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## Original article

# Risk Factors for the Development of Complications After Surgical Treatment for Bronchopulmonary Carcinoma<sup>☆</sup>

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## ABSTRACT

**Introduction:** The most suitable treatment in most early-stage lung cancer patients is surgical resection. Despite previously assessing each patient's status being relevant to detect possible complications inherent to surgery, no consensus has been reached on which factors are "high risk" in such patients. Our study aimed to analyze the morbidity and the mortality incidence associated with this surgery in our setting with a multicentre study and to detect risk parameters.

**Methods:** A prospective analysis study with 3307 patients operated for bronchopulmonary carcinoma in 24 hospitals. Study variables were age, TNM, gender, stage, smoking habit, surgery approach, surgical resection, ECOG, neoadjuvant therapy, comorbidity, spirometric values, and intraoperative and postoperative morbidity and mortality. A multivariate logistic regression analysis of the morbidity and mortality predictor factors was done.

**Results:** We recorded 34.2% postoperative morbidity and 2.1% postoperative mortality. Gender, myocardial infarction, angina, ECOG  $\geq 1$ , COPD, DLCO  $< 60\%$ , clinical pathological status, surgical resection and surgery approach were shown as morbidity and mortality predictor factors in lung cancer surgery in our series.

**Conclusions:** The main variables to consider when assessing the lung cancer patients to undergo surgery are gender, myocardial infarction, angina, ECOG, COPD, DLCO, clinical pathological status, surgical resection and surgery approach.

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## Factores de riesgo para el desarrollo de complicaciones tras tratamiento quirúrgico del carcinoma broncopulmonar

### R E S U M E N

#### Palabras clave:

Cáncer de pulmón  
Intervención quirúrgica  
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Mortalidad

**Introducción:** El tratamiento más adecuado en la mayoría de los pacientes con cáncer de pulmón en estadio inicial es la resección quirúrgica. A pesar de evaluar anteriormente que el estado de cada paciente sea el adecuado para detectar posibles complicaciones inherentes a la intervención quirúrgica, no se ha alcanzado ningún consenso sobre los factores que son de «alto riesgo» en esos pacientes. Nuestro estudio tuvo como objetivo analizar la morbilidad y la incidencia de mortalidad asociada con esta intervención quirúrgica en nuestro entorno con un estudio multicéntrico y descubrir los parámetros de riesgo.

**Métodos:** Se trata de un estudio de análisis prospectivo con 3.307 pacientes operados de carcinoma broncopulmonar en 24 hospitales. Las variables de estudio fueron edad, sistema TNM, sexo, estadio, tabaquismo, abordaje quirúrgico, resección quirúrgica, escala ECOG, tratamiento neoadyuvante, comorbilidad, valores espirométricos y morbimortalidad intra- y postoperatoria. Se realizó un análisis de regresión logística multivariante de los factores pronósticos de morbilidad y mortalidad.

**Resultados:** Registramos el 34,2% de morbilidad postoperatoria y el 2,1% de mortalidad postoperatoria. Sexo, infarto de miocardio, angina, ECOG  $\geq 1$ , EPOC, DLCO  $< 60\%$ , estado clínico patológico, resección quirúrgica y abordaje quirúrgico aparecieron como factores pronósticos de morbilidad y mortalidad en cirugía de cáncer de pulmón en nuestra serie. **Conclusiones:** Las principales variables que deben tenerse en cuenta al evaluar a pacientes con cáncer de pulmón para realizarles una intervención quirúrgica son sexo, infarto de miocardio, angina, ECOG, EPOC, DLCO, estado clínico patológico, resección quirúrgica y abordaje quirúrgico.

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## Introduction

Nowadays, bronchopulmonary carcinoma (BC) is the main cause of death by cancer worldwide. In early stages, surgical resection is still the most suitable treatment for most patients, and assessing each patient's status is of utmost importance before operating and foreseeing the appearance of any complications inherent to this treatment.<sup>1</sup> One in every five stage-I non-cell lung cancer (NSCLC) patients is considered to be at high risk for postoperative complications<sup>2</sup> and mortality rates of 2.2% have been published for patients undergoing NSCLC resection.<sup>3</sup>

Several factors have been proved to increase surgical risk for BC resection and impact patient outcomes. They include among others: age, chronic obstructive lung diseases (COPD), former myocardial infarction (MI), smoking and/or carbon monoxide diffusing capacity (DLCO) under 60%.<sup>4,5</sup> Different risk staging models have been recently developed trying to propose tools for chest surgeons.<sup>3,5,6</sup> To date, however, no consensus has been reached about the definition of "high risks" in such patients, finding only weak recommendations in the literature. This makes selecting the plan to be followed in each patient a difficult task.

