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Complications After Major Pulmonary Resections for Lung Cancer: A Prospective Study

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Abstract

Aim-Background: The aim of this study was to evaluate the complications after major pulmonary resections for lung cancer and identify the risk factors associated with the occurrence of complications. We studied risk factors related to both clinical and laboratory characteristics of patients and those related to tumour stage, histology and type of surgery.

Methods: Between January 2011 and June 2012, 89 patients (mean age 64.4, ranging from 37 to 82 years) underwent major pulmonary resection at our institution for treatment of lung cancer. A univariate analysis was conducted to determine whether there were statistically significant group differences in the variables. Logistic regression analysis was performed to assess the impact of variables on the emergence of complications after the operation, including categorical and continuous variables.

Results: Complications occurred in 64% of patients, 79% of whom displayed complications that were not potentially life-threatening, 12.4% experienced a life-threatening complication, and 4.5% died. Intraoperative and postoperative bleeding, myocardial infarction, pulmonary embolism, bronchopleural fistula, adult respiratory distress syndrome, postoperative pneumonia and need for reoperation were among the complications that were considered as being potentially dangerous.

Conclusions: The preoperative haemoglobin levels and the need for transfusion are strongly associated with the occurrence of complications. Complications occurred in 75% of patients with chronic obstructive pulmonary disease, albeit these complications were not life-threatening. Diabetes mellitus is associated with critical complications. Prolonged hospitalization was observed primarily for persistent air leak, atelectasis, fever, and particularly after a right-sided procedure.

Key words: *Thoracotomy; lobectomy; pneumonectomy; complications; non-small cell lung cancer*

Introduction-aim

The basic aim of this study was to identify complications after major pulmonary resections for lung cancer and identify the risk factors associated with the occurrence of complications. We studied risk factors related to both clinical and laboratory characteristics of patients and those related to tumour stage, histology and type of surgery.

The secondary objective of the study was to identify the causes and risk factors that lead to prolonged hospitalization and hence a significant increase in healthcare costs, as well as to describe the characteristics of patients who either died or experienced serious complications such as adult respiratory distress syndrome (ARDS), bronchopleural fistula (BPF).

Complications tend to be classified according to when they occur: in the intraoperative or postoperative period. Early complications are conditions appearing in the immediate postoperative period within 30 days after thoracotomy [1]-[10]. For the purposes of this study, late complications are considered all events occurring beyond 30 days (Table 1).

Methods

Patients and preoperative assessment

From January 2011 to June 2012, 89 patients (19 females)

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Table 1. *Complications after major pulmonary resections for lung cancer. A bibliographic review*

1. Intraoperative complications
1.1. Vessel injury (pulmonary vein or branch of the pulmonary artery)
1.2. Cardiac complications (arrhythmias, myocardial ischaemia)
1.3. Contralateral pneumothorax
2. Early postoperative complications
2.1. Postoperative haemorrhage
2.2. Bronchovascular fistula
2.3. Cardiac Herniation
2.4. Tamponade
2.5. Arrhythmias
2.6. Cardiac failure
2.7. Myocardial ischaemia - Myocardial infarct
2.8. Deep venous thrombosis – Pulmonary embolism
2.9. Shunt Dx→Sx
2.10. Pneumonia
2.11. Post- pneumonectomy pulmonary oedema
2.12. Respiratory failure
2.13. Atelectasis
2.14. Lobar torsion
2.15. Lung infarct after angioplastic resection
2.16. Air leak
2.17. Emphysema subcutaneous
2.18. Residual pleural space
2.19. Pleural effusion
2.20. Chylothorax
2.21. Bronchopleural fistula
2.22. Empyema
2.23. Oesophageal injury – Oesophagopleural fistula
2.24. Wound infection
2.25. Wound dehiscence
2.26. Peripheral embolism from tumour emboli
2.27. Acute renal failure
2.28. Massive gastrointestinal bleeding
2.29. Stroke
2.30. Phrenic nerve injury
2.31. Recurrent laryngeal nerve injury
2.32. Spinal cord injury
2.33. Dura Madre injury
2.34. Fever
3. Late postoperative complications
3.1. Post-thoracotomy pain
3.2. Post-pneumonectomy syndrome
3.3. Late empyema
3.4. Intrathoracic haematoma
3.5. Mycetoma
4. Death

aged 37-82 years underwent major pulmonary resection (lobectomy, bilobectomy or pneumonectomy) for lung cancer at Sismanogleio General Hospital in Athens.

