Prognostic factors for complications following pulmonary resection: pre-albumin analysis, time on mechanical ventilation, and other factors*

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ABSTRACT

Objective: To determine whether pre-operative nutritional status and post-operative time on mechanical ventilation, as well as others factors, are correlated with post-operative complications (general or pulmonary) in patients undergoing elective thoracic surgery. Methods: A prospective study was conducted, involving 71 patients undergoing elective pulmonary resection. The data collected pre-operatively included gender, age, smoking status, pre-albumin level, lymphocyte count, and body mass index. The peri-operative data included type of surgery and surgical time, as well as post-operative time on mechanical ventilation. Results: Post-operative complications were found to correlate with low pre-albumin concentration, type of resection, surgical time, and post-operative time on mechanical ventilation. Surgical time and post-operative time on mechanical ventilation were also implicated in the post-operative pulmonary complications observed in 22 (30.99%) of the patients studied. Conclusion: Our results suggest that pre-albumin concentration, type of surgery and surgical time, as well as post-operative time on mechanical ventilation, serve as predictive indices of post-operative complications in patients undergoing elective pulmonary resection. In the analysis of the post-operative pulmonary complications, statistically significant correlations were found between such complications and increases in surgical time or post-operative time on mechanical ventilation.

Keywords: Thoracic surgery; Postoperative complications; Mechanical ventilation; Nutritional status; Prealbumin

INTRODUCTION

When a patient is submitted to surgery under general anesthesia, there is a certain impact on pulmonary function, even if the surgery is extrathoracic. This impact is undoubtedly greater in thoracic surgery, which can lead to significant post-operative complications (POCs).[1]

A prolonged anesthesia period, the location of the incision, hypercapnia, severe dyspnea and advanced age accompanied by a long history of cardiopulmonary illness are also considered risk factors for post-operative pulmonary complications (POPCs),[2] as are smoking, obesity and abnormal blood gas/spirometry values.[3] Awareness of patient nutritional status is crucial to the post-operative assessment since malnutrition implies greater intra-operative and post-operative risks.[4] General body measurements, such as weight and height, are easily assessed and can provide valuable information regarding nutritional status.[4] There also seems to be a correlation between visceral protein deficiencies and morbidity.[5] Laboratory testing for nutritional status variables,[5] using methods such as determining the pre-albumin levels and performing lymphocyte counts, can also be important.

Studies have shown that mechanical ventilation (MV) and surgical time influence POCs. To maintain respiratory function during surgical interventions, MV is extensively used during, and in some cases after, anesthesia. However, prolonged use of MV can lead to POCs. Despite being considered a support method, MV can either reduce or aggravate pulmonary injury. High peak inspiratory pressure values result in pulmonary edema, alveolar destruction, surfactant dysfunction and death.[6] It is estimated that POPCs account for 24% of all deaths occurring within the fist six post-operative days.[7] Conceptually, POPCs are defined as pulmonary abnormalities that occur during the post-operative period and produce an identifiable disease or clinically significant dysfunctions that unfavorably affect the clinical evolution.[8] The predominant POPCs are atelectasis and pneumonia.[9-10] In addition, the patient might present acute respiratory failure, acute respiratory distress syndrome, pulmonary embolism or bronchopleural fistula.

The objective of this study was to assess nutritional indices such as pre-albumin levels and lymphocyte counts, as well as surgical time and time on MV, in order to characterize the influence of these factors on post-operative morbidity.

METHODS

A prospective cohort study was conducted from May of 2002 to October of 2003 in the Thoracic Surgery Department of the Campinas State University Hospital de Clínicas.

A total of 71 consecutive patients, of both genders, submitted to pulmonary resection met the inclusion criteria and comprised the study sample. During the data collection period, no modifications that might interfere with patient post-operative evolution were made to the basic intra-operative treatment protocols.

