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Identification of Risk Factors in Post Operative Morbidity and Mortality After Pulmonary Resections

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ABSTRACT

OBJECTIVE: *To identify preoperative and intraoperative risks factors for postoperative complications developed in lung resection surgery.* ***METHODS:*** *During 12 months from jan 2015 to dec 2015; 100 patients underwent pulmonary resection and were enrolled to the study. After a clinical interview, patients were evaluated by laboratory, pulmonary function tests and radiography, submitted to a surgical procedure, and were followed during their stay in the ICU and hospital, evaluating postoperatory complications and death.* ***RESULTS:*** *The postoperative rate of complications was 30%: respiratory (16%), infectious (10%), and cardiovascular (4%). Respiratory complications were related to smoking ($p < 0.01$, RR 2.31), airway obstruction by spirometry ($p = 0.01$, RR 2.60), presence of anemia ($p < 0.01$, RR 2.13), and prolonged protrombine time [PT] ($p = 0.03$, RR 1.77). Infection complications were related to smoking ($p < 0.01$, RR 2.69), airway obstruction by spirometry ($p = 0.01$, RR 3.31), presence of anemia ($p < 0.01$, RR 2.10), and prolonged PT ($p = 0.03$, RR 2.29). Cardiovascular problems were related with older age ($p < 0.01$, RR 2.66), cigarette smoking ($p < 0.01$, RR 4.55), and hypoxemia ($p = 0.03$, RR 2.43). The postoperative mortality rate was 7.1%.* ***CONCLUSION:*** *A preoperative evaluation can provide a suitable and safe postoperative prediction of complications in patients submitted to lung resection. Patients with COPD, hypoxemic, older, and anemic patients must be classified as high-risk for developing these complications.*

KEYWORDS : Thoracic surgery; preoperative care; risk factors; prognosis hospital mortality.

Introduction

Benefits of pulmonary surgical treatment are well-established. Life expectation of patients with non-small cell lung cancer is increased to 48 months, compared to 17 months of survival of patients submitted only to medical treatment[1]. Furthermore, surgery for bronchiectasis increases the quality of life[2] and survival of these patients[3]. However, postoperative complications are a significant cause of morbidity and mortality in patients submitted to thoracic or abdominal surgeries[4].

Managing of these patients requires an understanding of the predictable changes in pulmonary physiology occurring with surgery and anesthesia as well as a knowledge of factors associated with development of postsurgical complications. The surgical procedure causes reduction of lung capacity (represented by forced vital capacity [FVC] and forced expiratory volume in one second [FEV_1]) diaphragm dysfunction, impairs gas exchange, and cough and mucociliary clearance leading to development of microatelectasis and postoperative hypoxemia[4,5]. These modifications are exacerbated in chronic obstructive pulmonary disease [COPD][6,7], as well as in older patients[8], survivors of recent myocardial infarction[9], in starvation[10] and smoking patients[11].

The patients submitted to pulmonary resection procedures developed severe and frequent postoperative complications, so these patients frequently are submitted to the preoperative risk evaluation[12]. Advances in surgical and anesthetic techniques, combined with a detailed preoperative and sophisticated perioperative assessment, have contributed to an increasing number of adults undergoing these procedures[12-14].

The objective of this study was to identify preoperative, and transoperative risks factors for developed postoperative complications in lung resection surgery.

Methods

Patient management

All patients submitted to lung surgery at V.S.G.H.and pts. Were followed over a 12 month period were prospectively studied. All subjects enrolled underwent elective lung resection surgeries (lobectomy and pneumonectomy) with or without chest wall resection due to cancer, abscesses, or bronchiectasies. Exclusion criteria were: < 18 years of age, palliative resection, lung transplantation, thoracic trauma, thoracic surgery with no lung resection, thoracoscopy or thoracotomy for lung nodule biopsy, tracheostomy, emergency surgery, and informed consent declined

The preoperative evaluation included a complete history, physical examination, blood cell count, biochemical profile, chest film, 12-lead ECG, and pulmonary function tests... Transthoracic echocardiography, thallium-dipyridamole myocardial scintigraphy, or coronary angiogram were performed in patients with risk factors for coronary artery disease [CAD] and in those patients with low functional capacity, according to guidelines published by the American College of Physicians [ACP][15,16]. Preoperatively, as routine a thoracic epidural catheter was inserted, except for patients who refused placement of the catheter, patients with coagulation disorders, acute neurologic problems, local or systemic infections, or technical failures (i.e., catheter malpositioning or malfunction). Prophylactic antibiotic therapy (i.e., cefuroxime, 1.5 g every 8 h for 24 h) was administered routinely. All patients were operated by one of four specialized surgeons in thoracic surgeries and were managed by the same team of anesthesiologists and chest critical care physicians.