This study aimed to analyze the incidence of morbidity and mortality associated with BC resection in our setting by a multicentre study with patients from 24 Spanish departments of Thoracic, and to evaluate the risk factors that impact morbidity and mortality, which must be considered in order to plan the most suitable therapeutic strategies for each patient. This analysis also provides us with a valuable tool to assess the outcomes in our network.

## Patients and Methods

### Patients

This study is a prospective analysis that includes 3307 patients with suspected NSCLC undergoing surgery with curative purpose in 24 Spanish departments of Thoracic Surgery from 1 June 2012 to 30 November 2014. Patients with unresectable disease undergoing exploratory thoracotomies were excluded. All the involved hospitals recorded the same data for the disease, treatment and patient progress, being cares reviewed by the individual surgeons. Later, an external data manager collected data in a uniform manner. An auditor ensured the proper collection of data. Histology different from BC were excluded. The European guidelines criteria were followed for the surgery, neoadjuvant therapy and posterior diagnosis.<sup>7</sup>

The study variables were chosen according to previous literature<sup>7,8</sup> and they were defined in advance and agreed by all the authors: age, stage, gender, pathological stage, smoking habit, surgery approach, surgical resection, clinical status, neoadjuvant therapy (chemotherapy or chemo-radiotherapy), comorbidity, spirometric values (DLCO, forced expiratory volume in one second (FEV1), and intraoperative and postoperative morbidity and mortality. Postoperative morbidity and mortality was assessed by considering the first 30 days for the purpose. Tumors were staged using the 7<sup>th</sup> Revision in the International System for Staging Lung Cancer (TNM). The Eastern Cooperative Oncology Group (ECOG) scale was used for classifying clinical status (Table 1).

All complications collected in data had clinical transcendence. To analyze morbidity, the systematic classification of

**Table 1 – Hospitals That Have Participated in the Study.**

Hospital General de Asturias
Hospital General de Valencia
Hospital de Jaén
Hospital U. N. S. de la Candelaria (Tenerife)
Hospital Clínico de Madrid
Hospital de Palma de Mallorca
Hospital Puerta de Hierro (Madrid)
Hospital de Albacete
Hospital Clínic (Barcelona)
Hospital Sagrado Corazón (Barcelona)
Hospital Virgen del Rocío (Sevilla)
Hospital Gregorio Marañón (Madrid)
Hospital Germans Trias i Pujol
Hospital U. Virgen de las Nieves (Granada)
Hospital Carlos Haya (Málaga)
Hospital de Alicante
Hospital de la Ribera (Alzira, Valencia)
Hospital La Paz (Madrid)
Hospital A Coruña
Hospital Islas Cies (Vigo)
Hospital Reina Sofía (Córdoba)
Hospital U. de Girona Dr. Josep Trueta
Hospital Universitario Donostia
Hospital de Santiago de Compostela

operative morbidity into five normalized groups (Table 2), proposed by Dindo et al.,<sup>9</sup> was used. It helped to make an objective comparison of surgical procedures and patient series, and also between different surgeons and operating teams. Hemorrhage was considered a complication when it was >200 ml/h with hemodynamic instability and/or a total of 1500 ml, and air leak when it lasted at least 5 days. A possible occurrence of atelectasis was reviewed after surgery in all patients. Hypoxia was considered when <60 O<sub>2</sub>mmHg, angina pectoris in the absence of obstructive coronary artery disease and myocardial infarction when coronary artery was obstructed. All myocardial infarction were remote. Ischemic cardiomyopathy was considered when patients suffered simultaneously angina pectoris and myocardial infarction.

Each patient was enrolled after acceptance of informed consent document. Study protocol was approved by the ethics committees of the Hospitals involved in the study and conducted in accordance with the Declaration of Helsinki.

## Statistical Analysis

Categorical variables were expressed as absolute values and percentages (%). A multivariate logistics regression analysis was done to analyze the correlation between morbidity (including minor and major complications), mortality and clinical characteristics of patients (age, TNM, gender, pathological stage, smoking habit, surgery approach, surgical resection, ECOG, neoadjuvant therapy, comorbidity, spirometric values). The correlation between clinical characteristics and intraoperative mortality was not shown due to limited number of patients in this group (n=3). Variables showing a minimum significance threshold on the univariate analysis were included for the multivariate test. Level of significance was considered for a P-value of ≤.05. Statistical analysis was run with the SPSS package, v. 20.0 (SPSS Inc, Chicago, IL, USA).