The following inclusion criteria were applied: undergoing elective pulmonary resection surgery (pneumonectomy, lobectomy, bilobectomy, segmentectomy or nodulectomy); being 18 years of age or older; and giving written informed consent.

Patients who died during the intra-operative period were excluded from the analysis.

The study design was approved by the Ethics Committee of the Campinas State University School of Medicine (Opinion no., 231/2002).

The following pre-operative data were gathered from patient medical charts: gender; age; working diagnosis; smoking status; pre-albumin values and lymphocyte counts (up to five days prior to surgery); body mass index (BMI); and correlated morbidities, such as diabetes mellitus, systemic arterial hypertension and alcoholism. All patients underwent anesthesia administered by the same team, using the same anesthetic methods and involving selective ventilation.

The following intra-operative data were collected: Type and time (in hours) of thoracic surgery; type of surgical incision; and complications, such as hemorrhage, hypotension or death.

The following post-operative data were collected: time on MV (in hours) from intubation to extubation in the operating room or in the intensive care unit; general POCs; and specific POCs. The specific POCs were further subdivided: POPCs (acute respiratory failure, atelectasis, pleural effusion, acute respiratory distress syndrome, pneumothorax and dyspnea); infectious POCs (pneumonia, tuberculosis and infectious nodules); and cardiovascular POCs (pulmonary thromboembolism, cor pulmonale and arrhythmias).

Prognostic factors for complications following pulmonary resection:
pre-albumin analysis, time on mechanical ventilation, and other factors

491

In order to describe the sample profile according to the many variables under study, descriptive statistical tables of the continuous variables were prepared, as were tables describing the frequency of the categorical variables. For the purposes of comparing POCs and POPCs in terms of categorical variables, the chi-square test or, when necessary, Fisher's exact test, was used. To compare POCs and POPCs in terms of continuous variables, the Mann-Whitney non-parametric test, which compares the observation posts, was used. In order to determine which factors influenced pulmonary complications, logistic regression was used via univariate analysis, together with stepwise multivariate analysis.(12-13) A significance level of 5% (i.e., p < 0.05) was adopted.

RESULTS

A total of 63 patients were diagnosed with pulmonary neoplasia, whereas 8 were diagnosed with pulmonary mycetoma. There were 44 males (61.97%). Ages ranged from 19 to 77 years of age, with a mean of 55.69 years. Of the 71 patients evaluated, 24 (33.8%) were smokers, 26 (36.62%) were nonsmokers, and 21 (29.58%) were former smokers.

The types of pulmonary resection were bilobectomy in 3 patients (4.23%), lobectomy in 35 (49.3%), nodulectomy in 13 (18.31%), pneumonectomy in 14 (19.72%) and segmentectomy in 6 (8.45%). lobectomia eTypes of surgery were grouped as follows: lobectomy and bilobectomy; nodulectomy plus segmentectomy; and pneumonectomy.

In the present study, there was no statistical significance for the occurrence of POCs or POPCs based on age or lymphocyte count.

A total of 28 patients (39.44%) presented POCs, whereas 22 (30.99%) presented POPCs.

The present study compared POCs and POPCs in terms of categorical variables (gender, smoking status

and type of surgery). Comparisons were also made in terms of general intra-operative complications, intra-operative respiratory complications and intra-operative hemodynamic complications. These variables (POCs and POPCs) were also compared with continuous variables (age, pre-albumin level, lymphocyte count, surgical time, time on MV and BMI).

In reference to time on MV, 63 patients were extubated in the operating room, and 6 were extubated in the intensive care unit. For 2 patients, it was not possible to determine the moment of extubation. The type of surgery was found to have statistical significance in the comparison among the POCs: pneumonectomy, lobectomy, bilobectomy, nodulectomy and segmentectomy (p = 0.01 for all). There were also statistically significant correlations for the following: POCs with surgical time (p = 0.004), POCs with time on MV (p = 0.01) and POCs with pre-albumin level (p = 0.009); POPCs with surgical time (p = 0.003); and POPCs with time on MV (p = 0.04). The remaining results (for gender, smoking status, BMI, intra-operative complications, intra-operative respiratory complications and intra-operative hemodynamic complications) were not statistically significant. Tables 1 and 2 show the most important results, whereas Tables 3 and 4 show the logistic regression for POCs and POPCs.