A preoperative diagnosis was made in 72 patients (80.9 %). Neoadjuvant chemotherapy was given in five cases for downstaging. Standard preoperative evaluation included a detailed clinical history and physical examination, chest radiography, fibre optic bronchoscopy, chest, upper abdomen and brain CT scanning. Twelve patients were submitted to bone scintigraphy with technetium 99 (^{99}Tc) due to clinical suspicion of bone metastasis, and eight underwent positron tomography (PET) in the context of investigating suspicious mediastinal lymphadenopathy[11]. No patient was subjected to invasive mediastinal exploration with cervical mediastinoscopy or anterior mediastinotomy. Transthoracic needle biopsy (TTNB) enabled diagnosis in 32 patients.

As part of the preoperative assessment, a fibre optic bronchoscopy was performed on all patients. Endobronchial biopsies and bronchial washings followed, with a daily collection of three sputum specimens for at least three days. Transbronchial needle biopsy (TBNA) confirmed a preoperative diagnosis in 14 patients.

All patients underwent spirometric pulmonary function tests. Pulmonary function tests were performed while the patient was at rest in a seated upright position. These tests consisted of spirometry using the Cosmed FX pony spirometer (Cosmed Srl, Rome, Italy). All respiratory function tests were performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines [12].

In 25 cases presenting low forced expiratory volume in the first second (FEV_1), in whom a major lung resection could increase morbidity or even be prohibitive, further testing was carried out to measure the diffusion capacity for carbon monoxide (DLCO). According to radiological and endoscopic findings, four of these patients seemed to be candidates for pneumonectomy, and were hence submitted to lung perfusion scintigraphy calculating the postoperative FEV_1. All patients were evaluated preoperatively by a cardiologist and underwent a complete electrocardiogram and echocardiogram.

A preoperative anaesthetic assessment of the patients was made. All patients were informed in detail of the type of surgery, possible alternatives, potential complications and risks, as well as the impact of the operation on the quality of life (work, hobbies, sport activities and social life). They were also informed about the possible need for supplementary treatments (chemotherapy or radiotherapy) based on intraoperative and histological findings.

Surgical treatment

All patients were operated on by the same surgical team.

The majority of patients (92%) underwent endotracheal intubation with a single lumen tube. Only seven patients were intubated with a double lumen endotracheal tube. All patients had two peripheral venous catheters and an arterial line for continuous intraoperative blood pressure monitoring. A central venous catheter was usually inserted only in candidates for pneumonectomy. Antibiotic intraoperative prophylaxis consisted of 1.5 gr cefuroxime administered intravenously, unless it was contraindicated.

All patients were operated on through a standard posterolateral thoracotomy. Intraoperative pathologic consultation was available. In the case of 17 patients who had no preoperative diagnosis (19.1%), the frozen section procedure led us to decide on the type of surgery. Hilar and mediastinal lymph nodes were systematically dissected according to the guidelines of the European Society of Thoracic Surgeons (ESTS)[13]. In all cases, we asked for the pathological determination of surgical margins.

The bronchial closure was performed manually with interrupted 4-0 sutures of polypropylene (Prolene, Ethicon, Sommerville,NJ) in 11 cases (11.4%), and with staplers (Ethicon, EndoSurgery, Inc. Cincinnati) in 78 patients (87.6%). Bronchoplastic techniques were performed in four cases. The bronchial stump was covered with autologous tissue in all cases of pneumonectomy. For this purpose, several tissues were used: mediastinal fat pad (n =4), parietal pleura (n =8), and azygos vein (n = 8). Extended resections were needed in 21 tumours involving the chest wall (4.5%), parietal pleura (13.4%), pericardium (4.5%), diaphragm (1.1%), and other mediastinal structures (5.6%). An intrapericardial pneumonectomy was required in four cases (4.5%), and two patients (2.2%) underwent a completion pneumonectomy. The histological distribution of the tumours was as follows (Table 2): adenocarcinoma (n = 38; 43%), squamous (n = 30; 33.5%), large cell (n = 9;10%), carcinoid (n = 4; 4.5%), and other (n = 8; 9%).