## Results

Table 3 offers the clinical-pathological characteristics of the patients included in our study. From 3307 cases, 77.6% were male, with a median age of 66 years. Adenocarcinoma was the most frequent histological subtype (55.1%). Distribution by stages was as follows: I: 55.1%, II: 24.9%, III: 14%, IV: 1.9%. A total of 263 patients (8%) received neoadjuvant treatment. The most frequent surgery approach was thoracotomy (67%). Lobectomy was the most widely performed surgical resection (71.8%). Regarding comorbidity (Table 4), COPD criteria (28.4%) was the most frequent, followed by ischemic cardiomyopathy (9.2%), vascular disease (8.1%) and atrial fibrillation (6.7%).

We recorded an intraoperative morbidity of 7.5%. We found 279 complications, being the most frequent hypoxia (<60 O<sub>2</sub>mmh) (2.7%), hemorrhage (by iatrogenic section of artery or vein) (1.8%) and costal fracture (1.7%). Postoperative morbidity was 34.2%, where air leaks (10.6%), arrhythmia (6.3%) and pneumonia (6.2%) stood out (Table 5). Overall, we found that the majority of patients' complications were minor (78.4%; Table 2). Intraoperative mortality was 0.1%. 30-days postoperative mortality rate was 2.1% (69 patients). From them, 41 had undergone lobectomy, 19 pneumonectomy, 5 sublobar resection and 4 bilobectomy, which means a higher rate of deaths in

**Table 2 – Grade Complication of Patients' Morbidity.**

Grade	Definition	n	Percentage
<b>Minor complication</b>			
I	No pharmacological or other treatment is required	786	23.7%
II	Minor intervention or extra pharmacological treatment is needed	565	17%
<b>Major complication</b>			
III	Surgical, radiological or endoscopic surgery, or multiple treatments, is required		
IIIa	Intervention does not require general anesthesia	129	3.9%
IIIb	Intervention requires general anesthesia	94	2.8%
IV	Treatment in intensive care and life support unit is needed		
IVa	Dysfunction of a single organ	49	1.5%
IVb	Multiorgan dysfunction	30	0.9%
V	Patient's death caused by the complication	71	2.1%

**Table 3 – Univariate Analysis Results for the Association Between Patients' Characteristics and Morbidity/mortality.**

Variable	n	Percentage	Postoperative Mortality P	Morbidity P	Intraoperative Morbidity P
Age (years)					
<65	1400	42.33%	.005*	.049*	.044*
65–79	1732	52.37%			
>79	175	5.29%			
Gender					
Female	741	22.40%	.000***	.000***	.045*
Male	2566	77.60%			
Histology					
Adenocarcinoma	1704	51.52%			
Squamous	1212	36.64%	.234	.078	.551
Large cell tumor	96	2.90%			
Microcytic	28	0.84%			
Adenosquamous	55	1.66%			
Others	212	6.41%			
Pathological stage					
I	1821	55.06%			
II	825	24.94%	.043*	.049*	.039*
III	463	14%			
IV	63	1.90%			
Complete response	28	0.85%			
Not known	107	3.23%			
Neoadjuvant treatment					
Yes	263	7.95%	.150	.298	.345
No	3044	92.05%			
Smoking status					
Smoker	1042	31.51%			
Former Smoker	1751	52.95%	.029*	.000***	.046*
Never-smoker	393	11.88%			
Not known	121	3.66%			
Surgery approach					
Toracotomy	2233	67.52%			
VATS	1030	31.15%	.003***	.045*	.039*
Others	44	1.33%			
Surgical resection					
Pneumonectomy	314	9.49%			
Lobectomy	2376	71.85%	.005***	.034*	.045*
Bilobectomy	169	5.11%			
Anatomical segmentectomy	143	4.2%			
Wedge	308	9.31%			
General state					
ECOG 0	1988	60.11%			
ECOG 1	1090	32.96%	.005***	.002***	.047*
ECOG 2	109	3.30%			
ECOG 3	8	0.24%			
ECOG 4	2	0.06%			
No assessable	110	3.33%			
Comorbidity					
Yes	2832	85.64%	–	–	–
No	475	14.36%			

Video-assisted-Thoracic Surgery (VATS).

The Eastern Cooperative Oncology Group scale (ECOG).

