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CLINICAL RESEARCH

Risk factors for postoperative pulmonary complications and prolonged hospital stay in pulmonary resection patients: a retrospective study

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Abstract
Background: Postoperative pulmonary complications are the main cause of morbidity and mortality after pulmonary resection. This study was undertaken to determine the risk factors associated with postoperative pulmonary complications (PPCs) and length of hospital stay (LOS) in pulmonary resection patients in a tertiary teaching hospital in Brazil.
Methods: A retrospective data gathering from 196 patients who underwent pulmonary resection between 2012 and 2016 was conducted. Demographic and hospital admission data were collected from patients with complete medical records. Univariate analysis was performed, followed by Poisson's regression for predicting the prevalence of postoperative pulmonary complications and length of hospital stay.
Results: Thirty-nine patients (20%) displayed pulmonary complications in the postoperative period. The risk factors associated with an increased prevalence of postoperative pulmonary complications in a multivariate analysis were: American Society of Anesthesiologists physical status (ASA) $\geq$ 3 (PR 4.77, $p = 0.03$, 95% CI: 1.17 to 19.46), predicted diffusion capacity of the lungs for carbon monoxide – corrected single breath (PR 0.98, $p < 0.001$, 95% CI: 0.96 to 0.99) and age of the patient (PR 1.04; $p = 0.01$; 95% CI: 1.01 to 1.06). Those associated with an increased prevalence of prolonged hospital stay were: duration of surgical procedure longer than five hours (PR 6.94, $p = 0.01$, 95% CI: 1.66 to 12.23), male sex (PR 5.72, $p < 0.001$, 95% CI: 1.87 to 9.58), and presence of postoperative pulmonary complications (PR 11.92, $p < 0.001$, 95% CI: 7.42 to 16.42).
Conclusions: The rate of postoperative pulmonary complications in the study population is in line with the world average. Recognizing risk factors for the development of PPCs may help optimize allocation resources and preventive efforts.

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Introduction

Despite advances in perioperative care, morbidity and mortality associated with pulmonary resection remain relatively high.[1] A review published in 2009 using the Society of Thoracic Surgeons (STS) database revealed a general rate of postoperative pulmonary complications (PPCs) of 13%.[2] The challenge during the preoperative evaluation is to identify which patients are at increased risk for these complications. The preoperative evaluation in patients submitted to this type of procedure is difficult due to the scarcity of knowledge on the risks related to these complications.[3] The study of PPCs is relatively recent when compared to perioperative cardiovascular complications.

Recommendations of European and North American societies of thoracic surgery are usually taken into account during preoperative evaluation of candidates for pulmonary resection.[1] Few risk scores have been adapted to stratify patients candidates for pulmonary resection,[4,5] other scores have been developed to stratify patients according to risk of complications or in-hospital mortality following pulmonary resection.[3,6–10] To the best of our knowledge, there seem to be only a few models capable of assessing the risk of PPCs in pulmonary resection patients.

This study aims to determine the risk factors related to the presence of PPCs and length of hospital stay (LOS) in a tertiary teaching hospital in Brazil.

Methods

Ethical approval for this study (Ethical Committee N° NAC 2.230.948) was provided by the Ethical Committee NAC of Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil (Chairperson Marcia Mocellin Raymundo) on 21 August 2017. The study was conducted retrospectively from January 2012 to December 2016. Informed consent was waived.

According to a previous prospective observational study,[11] we estimated the incidence of PPC of approximately 14,5%. It would be necessary to recruit at least 168 patients to complete the study analysis, considering an alpha level of 5% and an absolute error of 5%.[12]

This retrospective cross-sectional study was performed in a regional thoracic center on all consecutive patients who underwent thoracotomy and lung resection between January 2012 and December 2016. Data from 200 consecutive patient records were screened from the electronic medical charts database of the Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. One hundred and ninety six patients had complete data for statistical analysis. Patients were identified through a structured search using the Query system and the following keywords: segmentectomy, bullectomy, lobectomy, bilobectomy and pneumonectomy.

Data concerning in-hospital mortality (death within 30 days postoperatively or at the same hospital stay) and unplanned reoperation within the 30-day postoperative period were also collected.