After surgery, patients were monitored for at least 48 h in the postanesthesia care unit or intensive care unit [ICU] to provide intensive nursing and respiratory care with emphasis on pain control, diaphragmatic breathing, aggressive pulmonary toilet by aggressive postoperative physical therapy, as well as early mobilization, ambulation, and feeding. Intravenous [IV] fluid infusion was limited to compensate for volume of blood loss with 0.9% saline solution and to replace evaporation loss with 5% glucose in saline solution at a rate of 1 mL/kg/h. Postoperative pain was assessed at rest and during coughing with a visual analog scale. The analgesic regimen was titrated to keep the visual analog scale at < 4/10 using either IV (nonsteroidal anti-inflammatory drugs) or epidural catheter (ropivacaine infusion) from 2 to 4 days.

Data collection and extraction

The preoperative data registered during standard interview and physical exam included: age, gender, smoking history (positive when smoking more than 20 pack years), presence of concomitant diseases (diabetes, cardiovascular, renal, and pulmonary disease). Other preoperative data registered were: arterial blood gases on air, blood cell count, biochemical profile, pulmonary function test [PFT](FEV1 and FVC as percentage of predicted), 12-lead ECG, type of malignancy, and informed consent. Diagnosis of chronic obstrutive pulmonary disease [COPD] was based on a history of myocardial infarction or angina, or typical Q waves seen on the ECG. Elevated blood pressure, arrhythmias, and diabetes mellitus requiring medication were considered significant comorbidities. Peripheral artery disease was defined

by clinical evidence (i.e., claudication at exercise and past or current vascular surgery) or arteriography. Diagnosis of COPD was based on criteria of the American Thoracic Society [ATS] and on results of pulmonary functional tests (i.e., FEV1/FVC, $\leq$ 70% of predicted value)17. Specific cutoff points were selected to define risk factors: (a) advanced age: $\geq$ 65 years; (b) moderate to severe COPD: FVC or FEV1 $\leq$ 60% of the predicted; (c) hypoxemia in room air: PaO2 $\leq$ 60 mmHg; (d) hypercapnia: PaCO2 $\geq$ 45 mmHg; (e) lymphocytopenia: lymphocyte count < 1500/μL; (f) increased hemorrhage risk: prothrombin time [PT] > 13 sec; and (g) anemia: hemoglobin $\leq$ 10 g/dL.

Intraoperative risk factors studied were perioperative estimated blood loss (3 or more packed red blood cells requirement), and occurrence of a hemodynamic instability defined as need for IV vasopressor or IV vasodilator during procedure. Patients were followed during ICU and hospital stay to evaluate postoperative complications and mortality. Complications were grouped as (a) respiratory: atelectasis, endotracheal reintubation, mechanical ventilation requirement > 24 h, and pleural air leak for more than 7 days; (b) cardiovascular: arrhythmias, hemodynamic instability with need for inotropic or vasodilators and coronary acute syndrome; (c) infectious: pneumonia (defined as new and persistent lung infiltrates at chest film, axillary temperature > 38.5ºC, and macroscopically proven purulent tracheal secretions), wound infection and pleural empyema; (d) metabolic: hyperglycemia (need of continuous insulin), eletrolite disturbances, and acute renal insufficiency (need of dyalisis); and (e) prognosis (survival or death). Severe postoperative complications were considered: endotracheal reintubation, hemodynamic instability with need for inotropic or vasodilators, coronary acute syndrome, pneumonia, pleural empyema, acute renal insufficiency, and death. Each patient could have one or more complications therefore, the number of complications was greater than the number of patients. Operative mortality was defined as death until 30th day after procedure.