DISCUSSION

The majority of the studied patients underwent resection of the pulmonary parenchyma due to neoplasia. According to some authors,[14] lung cancer is the leading cause of death from cancer, for men and women, in the USA, despite the fact that surgical resection offers a better chance for cure in patients with non-small cell lung cancer.

The POPC incidence following thoracotomy

TABLE 1

Principle variables with statistical significance for post-operative complications

Variables	Surgical time (hours:minutes)	Time on MV (hours:minutes)	Pre-albumin (mg/dl)
Patients with POCs (n)	28	28	21
Mean	4:15 h	8:55 h	11,37 mg/dl
Patients without POCs (n)	38	38	27
Mean	3:30 h	4:52 h	15,86 mg/dl
p	0,004	0,01	0,009

POCs: Post-Operative Complications; MV: Mechanical Ventilation

TABLE 2

Principal variables of statistical significance for post-operative pulmonary complications

Variables	Surgical time (hours:minutes)	Time on MV (hours:minutes)
Patients with POPCs (n)	22	22
Mean	4:26 h	6:25 h
Patients without POPCs (n)	44	44
Mean	3:35 h	6:22 h
p	0,003	0,04

POPC: post-operative pulmonary complications; MV: mechanical ventilation

TABLE 3

Significant variables in the univariate analysis of post-operative complications and post-operative pulmonary complications

Post-operative complications			
Variable	95% CI	p	OR
Pre-albumin	(0.988-0.803)	0.0292	0.891
Type of surgery	(23.515-1.374)	0.0165	5.684
Surgical time	(2.967-1.160)	0.0099	1.855
Post-operative pulmonary complications			
Variable	95% CI	p	OR
Surgical time	(3.206-1.181)	0.009	01.946

95% CI: 95% confidence interval; OR: odds ratio

accompanied by pulmonary resection stands at approximately 30%. It has been reported that this occurs not only due to the removal of pulmonary tissue, but also as a result of an alteration in the nutritional status, as well as of alterations in the chest-wall mechanics, of the thoracotomy itself, of the anesthesia and of the MV.[15] The nutritional indices used herein were chosen due to their ease of application and low cost, as well as to the fact that they are considered satisfactory predictors of post-operative morbidity. This can be observed in the current study, in which POPCs occurred at a rate of 30.99%, compared with 39.44% for POCs.

The highest rate of respiratory complications was associated with longer surgical times. According to some authors,[16] the most common post-operative complication following operations lasting over four hours is pneumonia, regardless of which lung is affected.

Various other authors have confirmed that being over the age of 70 represents an independent risk factor for pulmonary resection.[17] In contrast, other authors[18] have arrived at the conclusion that, for malignant diseases in elderly patients, pulmonary resection is beneficial. Still other authors,[19] have stated that elderly patients presenting good general health status do not display an increased number of POCs and should therefore not be excluded from surgery exclusively on the grounds of age. In the present study, patient age was not predictive of POCs.

We also found that smoking status had no influence on POCs, although the literature shows

TABLE 4

Significant variables in the univariate analysis of post-operative complications and post-operative pulmonary complications

Post-operative complications						
Variable	95% CI	Estimate	EP	chi-square	p	OR
Pre-albumin	(0.680-0.949)	- 0.2194	0.0852	6.6381	0.0100	0.803
Lymphocytes	(1.014-2.059)	0.3681	0.1807	4.1486	0.0417	1.445
Surgical time	(1.163-5.348)	0.9138	0.3892	5.5120	0.0189	2.494
Post-operative pulmonary complications						
Variable	95% CI	Estimate	EP	chi-square	p	OR
Surgical time	(1.181-3.206)	0.6655	0.2549	6.8192	0.0090	1.946