The outcome is composed of eight clinically relevant PPCs (pneumonia, atelectasis requiring fibrobroncoscopic intervention, bronchospasm requiring pharmacological treatment for more than 24 hours, acute respiratory distress syndrome (ARDS), pleural effusion requiring surgical intervention, aspiration of gastric contents, hypoxemia and pneumothorax). Medical records were evaluated by three team members applying diagnostic criteria established in the literature for assessment of complications.[13–19] Diagnosis of hypoxemia was considered if patients presented with pulse oximetry (SpO_2) value less than 90% for more than 24 hours, along with the necessity of oxygen therapy. Patients whose charts did not contained laboratory or imaging data confirming the diagnosis on any of PPCs considered were excluded. All patients were prescribed postoperative physical therapy and were handled according to the local institutional pain management protocol. Patients in whom epidural catheter was used in the intraoperative period, but proved ineffective in controlling postoperative pain due to incorrect positioning were considered to have received general anesthesia alone. All pulmonary resection patients aged 16 years or older were included for analysis. Data were obtained manually with the aid of a structured questionnaire and inserted in an electronic spreadsheet (*Microsoft Excel 2013*). Statistical analysis was performed with Statistical Package for the Social Sciences for Windows, release 23 – 2015 (IBM SPSS Statistics, IBM Corp., Armonk, NY, EUA).

Patients who underwent pulmonary resection due to complications caused by non-bacterial active infection, such as pulmonary tuberculosis or aspergillosis, were considered as having non-pyogenic lung infection. All patients who were discharged from the hospital were followed up in an outpatient setting according to the routine of the thoracic surgery service.

The length of hospital stay was recorded on days, from date of hospitalization (or surgical appointment for patients hospitalized for other reasons) to the date of discharge (or death). Studies point out a great variability in the concept of LOS after pulmonary resection surgeries.[20] Prolonged LOS is dependent on factors related to the surgical procedure, characteristics of patients,[21] institutional protocols and development of perioperative complications.[22] Even in patients undergoing uncomplicated lobectomies, the variability of LOS is considerable. In this study, we considered prolonged hospital stay a period of hospitalization greater than 10 days.

In order to determine the risk factors associated with increased prevalence of PPCs (dependent variable, binary type) a univariate analysis was performed followed by multivariate analysis (Poisson's regression). The logistic regression model was constructed using a backward stepwise selection procedure in which the presence of a PPC and LOS were the dependent variables. Independent predictors were entered into the model on the basis of the bivariate analysis ($p < 0.05$) and correlation coefficients between variables lower than 0.4. Potential predictors were sequentially removed if this exclusion did not result in a significant change in the log-likelihood ratio test. The cutoff for variable removal was set at a significance level of 0.05. We then calculated the adjusted odds ratios and the corresponding 95% CI value. Some variables were reconfigured to meet the purpose of the multivariate analysis as follows: ASA (1–2 vs 3 vs 4), chronic obstructive pulmonary disease (absent vs mild vs moderate–severe), and surgical procedure time (0–2 hours vs 2–3 hours vs 3–4 hours vs. 4–5 hours vs more than 5 hours). Surgical technique was divided according to the procedure performed in: segmentectomy, lobectomy,

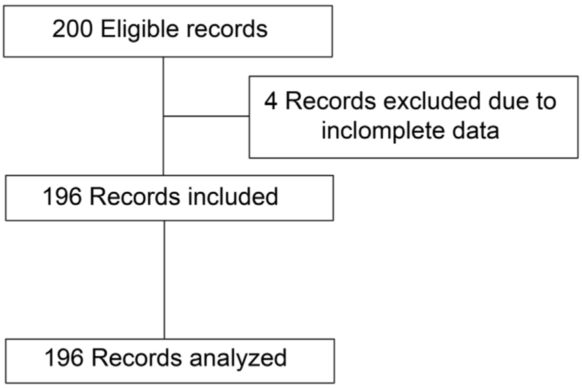

Figure 1 Recruitment flowchart.

bilobectomy and pneumonectomy. The variables postoperative predicted Diffusion Capacity of the Lungs for carbon monoxide – corrected single breath (ppoDL$_{co}$-cSB) and postoperative predicted Forced Expiratory Volume in the first second (ppoFEV$_1$) were calculated as previously published[26] and analyzed as continuous variables. Remaining data were analyzed as binary.

Results

Two hundred and fifty consecutive patients were identified through electronic research. One hundred ninety six different patients showed more than 95% complete data and were included in the statistical analysis, representing 196 elective surgical procedures (Fig. 1). Four patients (1%) had incomplete data and, therefore, were excluded from final analysis. Information on demographic and clinical variables is summarized on Table 1.