Table 2. *Demographic and clinical data*

Age (mean age/ range)	64.4/37-82
Gender (Male/Female)	70/19
Histology	
Adenocarcinomas	38
Squamous cell carcinoma	30
Large cell carcinoma	9
Adenosquamous cell carcinoma	3
Carcinoid tumour	4
Other	5
TNM staging	
T1aN0M0	6
T1bN0M0	11
T2aN0M0	19
T1aN1M0	4
T1bN1M0	2
T2aN1M0	7
T2bN0M0	6
T2bN1M0	2
T3N0M0	10
T1aN2M0	1
T1bN2M0	2
T2aN2M0	2
T2bN2M0	3
T3N1M0	2
T3N2M0	3
T4N0M0	3
T4N1M0	2
T4N2M0	1
T2aN0M1b	1
T3N2M1b	1
Surgical procedures	
Right upper lobectomy	18
Left upper lobectomy	16
Right upper and middle lobectomy	7
Left lower lobectomy	11
Right lower lobectomy	10
Middle lobectomy	4
Right lower and middle lobectomy	3
Left pneumonectomy	10
Right pneumonectomy	10

Staging

Patients were staged postoperatively according to the seventh edition of the TNM staging system. Postoperative staging was as follows: stage IA (n =17; 19.1%), stage IB(n = 19; 21.3%), stage IIA (n = 19; 21.3%), stage IIB (n =12; 13.5%), stage IIIA (n = 18; 20.3%), stage IIIB (n = 1; 1.1%), and stage IV (n = 3; 3.4%).

Postoperative management

Postoperatively, all patients, with the exception of four, were managed on the thoracic ward. Early extubation in the operating room was achieved in 85 patients (95%). Only four patients required prolonged mechanical ventilation and were admitted to the intensive care unit (ICU). Postoperative

chest pain was treated with epidural analgesia in 26 cases (29%). Thirty-one patients (35%) had a PCA intravenous pump, and an extrapleural special catheter for continuous infusion of ropivacaine 7% solution was inserted in eight patients (9%). Twenty-four patients (27%) needed no kind of pain control device, and were simply treated with IM administration of pethidine plus 1000mg of paracetamol intravenously.

Antibiotic (cefuroxime, 20mg/kg IV) and thromboembolic prophylaxis (tinzaparin, 175 Anti-Xa IU/Kg subcutaneous) were used routinely, and all patients during the postoperative period received an intensive programme of chest physiotherapy including deep breathing exercises and incentive spirometry.

For the first 48 postoperative hours, the patients were under continuous monitoring and vital signs (pulse rate, arterial blood pressure, oxygen saturation, temperature central venous pressure and urine output) were recorded. Data concerning the patient's course including physical examinations and roentgenograms were documented.

Data collection

A systematic literature search was performed between December 2012 and February 2013 to identify relevant reports. Studies and articles were identified using online searches of The U.S. National Library of Medicine via www.pubmed.com. Several searches were conducted to retrieve all potentially relevant articles. The following keywords were used to identify relevant case series, guidelines, and reviews: thoracotomy, lobectomy, pneumonectomy, complications, non-small cell lung cancer. Preoperative, intraoperative, and postoperative variables were recorded including general demographic data, Karnofsky index (KI), preoperative and postoperative packed cell volume (PCV) and haemoglobin (Hb), preoperative arterial blood gas levels, preoperative and predicted FEV_1 and FVC values, type of surgical procedure, histology, tumour stage, transfusions of packed red blood cells (RBC) and fresh frozen plasma (FFP), values of perioperative vital signs (temperature, arterial blood pressure, pulse rate, oxygen saturation), hospital stay, days in the ICU, patient comorbidity including coronary artery disease (CAD), arterial hypertension (AH), atrial fibrillation (AF), peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), chronic renal failure (CRF), diabetes mellitus (DM) and other malignancy, neoadjuvant chemotherapy or radiotherapy, postoperative pain assessment using a visual analogue scale and complications.

Statistical analysis

Descriptive statistics were used initially. Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as frequency (%). Univariate analysis was performed to determine whether there were statistically significant group differences in the variables. Continuous and categorical variables were compared between groups by analysis of independent samples t-test and chi-square analysis, respectively.

Logistic regression analysis was performed to assess the impact of variables on the presentation of side-effects after surgery, including categorical and continuous variables.

The risk of complications was evaluated by using a backward stepwise logistic regression analysis to estimate odds ratios (OR) and their 95% confidence intervals (CI). Those variables with p values less than 0.03 in the univariate analysis were included in the multivariate analysis. The final model included factors that remained significant with a p value less than 0.10. Goodness-of-fit was assessed by the Hosmer and Lemeshow test.

Statistical analysis was performed using Stata 9.1 for Windows (StataCorp LP, 4905 Lakeway Drive, College Station, Texas 77845-4512,USA).

Results

From 1 January 2011 to 30 June 2012, 89 patients, (19 women), aged from 37-82 years (mean age 64.4) underwent major pulmonary resection (lobectomy, bilobectomy or pneumonectomy) for lung cancer at Sismanogleio General Hospital in Athens. The majority of patients were male (78.6%), aged from 65-69 years. Fifty-nine patients underwent lobectomy, 10 bilobectomy and 20 pneumonectomy (Table 2). The decision on the type of procedure to be carried out was based on radiological and endoscopic findings in the context of preoperative staging, on operative findings and on the general condition of the patient. All patients had a Karnofsky index (KI) score of 90 - 100.