Data were classified as preoperative, and intraoperative, risk factors and as postoperative complications.

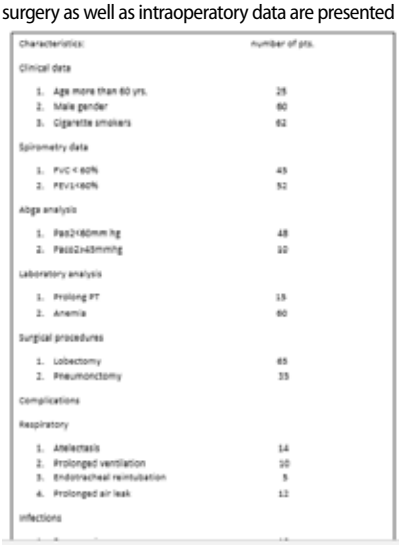
Statistical analysis

Data were analyzed using statistical software and Univariate analysis was carried out using the χ^2 test or Fisher's Exact Test for categorical variables and the Wilcoxon or Kruskal-Wallis test for continuous variables. Multivariate analysis (multiple logistic regression) was used to determine the relative risk (RR) and odds ratio (OR) and their 95% confidence intervals (95%CI) in variables with a p value <0.05 in univariate analysis for postoperative complications and death. All tests were two sided, and p values of < 0.05 were considered statistically significant.

Results

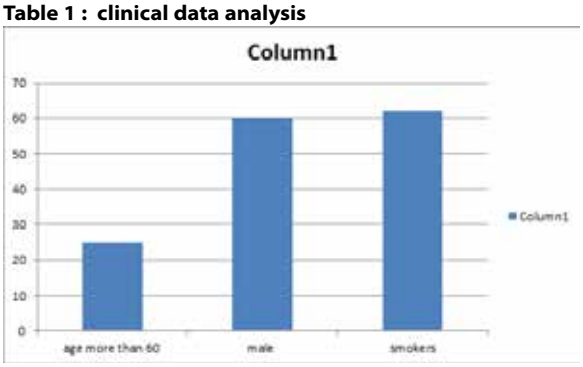
Study population

During the 12 months reference period, 380 thoracic surgeries were performed, and 100 patients were prospectively enrolled, and submitted to elective lung resection surgery (lung lobectomy and pneumonectomy). 65% were male, mean age of 48+-2 years, and 62 pts. smokers (mean cigarette consumption was 30 pack years). More men than women were smoking (52 and 10, respectively). Lung cancer was present in 20% of the cases. Preoperative clinical characteristics of patients, laboratory data and type of surgery as well as intraoperatory data are presented in Table 1.



Characteristics:	number of pts.
Clinical data	
1. Age more than 60 yrs.	28
2. Male gender	60
3. Cigarette smokers	62
Spirometry data	
1. FVC < 60%	45
2. FEV1<60%	52
Abga analysis	
1. Pao2<60mm hg	48
2. Paco2>45mmhg	10
Laboratory analysis	
1. Prolong PT	15
2. Anemia	60
Surgical procedures	
1. Lobectomy	65
2. Pneumonctomy	35
Complications	
Respiratory	
1. Atelectasis	14
2. Prolonged ventilation	10
3. Endotracheal reintubation	5
4. Prolonged air leak	12
Infections	

Table 1 : clinical data analysis



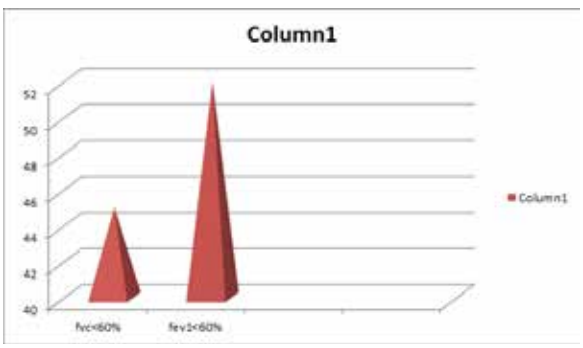
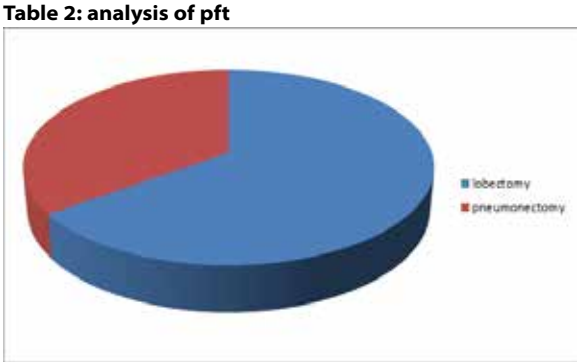