Thirty-nine patients displayed PPCs (20%), being pneumonia the most frequent complication (Table 2). Mean time of hospitalization was 10.06 ± 10.60 days; among patients, who developed some type of PPC, mean LOS was 23.5 ± 16.86 days. This study detected a mortality rate of five percent (10 patients). Eight patients (4%) died from postoperative pulmonary complications (six patients had pneumonia in the postoperative period, one patient presented lobar atelectasis, which was followed by pulmonary sepsis, and one presented with ARDS). One patient died from pulmonary thromboembolism and one from sepsis due to pulmonary empyema after lobectomy, followed by multiple organ dysfunction. None of patients presented with immunosuppression and none received chemotherapy in the perioperative period. Lobectomy was the most commonly performed procedure (50%), followed by segmentectomy (43.9%), bilobectomy (4.1%), and pneumonectomy (2%). None of patients underwent emergency surgery.

Factors related to the presence of PPCs in the univariate analysis are depicted on Table 3. The multivariate analysis using Poisson's distribution resulted in a model in which patients classified as ASA score ≥ 3 had almost five fold higher prevalence of pulmonary complications when compared to those with ASA score ≤ 2 (PR = 4.77, p = 0.03, 95% CI: 1.17–19.46). Age was also independently related with PPCs, with a prevalence increase of 4% per year after 16 years of age. (PR = 1.04, p = 0.01, 95% CI: 1.01–1.06). The ppoDL$_{co}$-cSB showed an inverse correlation with the occurrence of PPCs (PR = 0.98, p < 0.001, 95% CI: 0.96–0.99). For each percentage point reduction of ppoDL$_{co}$-cSB from 100%, the prevalence of PPCs increased by 2% Table 4.

Table 1 Demographic and clinical characteristics.

Variable	Patients (%)	Patients with PPC (%)
Age		
< 55 years	61 (31.1)	4 (10.3)
55–65 years	56 (28.6)	8 (20.5)
≥ 65 years	79 (40.3)	27 (69.2)
Gender		
Male	97 (49.5)	22 (65.4)
Female	99 (50.5)	17 (43.6)
ASA		
ASA 1	3 (1.5)	0
ASA 2	70 (35.7)	4 (10.3)
ASA 3 or higher	122 (62.2)	35 (89.7)
COPD		
Absent	75 (38.3)	9 (23.1)
Mild	90 (45.9)	16 (41)
Moderate	21 (10.7)	7 (17.9)
Severe	10 (5.1)	7 (17.9)
Surgical technique		
Segmentectomy	86 (43.9)	10 (25.6)
Lobectomy	98 (50)	25 (64.1)
Bilobectomy	8 (4.1)	3 (7.7)
Pneumonectomy	4 (2.0)	1 (2.6)
FVC[a]	83.16 ± 17.97%	76.74 ± 20.12%
FEV$_1$[a]	78.71 ± 20.80%	66.79 ± 23.18%
DL$_{CO}$[a]	60.73 ± 18.91%	51.75 ± 15.10%

PCC, postoperative pulmonary complication; ASA, American Society of Anesthesiologists physical status; COPD, chronic obstructive pulmonary disease; VATS, video assisted thoracoscopic surgery; FVC, forced vital capacity; FEV$_1$, forced expiratory volume in the first second; DL$_{CO}$, diffusion capacity of the lung for carbon monoxide.

[a] Values for FVC, FEV$_1$ and DL$_{CO}$ are presented as mean ± standard deviation.

Table 2 Frequency of postoperative pulmonary complications.

Postoperative pulmonary complication	Number of patients (%)
Pneumonia	32 (82)
Atelectasis	10 (26)
Bronchospasm	5 (13)
Pneumothorax	1 (3)
Pleural effusion	4 (10)
Acute Respiratory Distress Syndrome	2 (5)
Gastric content aspiration	0 (0)
Hypoxemia	6 (15)
Total Number of Patients with one or more PPC	39 (20)
Death from PPC	8 (4)

PPC, postoperative pulmonary complication.

Table 3 Independent variables for postoperative pulmonary complications in 196 patients identified in the univariate analysis.