In total, 65.2% of patients were former or current smokers consuming > 15 py; 24.7% presented preoperative anaemia with haemoglobin levels below 12 g /dl; 28.1% had preoperative values of FEV_1 <2 L; 16.8% presented CAD; 38.2% had moderate to severe AH; 31.5% had a history of COPD; 15.7% had DM; 5.6% underwent neoadjuvant chemotherapy for downstaging. 28.1% were transfused. and 5.6% received more than four units of red packed cells.

At least one complication presented in 64% of the patients. 79% of which complications were not potentially life-threatening. Eleven patients (12.4%) experienced a critical complication and four patients (4.5%) died. Intraoperative haemorrhage, postoperative haemorrhage, acute myocardial infarct (MI), pulmonary embolism (PE), BPF, ARDS, postoperative pneumonia and the need for re-intervention were considered as potentially dangerous complications.

Complications not deemed as life-threatening included

postoperative atrial fibrillation, air leak, residual space, wound infection, atelectasis, fever, sinus tachycardia, urinary tract infection, phrenic or laryngeal nerve injury, and thrombophlebitis (Table 3).

Discussion

Advances in surgical and anaesthetic techniques and perioperative care have rendered anatomic lung resections a common and almost routine procedure, with consistent improvements in operative mortality. Despite the observed improvement in mortality, the morbidity rates associated with pulmonary resections have not changed significantly in the last 30 years [14]-[16]. Prospective studies have found complications to occur in 38% of patients following major lung resection, a frequency that has not significantly changed with time. Given that the occurrence of a major complication is a risk factor for mortality, the overall improvement in mortality suggests an improvement in the management of potentially life-threatening complications, which less frequently result in death [17].

Non-life-threatening complications are nevertheless important, as the development of complications is associated with both longer hospitalization and higher costs. The risk factors for mortality similarly apply to morbidity (Table 4). Morbidity risk factors also include active cigarette smoking, significant preoperative functional impairment as indicated by a low KI, the extent and duration of surgery, with pneumonectomy being associated with more complications than lobectomy [18],[19].

With a mortality rate of 3.4–11.2%, extrapleural pneumonectomy carries higher mortality than simple pneumonectomy [20]. Completion pneumonectomy also has higher mortality rates of 10–23% [21], as does right-sided pneumonectomy compared to left pneumonectomy [22]. This difference could be attributed to the right pneumonectomy bearing higher rates of major complications, including BPF, empyema, and post pneumonectomy pulmonary oedema (PPPO).

Several early reports identified high rates of surgical complications after neoadjuvant chemotherapy and radiation therapy. Right pneumonectomy seemed particularly

Table 3. *Complications after major pulmonary resections for lung cancer in our institution (Jan. 2011- Jun 2012)*

Complications	Number of patients (%)	(%)[a]
Fever [b]	36 (40.5)	25-50
Extended LOS [c]	22 (24.7)	
Atelectasis	12 (13.5)	3.6-8.9
Persisting air leak [d]	8 (8.9)	6.8-15.6
ICU hospitalization [e]	6 (6.7)	5-15
Transfusion [f]	5 (5.6)	
Post-thoracotomy pain	5 (5.6)	5
Postoperative haemorrhage	4 (4.5)	2.5-3.9
Bronchopleural fistula	3 (15)	0.5-5.1
Intraoperative haemorrhage	3 (3.4)	
Atrial fibrillation	3 (3.4)	18-34
Need for reoperation	3 (3.4)	1.5
ARDS [g]	3 (3.4)	2.8-7.9
Acute myocardial infarction	2 (2.5)	0.6-1.2
Postoperative pneumonia	2 (2.5)	2-11.7
Wound infection	2 (2.5)	
Urinary tract infection	2 (2.5)	
Pulmonary embolism	1 (1.1)	0.4-5.4
Residual pleural space	1 (1.1)	
Phrenic nerve injury	1 (1.1)	
Recurrent laryngeal nerve injury	1 (1.1)	
Chylothorax	1 (1.1)	0.3-0.74
Thrombophlebitis	1 (1.1)	
Thirty-day mortality after lobectomy	1 (1.4)	0-3.9
Thirty-day mortality after pneumonectomy	3 (15)	0-9.2