**Table 4 – Univariate Analysis Results for the Association Between Patients' Comorbidity and Morbidity/Mortality.**

Previous Disease	n	Percentage	Postoperative Mortality P	Morbidity P	Intraoperative Morbidity P
Ischemic cardiomyopathy	304	9.19%	.144	.067	.125
Myocardial infarction	128	3.87%	.036*	.005***	.032*
Angina pectoris	54	1.63%	.020*	.056	.044*
Atrial fibrillation	221	6.68%	.043*	.060	.443
Vascular disease	267	8.07%	.030*	.106	.456
Valvular hearth disease	69	2.08%	.148	.138	.160
Atelectasis	25	0.76%	.045*	.020*	.455
COPD	940	28.42%	.000***	.000***	.048*
Lung disease	25	0.76%	.043*	.002***	.043*
Stroke sequel	78	2.36%	.017*	.328	.425
Chronic obstructive lung diseases (COPD).					

pneumonectomy (6.1% pneumonectomy vs 1.7% lobectomy, 2.4% bilobectomy and 1.1% sublobar resection).

Univariate analysis of the association between patients' characteristics and morbidity/mortality are shown in [Tables 3 and 4](#). Regarding the pre-surgery factors that influenced intraoperative and postoperative morbidity and mortality ([Table 6](#)), the multivariate analysis show that those patients with a background of MI (OR 1.4; 95%CI: 1–2.1), angina (OR 1.7; 95%CI: 1–3), DLCO <60% (OR 1.4; 95%CI: 1.1–1.7) and major resection (OR 1.3; 95%CI: 1–1.6) presented a higher probability of intraoperative morbidity. The patients with a background of

MI (OR 1.4; 95%CI: 1–2.1), COPD (OR 1.4; 95%CI: 1.2–1.7), lung disease (OR 3.1; 95%CI: 1.3–7.2), ECOG  $\geq 2$  (OR 1.7; 95%CI: 1.1–2.6), DLCO <60% (OR 1.6; 95%CI: 1.3–2.1) and major resection (OR 2.1; 95%CI: 1.6–2.7) presented a higher probability of postoperative morbidity. Females (OR 0.6; 95%CI: 0.4–0.7) and the patients undergoing for Video-assisted-Thoracic Surgery (VATS) (OR 0.6; 95%CI: 0.5–0.7) were less likely to present postoperative morbidity.

On the other hand, the patients with a background of angina (OR 4; 95%CI: 1.3–12.5), COPD (OR 2.1; 95%CI: 1.2–3.6), prior stroke with sequelae (OR 3.4; 95%CI: 1.2–9.1) and ECOG  $\geq 1$

**Table 5 – Patients' Morbidity.**

Complication	n	Percentage of Total Patients	Percentage on Morbidity
<i>Intraoperative</i>			
Arrhythmia	39	1.18%	13.98%
Hypoxia	89	2.69%	31.90%
Hemorrhage	61	1.84%	21.86%
Costal fracture	55	1.66%	19.71%
Others	35	1.06%	12.54%
Mortality	3	0.09%	–
N° total complications	279		
N° patients with complications	249		
<i>Postoperative</i>			
Pneumonia	204	6.17%	14.12%
Hemoptysis	6	0.18%	0.41%
Atelectasis	191	5.78%	13.22%
Intubation	57	1.72%	3.94%
Pleural effusion	70	2.12%	4.84%
Air leaks	355	10.6%	24.57%
Arrhythmia	208	6.29%	14.39%
Ischemic Cardiopathy	12	0.36%	0.83%
Pulmonary edema	35	1.06%	2.42%
Infarction	5	0.15%	0.35%
Hemorrhage	121	3.66%	8.37%
Fistula	38	1.15%	2.63%
Empyema	31	0.94%	2.14%
Infection	20	0.60%	1.38%
Dehiscence	12	0.36%	0.83%
Others	80	2.42%	5.54%
Mortality	69	2.08%	–
N° total complications	1445		
N° patients with complications	1132		