Table 2: analysis of pft



Analysis of surgical procedures

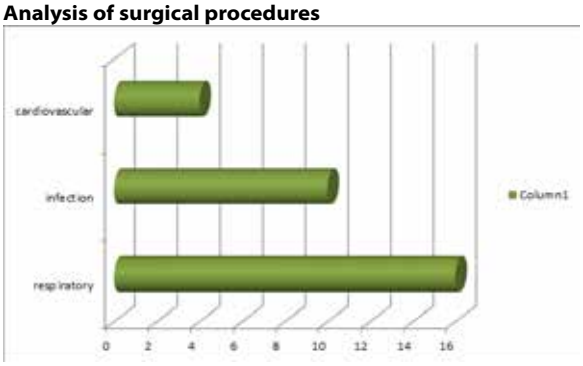


Chart showing analysis of complications

Postoperative complications

Postoperative complications are presented in Table 1. The postoperative rate of complications was 30%: respiratory (16%), infectious (10%), cardiovascular (4%). The mortality rate was 12%, and mostly due to sepsis following pneumonia or pleural empyema .

Respiratory postoperative complications were related with smoking (p < 0.01, RR 2.31 [95% CI 1.92 - 2.95]), airway obstruction in spirometry (p = 0.01, RR 2.6 [95% CI 1.8 - 3.1]), presence of anemia (p < 0.01, RR 2.13 [95% CI 1.12 - 3.92]), and prolonged PT (p = 0.03, RR 1.77

[95% CI 0.94 - 4.16]). Delay in extubation was the only respiratory complication that correlated individually with the cigarette smoking risk factor (p = 0.02, RR 2.76 [95%CI 1.53 - 3.38]). Table 2 shows the relationship between postoperative complications and preoperative characteristics, type of surgery, and intraoperative data.

Infectious postoperative complications were related with smoking (p < 0.01, RR 2.69 [95% CI 1.28 - 3.54]), airway obstruction in spirometry (p = 0.01, RR 3.31 [95% CI 2.56 - 3.85]), presence of anemia (p < 0.01, RR 2.10 [95% CI 1.25 - 3.12]), and prolonged PT (p = 0.03, RR 2.29 [95% CI 1.82 - 3.17). Pneumonia was the only infectious complication correlated with smoking (p < 0.01, RR 2.69 [95% CI 2.42 - 2.98]), airway obstruction in spirometry (p < 0.01, RR 3.31 [95% CI 2.96 - 3.77]), presence of anemia (p < 0.01, RR 2.12 [95% CI 1.37 - 3.75]), and prolonged PT (p < 0.01, RR 2.26 [95% CI 0.76 - 5.78]). Pre and intraoperative risk factors were unable to predict occurrence of wound infection or pleural empyema.

Cardiovascular problems were related with older age (p < 0.01, RR 2.66 [95% CI 2.21 - 2.96]), cigarette smoking (p < 0.01, RR 4.55 [95% CI 3.65 - 5.95]), and hypoxemia (p = 0.03, RR 2.43 [95% CI 1.02 - 3.68]).

Pneumonectomies did not present more postsurgical complications when compared with lobectomies. When evaluating arterial blood gases, hypercapnia did not relate with complications. Detailed analysis of preoperative ECG did not predict risk of surgical complications. It is important to remember that patients could have one or more postsurgical complications.

Postoperative mortality

Smoking (p = 0.01, RR 3.76 [95% CI 2.54 - 5.02]) and hypoxemia (p = 0.02, RR 3.56 [95% CI 3.08 - 3.97]) were the preoperative risk factors that increased patient postoperative mortality. Although requirement for intraoperative blood transfusion did no increase postoperative complications individually, it increased postoperative mortality (p = 0.01, RR 4.53 [95% CI 1.72 - 7.65]), as well as the need of pneumonectomy (p < 0.01, RR 2.31 [95% CI 1.22 - 4.19]).