[a]Percentage of complications in published studies, [b]Body temperature > 38 °C, [c]Length of stay exceeding 14 days, [d]Air leak exceeding 7 days, [e]Admission in Intensive care unit, [f]Administration ≥ 4 units of packed red blood cells, [g] Adult respiratory distress syndrome

Table 4. *Risk factors for morbidity and mortality after major pulmonary resections for lung cancer*

Age over 60 years
Male gender
Malnutrition
Diabetes Mellitus
COPD [a]
FEV_1 <2 L for pneumonectomy and FEV_1 <1.5 L for lobectomy[b]
Coronary disease or other heart disease
Advanced
Peripheral vascular disease
Intraoperative hemorrhage
Transfusion exceeding 4 units of packed red blood cells
Perioperative crystalloid's overload

[a]Chronic obstructive pulmonary disease, [b]Forced expiratory volume in the first second

hazardous presenting an increased complication risk and mortality of 23.9%. However, recent reports have shown no significant difference in mortality or morbidity in patients receiving surgery alone versus neoadjuvant chemotherapy followed by surgery for NSCLC. Right pneumonectomy has also been shown to be relatively safe.

Many studies showed age to be an important risk factor for morbidity and mortality after lobectomy or pneumonectomy. Patients younger than 70 years had mortality 0.4-4.1%, significantly lower compared with that in those aged over 70 years (2.0-7.1%)[23]. In contrast, recent studies found no relationship between mortality and age. The effect of age in earlier reports could have been due to increased comorbidities in the elderly; more recent improvements may possibly reflect better patient selection and preparation, as well as improved perioperative techniques that allow older patients to undergo surgery more safely [24],[25].

Preoperative respiratory function tests and arterial blood gases are particularly useful in selecting those patients who could tolerate a major pulmonary resection. The most useful parameters are the FEV_1 and the DLCO. The calculation of postoperative predicted values are very useful in determining the extent of resection. The most accurate method tends to be lung perfusion scintigraphy. The DLCO is an equally important method of assessment of postoperative morbidity and mortality. Predicted postoperative values of less than 40% indicate an increased risk of morbidity and mortality. In fact, patients with FEV_1 <30% of such patients will require prolonged postoperative mechanical ventilation or will die.

The best way to reduce the incidence of postoperative complications after lobectomy or pneumonectomy is prevention. Careful preoperative evaluation is linked to improvement in morbidity and mortality. Standard preoperative evaluation should include pulmonary function tests with diffusion measurement. Nuclear methods are useful for further evaluation of patients with borderline respiratory function, especially candidates for pneumonectomy. Particularly intensive respiratory physiotherapy is necessary in patients with borderline results on spirometric tests. All patients should abstain from cigarette smoking, and all chronic medical conditions should be optimally treated. Patients with poor nutrition should be treated before surgery with nutritional supplements or with enteric feeding tubes if necessary. A complete preoperative cardiac evaluation is obligatory.

Complications can be avoided with proper perioperative care. Adequate pain control is associated with fewer respiratory complications after pneumonectomy. Perioperative fluid administration should be controlled in combination with the use of diuretics in order to achieve proper diuresis. It is vital to achieve strict blood sugar control. Aggressive postoperative respiratory physiotherapy is mandatory along with strategies against thromboembolic events.

Univariate analysis

Statistically significant differences were observed between the development of a complication and preoperative (p=0.045) and postoperative PCV values (p=0.003), Hb concentration before (p= 0.032) and after (p = 0.004) surgery, number of units of RBC (p=0.010) and FFP (p = 0.030) administered (Table 5).

No significant differences were observed between the occurrence of a complication (life-threatening or not) and presumed risk factors such as gender, age, smoking, CAD, AF, AH, CRF and NCT.

Similarly, no correlation was found between the emergence of a complication (life-threatening or not) and the type of resection (pneumonectomy, lobectomy or bilobectomy),

Table 5. *Prolongation of LOS[a] related to complications after major pulmonary resections for lung cancer in our institution*

Complications	Number of patients (%)	
	LOS>10 days (n=39)	LOS>14 days (n=22)
Fever [b]	25 (64)*	14 (64)*
Sinus tachycardia	25 (64)*	15 (68)
Atelectasis	12 (31)*	9 (41)*
Persisting air leak [c]	8 (20.5)*	7 (32)*
ICU hospitalization [d]	3 (7.7)	2 (9)
Need for reoperation	3 (7.7)	3 (13.6)
Bronchopleural fistula	3 (7.7)	2 (9)
Post-thoracotomy pain	3 (7.7)	2 (9)
Postoperative pneumonia	2 (5)	2 (9)
ARDS [e]	2 (5)	1 (4.6)
Intraoperative haemorrhage	2 (5)	-
Postoperative haemorrhage	2 (5)	-
Wound infection	2 (5)	2 (9)
Postoperative atrial fibrillation	2 (5)	1 (4.6)
Residual pleural space	1 (2.5)	1 (4.6)
Recurrent laryngeal nerve injury	1 (2.5)	-
Chylothorax	1 (2.5)	1 (4.6)
Urinary tract infection	1 (2.5)	-
Thrombophlebitis	1 (2.5)	-