95% CI: confidence interval; SE: standard error; OR: odds ratio

Prognostic factors for complications following pulmonary resection:
pre-albumin analysis, time on mechanical ventilation, and other factors

493

that smokers are at greater risk for developing POPCs.[20]

Our results show that there was a statistically significant correlation between pre-albumin alterations and POCs, as evidenced by the finding that 43.75% of the patients presenting POCs had low levels of pre-albumin. Such correlations have also been reported in the literature,[21] underscoring the importance of assessing pre-albumin levels. In addition, the literature demonstrates that pre-albumin is the first serum protein to be altered under acute malnutrition conditions and is the most sensitive in terms of returning to its normal level following nutritional supplementation. The objective of determining pre-albumin levels is to indirectly measure visceral protein mass. Pre-albumin presents quite a small body reserve and a short half-life (of approximately two days).[22] Therefore, one must be careful when interpreting its levels prior to confirming a diagnosis of protein-calorie malnutrition, since hepatic production of pre-albumin drops in response to systemic inflammation, such as that seen in trauma or sepsis, the end result being that serum pre-albumin levels fall rapidly.[21] Due to these characteristics, certain authors[23] consider this protein the best nutritional assessment parameter.

Various studies have demonstrated a relationship between POCs and low lymphocyte counts. In order to complement the assessment of patients with suspected protein-calorie malnutrition, one must determine serum proteins such as pre-albumin, further to assessing the number of lymphocytes.[21] In the present study, lymphocyte count was not sufficiently sensitive to predict POCs, a finding that contradicts those of the articles cited. However, pre-albumin level proved to be a nutritional index that is predictive of POCs, although not specifically predictive of POPCs.

Life expectancy is lower in obese patients, although surgical mortality rates are not higher.[24] However, obese patients are at greater risk for pulmonary complications.[24] Nevertheless, in the present study, BMI, which characterizes obesity, did not prove sufficiently sensitive to predict POPCs.

The type of surgery parameter was an effective predictor of POCs but not of POPCs. According to some authors,[17] the mortality rate among patients undergoing pneumonectomy is typically twice as high as that among those undergoing lobectomy.

In addition, segmentectomy or nodulectomy carry the lowest risks, and pneumonectomy carries the highest risk. Therefore, there is a clear relationship between the extent of resection and post-operative morbidity/mortality.[19]

A gamut of adverse effects and complications are associated with MV. These complications occur with great frequency and yet are not frequently reported in literature. The potential adverse effects include a decrease in the cardiac index, respiratory alkalosis, increased intracranial pressure and gastric distension. Complications that are exclusively respiratory, such as pneumothorax, bronchopleural fistula and nosocomial pneumonia, can arise. Complications can also result from inappropriate handling of the mechanical ventilator, such as the use of incorrect settings or not heating/humidifying the inspired air.[25]

In a retrospective analysis of the incidence of intra-operative and immediate POCs, 65 patients with pulmonary emphysema and submitted to lung transplant were evaluated. The conclusion that time on MV > 48 hours and post-operative hemorrhage were the variables that best indicated death during the immediate post-operative period.[26]

Some authors performed a retrospective study of 508 patients undergoing gastroduodenal surgery, with the purpose of investigating risk factors for POPCs. The conclusion was that the intra-operative/post-operative time on MV contributed to the development of these complications.[27]

In the current study, the intra-operative time on MV correlated significantly with POCs (28 patients; $p = 0.0198$), as well as with POPCs (22 patients; $p = 0.0491$). Although our results suggest that there is a relationship between time on MV and POCs, there is still a shortage of studies in the literature evaluating POCs in relation to time on MV in pulmonary resections. Therefore, more studies are needed to determine whether a longer intra-operative time on MV results in POCs.

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