjuvant chemotherapy has been reported to increase the risk of both morbidity and mortality after surgery.²⁰ In our study neoadjuvant therapy did not prove to influence early post-operative mortality but did influence 10-year mortality rate in multivariate analysis, probably due to long-term systemic effects of chemotherapy treatments.²⁵

Early complications occurred in 35% of patients. The most frequent early complication was atrial fibrillation, which occurred in 20.6% of patients, an incidence concordant with the 11-28% frequency interval reported by Foroulis et al.³⁰ Although atrial fibrillation is even more common in pneumonectomies involving pericardial dissection, due to atrial irritation,²⁰ this did not seem to occur in our study, probably showing that our results underestimate the real incidence of arrhythmic events.

Bronchopleural fistula development is one of the most feared complications of pneumonectomy. In our study, we found a frequency of 9.5% of late bronchopleural fistulas, causing overwhelming morbidity in patients. All patients had a history of tobacco abuse which probably contributed to fistula development. Most studies have proposed right pneumonectomies as a risk factor for fistula development,^{10,14} although, our findings did not corroborate this statement. Nineteen patients were submitted to bronchial stump reinforcement either with intercostal muscle or U-sutures, although, this did not seem to influence the incidence of bronchopleural fistula.

One of the biggest limitations in our study is the short sample size and the high heterogeneity of our population. Although, we found this study to be relevant, since pneumonectomies are high risk procedures and risk factors are still contradictory and not well defined. We believe this surgery must be attempted whenever it is believed to be the treatment approach offering the longest survival expectancy with acceptable morbidity for each patient, as so, patients must be thoroughly studied, and indications should be individually defined. More studies evaluating the impact of cardiopulmonary status variables on outcome are in need.

CONCLUSIONS

Pneumonectomy is a safe and viable option for cases in which lung tumours are not accessible through less invasive resections and the patient is considered fit for surgery.

The procedure is safe in elders. Gender and diagnostic group do not seem to influence adverse event's risk after

a pneumonectomy, although benign disease might increase post-surgical adverse outcome risk. Right sided pneumonectomies may be associated with higher mortality rates. Tobacco seems to increase the risk of both early and late complications. Smoking cessation should be encouraged in all cases. Patients considered candidates for pneumonectomy should be carefully selected, accounting for their previous medical history and cardiopulmonary risk factors.

REFERENCES

- Deslauriers, J., et al., Long-term physiological consequences of pneumonectomy. *Semin Thorac Cardiovasc Surg*, 2011. 23(3): p. 196-202.
- Bryant, A.S., R.J. Cerfolio, and D.J. Minnich, Survival and quality of life at least 1 year after pneumonectomy. *J Thorac Cardiovasc Surg*, 2012. 144(5): p. 1139-43.
- James TW, F.L., Indications for pneumonectomy. *Pneumonectomy for malignant disease. Ann Thorac Surg*, 2011. (92): p. 244-50
- Mitsudomi, T., et al., Postoperative complications after pneumonectomy for treatment of lung cancer: multivariate analysis. *J Surg Oncol*, 1996. 61(3): p. 218-22.
- Llewellyn-Bennett, R., R. Wotton, and D. West, Prophylactic flap coverage and the incidence of bronchopleural fistulae after pneumonectomy. *Interact Cardiovasc Thorac Surg*, 2013. 16(5): p. 681-5.
- Kalathiya, R.J., D. Davenport, and S.P. Saha, Long-term survival after pneumonectomy for non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*, 2013. 21(5): p. 574-81.
- Rivera, C., et al., Pneumonectomy for benign disease: indications and postoperative outcomes, a nationwide study. *Eur J Cardiothorac Surg*, 2015. 48(3): p. 435-40; discussion 440.
- Kang, M.W., et al., Surgical treatment for multidrug-resistant and extensive drug-resistant tuberculosis. *Ann Thorac Surg*, 2010. 89(5): p. 1597-602.
- Shapiro, M., et al., Predictors of major morbidity and mortality after pneumonectomy utilizing the Society for Thoracic Surgeons General Thoracic Surgery Database. *Ann Thorac Surg*, 2010. 90(3): p. 927-34; discussion 934-5.
- Hu, X.F., et al., Risk factors for early postoperative complications after pneumonectomy for benign lung disease. *Ann Thorac Surg*, 2013. 95(6): p. 1899-904.
- Qadri, S.S., et al., Short- and long-term outcomes of pneumonectomy in a tertiary center. *Asian Cardiovasc Thorac Ann*, 2016. 24(3): p. 250-6.
- Leo, F., et al., The risk of pneumonectomy over the age of 70. A case-control study. *Eur J Cardiothorac Surg*, 2007. 31(5): p. 780-2.
- van Meerbeeck, J.P., R.A.M. Damhuis, and M.L. Vos de Wael, High postoperative risk after pneumonectomy in elderly patients with right-sided lung cancer. *European Respiratory Journal*, 2002. 19(1): p. 141-145.
- Dyszkiewicz, W., K. Pawlak, and L. Gasiorowski, Early post-pneumonectomy complications in the elderly. *Eur J Cardiothorac Surg*, 2000. 17(3): p. 246-50.
- Swartz, D.E., et al., Perioperative mortality after pneumonectomy: analysis of risk factors and review of the literature. *Can J Surg*, 1997. 40(6): p. 437-44.
- Licker, M., et al., Risk factors for early mortality and major complications following pneumonectomy for non-small cell carcinoma of the lung. *Chest*, 2002. 121(6): p. 1890-7.
- Ludwig, C., et al., Comparison of morbidity, 30-day mortality, and long-term survival after pneumonectomy and sleeve lobectomy for non-small cell lung carcinoma. *Ann Thorac Surg*, 2005. 79(3): p. 968-73.
- Patel, R.L., E.R. Townsend, and S.W. Fountain, Elective pneumonectomy: factors associated with morbidity and operative mortality. *Ann Thorac Surg*, 1992. 54(1): p. 84-8.
- Algar, F.J., et al., Predicting pulmonary complications after pneumonectomy for lung cancer. *Eur J Cardiothorac Surg*, 2003. 23(2): p. 201-8.
- Annessi, V., et al., Is age over 70 years a risk factor for pneumonectomy? *Asian Cardiovasc Thorac Ann*, 2009. 17(3): p. 272-7.
- Pagni, S., et al., Pulmonary resection for malignancy in the elderly: is age still a risk factor? *Eur J Cardiothorac Surg*, 1998. 14(1): p. 40-4; discussion 44-5.
- Bolukbas, S., M.H. Eberlein, and J. Schirren, Pneumonectomy vs. sleeve resection for non-small cell lung carcinoma in the elderly: analysis of short-term and long-term results. *Thorac Cardiovasc Surg*, 2011. 59(3): p. 142-7.
- Dell'Amore, A., et al., Early and long-term results of pulmonary resection for non-small-cell lung cancer in patients over 75 years of age: a multi-institutional study. *Interact Cardiovasc Thorac Surg*, 2013. 16(3): p. 250-6.
- Ginsberg, R.J., et al., Modern thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg*, 1983. 86(5): p. 654-8.
- Fernandez, F.G., et al., Impact of laterality on early and late survival after pneumonectomy. *Ann Thorac Surg*, 2011. 92(1): p. 244-9.