*[a]Length of stay, [b]Body temperature > 38 °C, [c]Air leak exceeding 7 days, [d]Admission in Intensive care unit, [e]Adult respiratory distress syndrome, *p<0.05*

side of procedure (right or left lung) and tumour histology.

Values of measured and predicted postoperative FEV_1 (and FVC) and preoperative values of pH, pO_2, pCO_2 and $SatO_2$ were not associated with the statistically increased incidence of pulmonary complications. Likewise, the type of pain control was not associated with the risk of complications.

Independent predictors of complications proved to be as follows:

a) DM (χ^2 =4.71, p= 0.03). Patients who experienced life-threatening complications were 4.7 times more likely to have diabetes than those who experienced non-life-threatening complications (OR = 4.7; 95% CI 1.07 to 21.03).

b) COPD (χ^2 = 4.83, p = 0.028). Only 13% of patients with potentially life-threatening complications had COPD compared to 45% of patients with non-life-threatening complications. Patients presenting COPD were 80% less likely to have any of the complications defined as life-threatening (OR = 0.18; 95% CI 0.037 to 0.929).

Overall, however, 75% of those who had COPD experienced some kind of complication, albeit generally non-life-threatening.

We also attempted to study the factors related to the prolonged length of stay (LOS). Thirty-nine patients were hospitalized over 10 days. Comparing this subgroup of patients with those having a shorter hospital stay, we found the patients to be of average age (67 ± 7 Vs. 62 ± 9, p = 0.011) and predominantly male (90%, p = 0.036). The prolongation of hospitalization over 10 days is not correlated with any other characteristics of the patient or the type of surgical procedure (Table 5).

We also arrived at similar conclusions when defining "extended LOS" as hospitalization exceeding 14 days. The most common complications to be associated with prolonged LOS were persistent air leak (8 subjects, p = 0.001), atelectasis (12 subjects, p = 0.000), fever (25 subjects, p = 0.000) and sinus tachycardia (25 subjects, p = 0.038).

In 22 patients (Table 6), extended LOS (>14 days) was associated with older age (p = 0.038), right side of thoracotomy (p = 0.039), persistent air leak (p = 0.000), fever (p = 0.011) and atelectasis (p = 0.001).

Multivariate analysis

We applied a retrograde procedure logistic regression model. The appearance or not of any complication was the dependent variable. The independent variables were selected based on the following criteria:

a) sufficient number of events

b) associated with a statistically significant mode with the dependent variable in the univariate analysis exhibiting p ≤ 0.3

c) considered in previous reports as significant risk factors for postoperative complications

It was necessary to limit the number of variables due to the limited sample size and the number of incidents of the dependent variable so as to create a reliable logistic regression model. Initially, the prognostic model included the subsequent variables: age, sex, preoperative Hb concen-

Table 6. *Patients characteristics related to LOS*[a]

	Number of patients (%)		
	LOS≤10 days (n=50)	LOS>10 days (n=39)	LOS>14 days (n=22)
Mean age ± SD[b] (years)	62±9	67±7*	68±9*
Gender Male	35(70)	35(90)*	19(86)
Female	15(30)	4(14)*	3 (14)
Tobacco consumption[c]	30(60)	14 (64)	14(63)
Coronary disease	9 (18)	6 (15)	2 (9)
COPD[d]	13(26)	15 (38)	10(45)
Hypertension	18(36)	16 (41)	7 (32)
CRF[e]	1 (2)	2 (5)	1 (5)
DM[f]	5 (10)	9 (23)	3 (14)
NCT[g]	4 (8)	1 (2.5)	1 (5)
AF[h]	3 (6)	0	0
Other	7 (14)	9(23)	7 (32)
Right side	29(58)	23 (59)	17 (77)*
Left side	21(42)	16(41)	5 (23)*
Pneumonectomy	13(26)	7 (18)	2 (9)
Bilobectomy	4 (8)	6 (15)	5 (23)
Lobectomy	33(66)	26 (67)	15 (68)
Tumour Stage			
I	19(38)	17 (44)	9 (41)
II	18(36)	13 (33)	6 (27)
III	12(24)	7(18)	5 (23)
IV	1 (2)	3 (5)	2 (9)
Tumour histology			
Adenocarcinoma	20(40)	18 (46)	12 (55)
Squamous	18(36)	12(31)	7 (32)
Large cell	7 (14)	2 (5)	1 (5)
Other	5 (10)	7 (18)	2 (9)