Variables entered into the Poisson's regression model	OR	*p*-value	95% CI (Wald)	
Age	1.04	< 0.001	1.02	1.07
Charlson Comorbidity Index	0.12	0.02	0.05	0.20
No. of pulmonary subsegments removed	1.05	0.02	1.01	1.10
$ppoDL_{CO}$-cSB	0.97	0.001	0.95	0.99
$ppoFEV_1$	0.89	0.002	0.82	0.96
ASA				
3 or higher	3.81	0.006	1.11	6.51
Smoking history				
> 21 packs-year	1.60	0.032	1.08	6.27
COPD				
Moderate–severe	3.76	< 0.001	1.82	7.77
Duration of surgical procedure				
> 5 hours	6.32	0.003	1.88	21.18
Non-pyogenic lung infection	3.97	< 0.001	2.17	6.94
Functional status (dependent-partially dependent)	4.74	< 0.001	3.00	7.48
Surgical technique*	2.26	0.015	1.17	4.39

$ppoDL_{CO}$, predicted postoperative diffusing capacity of lung for carbon monoxide; $ppoFEV_1$, predicted postoperative forced expiratory volume in the first second; ASA, American Society of Anesthesiologists physical status; COPD, chronic obstructive pulmonary disease. Surgical Technique*: for lobectomy. Bilobectomy or pneumonectomy procedures; CI, confidence interval.

Table 4 Independent predictors of risk for postoperative pulmonary complications identified in the multivariate analysis (Poisson's Regression Model).

	Prevalence ratio	*p*-value	95% CI (Wald)	
ASA 3 or higher	4.77	0.03	1.17	19.46
Age	1.04	0.01	1.01	1.06
$ppoDL_{CO}$-cSB	0.98	< 0.001	0.96	0.99

ASA, American Society of Anesthesiologists physical status; $ppoDL_{CO}$, predicted postoperative diffusing capacity of lung for carbon monoxide; CI, confidence interval.

Table 5 Independent variables for prolonged LOS in the 196 patients identified in the univariate analysis.

Variable	Odds Ratio	*p*-value	95% CI (Wald)	
BMI (kg m^{-2})	0.41	0.02	0.32	0.611
No. of pulmonary subsegments removed	0.40	< 0.001	0.12	0.67
Male sex	3.72	0.01	1.81	6.64
ASA-PS 3 or higher	3.82	< 0.001	1.12	6.52
COPD moderate-severe	5.9	0.01	1.59	10.21
Duration of surgical procedure > 5 hours	11.97	< 0.001	7.56	16.38
Non-pyogenic lung infection	19.20	< 0.001	11.69	26.71
Functional status (dependent–partially dependent)	14.96	< 0.001	9.77	20.11
Postoperative pulmonary complications	16.22	< 0.001	13.29	19.15
$ppoDL_{CO}$-cSB	0,88	0.29	0,78	0,98
$ppoFEV_1$	0.89	0.02	0.82	0.96

LOS, length of hospital stay; BMI, body mass index; ASA, American Society of Anesthesiologists physical status; $ppoDL_{CO}$, predicted postoperative diffusing capacity of lung for carbon monoxide; COPD, chronic obstructive pulmonary disease; $ppoFEV_1$, predicted postoperative forced expiratory volume in the first second; CI, confidence interval.

Table 6 Independent predictors of risk for prolonged los identified in the multivariate analysis (Poisson's Regression Model).

	Prevalence Ratio	*p*-value	95% CI (Wald)	
Male sex	5.72	< 0.001	1.87	9.58
Duration of Surgical Procedure > 5 hours	6.94	0.01	1.66	12.23
Postoperative Pulmonary Complications	11.92	< 0.001	7.42	16.42

LOS, Length of Hospital Stay; CI, Confidence Interval.

Factors related to the presence of LOS in the univariate analysis are depicted on Table 5. After multivariate analysis, only three variables showed correlation with an increased prevalence for prolonged LOS (Table 6). The presence of PPCs demonstrated greatest strength of association with prolonged LOS, with an increased prevalence ratio (PR = 11.92, $p < 0.001$, 95% CI: 7.42–16.42) when compared to patients with no PPCs. The variables male sex and surgical procedure time > 5 hours also showed a positive correlation with an increased prevalence ratio for longer LOS: (PR = 5.72, $p < 0.001$, 95% CI: 1.87–9.58) and (PR = 6.94, p = 0.01, 95% CI: 1.66–12.23), respectively.

Discussion

In our retrospective cross-sectional study, three variables (ASA, age and ppoDL$_{co}$-cSB) were shown to be independently related with an increased prevalence of PPCs and three variables with prolonged LOS (male sex, procedure time > 5 hours and the presence of postoperative pulmonary complications). In regard to the occurrence of PPCs, the American Society of Anesthesiologists (ASA) score was the most important predictor, followed by age and ppoDL$_{co}$-cSB.