Table 3 shows the increase of mortality due to finding of postsurgical complications.

Discussion

Thoracic surgeries are procedures associated with relatively high rates of postsurgical complications[18]. Incidence of pulmonary complications is uncertain, due to the variability of definitions used by different authors[19]. Although physicians involved in preoperative evaluations can base surgical risk assessment on extensive research, their ability to do so correctly is limited by methodological problems in literature such as poor standardization and definition of postoperative complications, inadequate blinding of observers, selection bias, limitation by study size, and reporting of non-clinical significant complications (e.g., microatelectasis) [20].

Patient-related risk factors

Age. Some authors consider advanced age as a risk factor for mortality and perioperative complications[8,21-24], others disagree with it[25-30]. Ergina et al.[31] demonstrated that older patients have more respiratory or cardiovascular complications, and Tisi et al.[7] suggested that it was due to the physiological effect of aging (reduction of the vital capacity, peakflow, elastic lung retraction, and increase of residual lung volume). Despite early suggestions of an increased risk of pulmonary complications with advanced age, this is not an independent risk factor for pulmonary complications. The healthy status of a patient, mainly cardiorespiratory seems to be much more important than age[26]. In our study, those older 65 years had no increase of postoperative mortality, and in agreement with Kroenke et al.[23], we observed an association with cardiovascular complications.

Smoking. The beneficial effects of smoking cessation, including improvement in ciliary and small airway function and a decrease in sputum production, occur gradually over several weeks. The risk is highest in patients who were smoking within the last 2 months, and patients who had quit smoking for more than 6 months, have a risk similar to those who do not smoke. Postoperative morbidity did not decrease in patients who had quit smoking for less than 4 weeks[32]. Our study showed increase of pulmonary and cardiovascular complications as well as increase of mortality rates.

Pulmonary function tests. Results of several retrospective studies of routine preoperative PFT disclosed only a marginal benefit in predicting postoperative complications in patients except in those undergoing lung resection. PFT could be used to identify high-risk patients for whom aggressive perioperative management is warranted. The ACP consensus statement[15,16,33] suggests the following indications for preoperative PFT: (a) patients undergoing cardiac or upper abdominal surgery with a history of smoking or dyspnea; (b) patients undergoing lower abdominal surgery if dyspnea or history of smoking indicates prolonged surgery; (c) patients undergoing orthopedic surgery with uncharacterized lung disease; (d) patients undergoing lung resection; (e) older than 60 years of age; (f) positive smoking history; (g) presence of pulmonary disease; and (h) presence of pulmonary symptoms. PFT results should not be the sole reason to change plans necessary for surgery.

PFT remain the standard screening tests performed before pulmonary resection. It is generally agreed that a minimum value of FEV_1 is required preoperatively (2 L before pneumonectomy and 1.5 L lobectomy, respectively) and that further cardiopulmonary testing is needed in patients with marginal lung function[34]. Variable cut-off values of FEV_1 (ranging from 35% to 80%) have been arbitrarily chosen to assess the severity of COPD and to predict the risk for pulmonary complications, but preoperative FEV_1 less than 60% is still a main predictor of perioperative mortality and respiratory morbidity[35].

COPD. Patients with severe COPD are 6 times more likely to have a major postoperative complication[35]. Elective surgery should be deferred in patients who are symptomatic, have poor exercise capacity, or have acute exacerbation. PFT results do not facilitate identification of the high-risk patients or of severity of dysfunction when risk of surgery is forbidding. Therefore, surgery should never be withheld based on PFT results[33]. Patients with severe COPD, classified as very high risk, may undergo surgery and will face a moderate risk of postoperative complications (29%)[23,35]. We use the Kroenke et al.[23] criteria and more than 40% of the patients presented with severe COPD based upon spirometric findings, and identifing an association between FEV_1 and respiratory, cardiovascular complications.