*[a]Length of stay, [b]Deviation standard, [c]Exceeding 15 py, [d]Chronic obstructive pulmonary disease, [e]Chronic renal failure, [f]Diabetes mellitus, [g]Neoadjuvant chemotherapy, [h]Atrial fibrillation, *p<0.05*

tration, CAD, COPD, DM, side of surgical procedure, type of resection (pneumonectomy, lobectomy or bilobectomy), disease stage and number of units of RBC administered.

Our prognostic model is shown in Table 7. The model shows a satisfactory fit to the data according to the standard of review Hosmer-Lemeshow (HL = 1.12, p = 0.29), correctly classifying 70.8% of the events. The receiver-operating characteristic (ROC) curve of the model is also satisfactory as the area under the curve was 0.79.

Accordingly, the transfusion of RBC was associated with the occurrence of complications. Every additional administration of just one unit of RBC appears to increase the probability of any type of complication by 3.5 times.

Patients with COPD presented 3.3 times higher incidence of complications [OR = 3.38, 95% CI (1.01 to 10.66)] compared to those without COPD.

Surgical procedures on the right side presented an almost three-fold incidence of complications [OR = 2.9, 95% CI (1.02 to 8.49)] taking into account all the other risk factors included in the model.

Table 7. *Retrograde procedure logistic regression model*

	OR	Z	P>|z|	[95% CI]
Age	1.03	1.05	0.294	0.97 1.09
Pre [Hb] [a]	0.69	-1.67	0.094	0.45 1.06
RBC [b]	**3.51**	**2.20**	**0.028**	1.14 10.74
COPD [c]	**3.29**	**1.98**	**0.048**	1.01 10.66
Right side of rocedure	**2.94**	**1.99**	**0.046**	1.02 8.49

[a]Preoperative haemoglobin concentration, [b]Units of packed red blood cells administered, [c]Chronic obstructive pulmonary disease

Conclusions

Studying the histology with multinomial logistic regression, patients with squamous cell carcinoma were 7.5 times more likely to be smokers than those with adenocarcinoma taking into account gender. This is entirely in keeping with results from previous reports.

The univariate analysis showed that preoperative Hb and the administration of RBC and FFP is associated with the occurrence of complications. The relationship of RBC administration is also confirmed by the multivariate analysis.

Seventy-five per cent of patients with COPD presented a non-life-threatening complication.

According to univariate analysis, DM is associated with life-threatening complications.

Prolonged LOS was incurred mainly by persistent air leak, atelectasis, and fever, particularly in the case of hospitalization exceeding 14 days that was frequently required after a right-sided surgical procedure.

Pain and type of analgesia were not correlated with score complications or prolonged hospitalization, but our study was not designed to study this aspect.

Due to the limited sample size, the model of our study was designed only for the occurrence or non-occurrence of life-threatening complications and non-life-threatening complications.

Transfusion of RBC is strongly associated with the development of complications. COPD and right-sided procedures are marginally statistically significant for the occurrence of any kind of complication.

Ethical Approval

The study has been approved by the ethics committee of our institutional board. All patients gave their informed consent prior to their inclusion in this study.

Conflict of interest

The authors declare that they have no conflict of interest. They have full control of all primary data and they agree to allow the journal to review their data if requested.

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Επιπλοκές μετά από μείζονες θωρακοχειρουργικές επεμβάσεις για καρκίνο πνεύμονα

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Περίληψη

Σκοπός: Κύριος σκοπός της μελέτης ήταν η καταγραφή των επιπλοκών μετά από μείζονες θωρακοχειρουργικές επεμβάσεις για καρκίνο του πνεύμονα και η αναζήτηση παραγόντων κινδύνου που συσχετίζονται με την εμφάνιση επιπλοκών. Μελετήθηκαν τόσο παράγοντες κινδύνου που αφορούν κλινικοεργαστηριακά χαρακτηριστικά των ασθενών όσο και παράγοντες που έχουν σχέση με τον τύπο της νεοπλασίας και το είδους του χειρουργείου στο οποίο υποβλήθηκαν.