When the ppoDL$_{co}$-cSB and ppoVEF$_1$ variables were analyzed together, only the former appears as independent predictor for PPCs, similar to the study performed by Amar et al.[24] According to Brunelli et al.,[25] the correlation between FEV$_1$ and DL$_{co}$ or ppoDL$_{co}$ is weak for predicting patients with or without postoperative complications and, even those patients who present a normal FEV$_1$ value should include a measurement of DL$_{co}$ in the perioperative evaluation. Although DL$_{co}$ alone is highly associated with PPCs, we chose to use ppoDL$_{co}$-cSB because it associates a measure of the extension of lung resection and preoperative lung function. None of the patients in our study received chemotherapy in the preoperative period. Therefore, the reduction in pulmonary diffusion capacity seems to be explained by lung disease or by the greater number of resected lung segments in the patients presenting PPCs.

Interestingly, despite its subjectivity, the ASA score in our study appears to be an independent predictor for PPCs. The same result was found by Falcoz et al.[3] in a prospective study involving 15,183 patients on mortality risk factors in pulmonary resection and in a study conducted by Canet et al.[26] involving 2,464 non-cardiac surgery patients.

The Charlson comorbidity index did not appear to be an independent predictor in this sample, as well as other scales, such as functional status and nonintentional preoperative weight loss. In a retrospective study, analyzing a database containing 493 patients undergoing lobectomy for lung cancer, Sanchez et al.[27] concluded that the Charlson comorbidity index, after multivariate analysis, showed to be an important predictor of risk for postoperative complications. A possible explanation for the difference presented between the study by Sanchez et al. and the current study is the fact that, when analyzed in conjunction with other collinear variables (ASA, functional status and preoperative weight loss), the predictability of the Charlson Comorbidity Index is impaired.

When compared to the younger population, elderly patients appear to present higher postoperative morbidity and mortality rates.[28] The current study corroborates this finding, since age appears to be a predictor of PPCs, even when other factors, such as associated comorbidities, are taken into account.[3,29]

We have demonstrated that the presence of postoperative pulmonary complications increased the prevalence for a longer LOS. In our study, 20% of patients presented some type of complication and in-hospital mortality was 4%. None of patients without pulmonary complications died. According to other studies, the percentage of pulmonary complications and mortality may vary depending on the definition used. Even so, some authors agree that pulmonary complications are as common, lethal and costly to the health system as cardiovascular complications.[15,24] The perioperative comorbidities presented by patients in our study did not influence the outcomes. The same happened with the anesthetic and surgical techniques used.

Length of hospital stay in patients undergoing pulmonary resection is quite variable and depends on several factors, such as: surgical factors, comorbidities presented by patients,[26] perioperative complications and different institutional protocols.[29] The study conducted by Freeman et al.[30] deserves to be mentioned. It identified a bimodal distribution in hospital readmissions. Those patients readmitted after an initial hospitalization period of 5 days, pleural effusion, pneumothorax and atelectasis were the main causes of readmission. Although described in several studies as PPCs, these complications may be associated with inadequate duration of postoperative pleural drainage.

Among patients readmitted after an initial hospitalization period of 16 days, several causes were identified, highlighting the development of pneumonia and the functional status. The relationship between prolonged LOS and the presence of PPCs has also been suggested by these authors.

In our study none of patients were readmitted and prolonged LOS (more than 10 days) were related to the presence of PPCs. male sex and duration of surgical procedure more than 5 hours.

It seems important to us to identify risk factors related to prolonged LOS and to adopt care protocols, in order to reduce the time of intention and the rate of readmissions.

Although the sample size was adequate and data were collected with support of a structured questionnaire, containing the *a priori* definitions of outcomes and reducing the chance of subjective evaluations, this study has an exploratory character. Therefore, we believe that a prospective, randomized and larger study, including multiple centers and different populations, is necessary for a better understanding of the risk factors involved in the genesis of PPCs after pulmonary resection. It seems to be adequate to follow the steps of Canet et al.,[26] using a large randomized sample divided into an assembly cohort and a validation cohort, in order to build a more comprehensive risk score.

Conclusions

We believe that data summarized here contributes to further understanding the genesis of postoperative pulmonary complications, especially considering the lack of information regarding pulmonary resection in patients outside the oncological scope. The present study findings appear to be in agreement with the results of previous literature. Further studies addressing the incidence of postoperative pulmonary complications following pulmonary resection surgery are warranted and should include a larger sample size, multicentric database, a prospective design, as well as contain information on mechanical ventilation parameters, the amount of fluid and blood products used and consider the intensity of postoperative physiotherapy treatment.

Conflicts of interest

The authors declare no conflicts of interest.

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