Arterial blood gases. A $PaCO_2$ of more than 45 mmHg often occurs in persons with severe COPD and indicates a high risk, although it is not necessarily prohibitive for surgery[7,36,37]. Hypoxemia is not a significant predictor of complications[36]. In our study, we verify that hypoxemia was associated with cardiac complications, principally occurrence of arrhythmias. We did not find an association between hypercapnia and prognosis, perhaps due to the small number of patients with this alteration.

Anemia. Anemia is present in 10% of patients admitted to general hospitals[38]. Hemoglobin values above of 10 g/dL do not significantly reduce oxygen transport and treatment is not required before surgery, and almost 45% of our patients had anemia, based in this criteria. Our data showed that anemic patients had more respiratory and infectious complications, probably due to nutritional deficiencies not identified during the preoperative evaluation.

Lymphocytopenia. This is a malnutrition marker just as albumin level, and malnutrition is a risk of morbidity and mortality in critical care and surgical patients[39,40]. Moreover, patients submitted to thoracic surgery, frequently have cancer and are smokers; predisposing factors to malnutrition. Busch et al.[41], in 106 patients submitted to lung surgery due to bronchogenic cancer, did not correlate lymphocytopenia with higher postoperative complications, in agreement with our study data.

Prothrombin time. High values of PT are a contraindication for surgical procedures, due to an increase of hemorrhagic complications[42]. Our data showed increased respiratory complications, which in our opinion is due to PT being a marker of hepatic synthesis capacity and not because of coagulation defects[43].

Intraoperative risk factors

Perioperative blood transfusion. Whitson et al.[44] showed that perioperative blood transfusion was associated with increased postoperative complications (53.5% vs. 30.5%, p < 0.001). In our study, blood transfusion was associated with an increased operative mortality (3.4% vs.

1.7%, p = 0.005) and length of stay after surgery (median 6 vs. 5 days, p < 0.001).

Postoperative complications

Keagy et al.[45,46] reported on 369 patients, 244 had postoperative complications during follow-up of 30 days, mainly cardiovascular (41%) and pulmonary (21%). Wahi et al.[28], in 197 pneumonectomies followed-up during 30 days, showed 23% of arrhythmias and prolonged MV in 9.1% of the cases. Ferguson et al.[47], evaluating 271 patients, showed postoperative complications in 52% of the cases; and Asamura et al.[48], in 267 patients submitted to thoracotomy, found 23.6% of arrhythmias. Our study found respiratory complications in 34.3% of the cases, and pneumonia in 29.7% of the cases.

Postoperative mortality

Some authors[34,45-47,49] described variables postoperative mortality rates (2.8% - 12.6%), and the higher mortality rates found in patients submitted to pneumonectomies (7.1% - 27.4%)[28,47,49]. Ginsberg et al.[50], reviewed 2,220 patients submitted to thoracotomies in North-American and Canadian reference hospitals, and showed mortality postsegmentectomies of 1.4%, after lobectomies of 2.9%, and after pneumonectomies of 6.7%. Our data demonstrated global mortality of 7.1%, and pneumonectomy mortality of 19.4%.

Strengths and limitations: We believe that the strengths of this paper are: (a) large sample; (b) research developed in a hospital specialized in respiratory diseases; and (c) follow-up of all patients studied. We are mindful of several limitations related to: (a) design of the study (cohort study); (b) no evaluation of preoperative creatinine values (despite all patients have values lower than 1.5 mg/dL); (c) single center report; (d) no evaluation of intraoperative data (e.g. duration of the surgery or anesthesia, and intraoperative fluid balance); and (e) no evaluation of stairs climbing test in patients with preoperative $VEF_1 < 2\ L$[51].

Conclusion

In an era of progressive cost containment and public scrutiny, the wisdom of aggressive preoperative evaluations for all surgical candidates have been questioned. Current data quantify the risks and morbidities associated with the care of seriously ill patients with coronary artery disease and demonstrate the need for professional and public discussions focusing on the association of a high preoperative risk status and the consumption of resources. A concise and standarized preoperative evaluation can provide a suitable and safe postoperative prediction of complications in patients submitted to lung resection, and patients with COPD, hypoxemic, older, anemic patients, and need of pneumonectomy must be classified as high-risk for develop postoperative complications.

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