Μέθοδος: Κατά την περίοδο 1/1/2011 – 30/6/2012 89 ασθενείς ηλικίας 37 - 82 ετών υποβλήθηκαν σε μείζονα πνευμονική εκτομή στο Θωρακοχειρουργικό τμήμα του Σισμανογλείου Γενικού Νοσοκομείου Αττικής για αντιμετώπιση καρκίνου πνεύμονα. Πραγματοποιήθηκε λεπτομερής καταγραφή όλων των επιπλοκών καθώς και συστηματική βιβλιογραφική έρευνα σχετικών αναφορών για επιπλοκές μετά από χειρουργικές επεμβάσεις για καρκίνο πνεύμονα. Έγινε διαδικτυακή αναζήτηση στα αρχεία της εθνικής ιατρικής βιβλιοθήκης των ΗΠΑ μέσω της διαδικτυακής πύλης Pub med. Για τη διερεύνηση της συσχέτισης της εμφάνισης ή μη επιπλοκών πραγματοποιήθηκε μονοπαραγοντική ανάλυση με τη χρήση κατάλληλων στατιστικών δοκιμασιών ανάλογα με τον τύπο των μεταβλητών. Στη συνέχεια προσαρμόστηκαν με ανάδρομη διαδικασία μοντέλα λογιστικής παλινδρόμησης.

Αποτελέσματα: Ποσοστό 64% των ασθενών εμφάνισε κάποιου είδους επιπλοκή. 79% των επιπλοκών αυτών δεν ήταν δυνητικά επικίνδυνες για τη ζωή. 12.4% εμφάνισαν κάποια επικίνδυνη για τη ζωή επιπλοκή και 4.5% απεβίωσαν. Ως δυνητικά επικίνδυνες θεωρήθηκαν οι εξής επιπλοκές: διεγχειρητική και μετεγχειρητική αιμορραγία, οξύ έμφραγμα του μυοκαρδίου, πνευμονική εμβολή, βρογχοϋπεζωκοτικό συρίγγιο, οξεία αναπνευστική ανεπάρκεια, μετεγχειρητική πνευμονία και η ανάγκη επανεπέμβασης. Ως μη επικίνδυνες για τη ζωή θεωρήθηκαν οι εξής επιπλοκές: μετεγχειρητική κολπική μαρμαρυγή, διαφυγή αέρα, υπολειπόμενο κενό, διαπύηση τραύματος, ατελεκτασία, πυρετός, φλεβοκομβική ταχυκαρδία, ουρολοίμωξη, τραυματισμός φρενικού και λαρυγγικού νεύρου, θρομβοφλεβίτιδα.

Συμπεράσματα: Με την μονοπαραγοντική ανάλυση βρέθηκε ότι η προεγχειρητική τιμή αιμοσφαιρίνης και η χορήγηση συμπυκνωμένων ερυθρών αιμοσφαιρίων και κατεψυγμένου πλάσματος σχετίζεται με την εμφάνιση επιπλοκών γενικότερα. Η σχέση κυρίως της χορήγησης ερυθρών επιβεβαιώθηκε και κατά την πολυπαραγοντική ανάλυση με την οποία βέβαια λαμβάνουμε υπόψη και τους άλλους παράγοντες κινδύνου που μπορεί να επηρεάζουν τη σχέση. 75% των ασθενών με χρόνια αποφρακτική πνευμονοπάθεια εμφάνισαν κάποια επιπλοκή παρόλο που γενικά οι επιπλοκές αυτές εντάσσονταν στις μη επικίνδυνες για τη ζωή. Ο σακχαρώδης διαβήτης σχετίζονταν με επικίνδυνες για τη ζωή επιπλοκές στην μονοπαραγοντική ανάλυση. Η παράταση νοσηλείας παρατηρήθηκε κατά κύριο λόγο για εμμένουσα διαφυγή αέρα, ατελεκτασία, πυρετό και, ειδικά στην περίπτωση νοσηλείας άνω των 14 ημερών ήταν συχνό φαινόμενο μετά από δεξιές θωρακοτομές. Πόνος και είδος αναλγησίας δεν είχαν σχέση με την εμφάνιση επιπλοκών ή με την παράταση νοσηλείας. Από το μοντέλο μας η σχέση με τη χορήγηση ερυθρών αιμοσφαιρίων είναι ξεκάθαρη ενώ οριακά στατιστικά σημαντική είναι η παρουσία χρόνιας αποφρακτικής πνευμονοπάθειας και η πλευρά της θωρακοτομής (δεξιά).

Λέξεις κλειδιά: *Θωρακοτομή, λοβεκτομή, πνευμονεκτομή, επιπλοκές, μη μικροκυτταρικός καρκίνος πνεύμονα*

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