**Table 6 – Multivariate Analysis for the Association Between Patients' Variables and Morbidity/Mortality.**

Intraoperative Morbidity Variable	Exp(B)	I.C. 95%	P	Exp(B)	30 Days-Morbidity I.C. 95%	P
Gender	1.083	0.902–1.300	.391	0.565	0.458–0.696	.000
Age (<80/≥80)	0.917	0.670–1.254	.586	1.230	0.887–1.704	.214
Smoking status	0.915	0.724–1.156	.456	0.976	0.748–1.274	.860
Myocardial infarction	1.461	1.022–2.088	.038	1.470	1.017–2.124	.040
Angina pectoris	1.754	1.014–3.036	.045	1.277	0.724–2.254	.398
Atelectasis	0.909	0.405–2.042	.817	2.109	0.937–4.746	.072
Pneumonia	0.967	0.592–1.579	.893	1.188	0.716–1.972	.504
COPD	0.949	0.804–1.119	.533	1.453	1.224–1.724	.000
Lung disease	0.422	0.172–1.031	.058	3.017	1.271–7.162	.012
DLCO (<60/≥60)	1.426	1.156–1.758	.001	1.653	1.330–2.054	.000
FEV1 (<60/≥60)	1.178	0.933–1.486	.169	0.824	0.647–1.048	.114
Surgery approach (VATS vs Thoracotomy)	0.936	0.805–1.087	.386	0.638	0.539–0.753	.000
Surgical resection (Minor vs major)	1.290	1.036–1.607	.023	2.107	1.632–2.719	.000
ECOG (0 vs 1/2)	1.336	0.894–1.995	.157	1.715	1.149–2.560	.008
Stage	0.970	0.648–1.452	.883	0.878	0.574–1.343	.548
Intraoperative mortality				30 days-mortality		
Gender	–	–	–	0.180	0.042–0.770	.021
Age (<80/≥80)	–	–	–	1.506	0.578–3.928	.402
Smoking status	–	–	–	1.529	0.354–6.609	.570
Myocardial infarction	–	–	–	2.121	0.858–5.244	.103
Angina pectoris	–	–	–	4.009	1.286–12.497	.017
Atelectasis	–	–	–	1.532	0.194–12.094	.686
Pneumonia	–	–	–	2.895	0.979–8.562	.055
COPD	–	–	–	2.124	1.246–3.621	.006
Lung disease	–	–	–	2.964	0.564–15.578	.199
DLCO (<60/≥60)	–	–	–	1.066	0.537–2.116	.854
FEV1 (<60/≥60)	–	–	–	0.871	0.426–1.781	.705
Surgery approach (VATS vs Thoracotomy)	–	–	–	0.307	0.138–0.682	.004
Surgical resection (Minor vs major)	–	–	–	2.116	0.811–5.517	.125
Stage	–	–	–	0.345	0.128–0.927	.035
ECOG (0 vs 1/2)	–	–	–	2.910	1.258–6.731	.013
Stroke sequel	–	–	–	3.378	1.259–9.064	.016
Vascular disease	–	–	–	1.492	0.728–3.06	.274
Fibrillation	–	–	–	1.549	0.678–3.535	.299
Chronic obstructive lung diseases (COPD).						
Carbon monoxide diffusing capacity (DLCO).						
Forced expiratory volume in one second (FEV1).						
Video-assisted-Thoracic Surgery (VATS).						
The Eastern Cooperative Oncology Group scale (ECOG).						

(OR 2.9; 95%CI: 1.2–6.4) had a higher probability of postoperative mortality, while females (OR 0.2; 95%CI: 0.1–0.8), the patients operated for VATS (OR 0.3; 95%CI: 0.1–0.7), and stage I and II patients (OR 0.3; 95%CI: 0.1–0.9) presented a lower probability of postoperative mortality.

## Discussion

Surgical resection continues to be the treatment of choice in early stages of NSCLC, and its results depend on both correct oncological assessments and careful overall perioperative selection, which prevent complications inherent to this treatment from appearing.<sup>1–3</sup>

In our series, we found an intraoperative morbidity of 7.5% and a postoperative morbidity within the first 30 days of 34.2%. Postoperative and intraoperative mortality were of 2.1% and

0.1%, respectively. These data agree with the figures described in the literature.<sup>2,3,10</sup> The decrease in postoperative mortality found in latest studies was particularly significant when comparing to the Sociedad Española de Patología del Aparato Respiratorio (SEPAR) study reporting morbidity and mortality rates of 35.2% and 6.8%, respectively, for patients undergoing thoracotomy between 1993 and 1997.<sup>1</sup> Several issues may explain this positive tender in quality of surgery for NSCLC, such as a better patient selection for surgery (thanks to the introduction of PET images within preoperative clinical staging tools), and the implementation of perioperative programs of respiratory rehabilitation.

In our study, we found that surgical complications resulting from BC resection were mainly minor, highlighting air leaks (10.6%), which were more frequent than those found in other series.<sup>1</sup> Cardiac arrhythmia was the most frequently observed complication behind persistent air leaks, and was



also the most frequent postoperative medical complication. It is usually described in most similar studies, with rates ranging between 3.8 and 40% after lung cancer surgery.

One of the most important predictors of morbimortality after NSCLC surgical resection is patient clinical status before surgery.<sup>11</sup> As expected, this variable was significantly statistical in our series in the patients with ECOG values above or equal to 1, who presented a higher probability of intra- and postoperative morbidity and mortality.

One of the most controversial questions is whether age is a limiting factor for lung surgery, specifically in patients aged over 80.<sup>12</sup> In our series, octogenarian patients shown similar morbidity and mortality rates than other age groups. Many studies corroborate this finding,<sup>4,13,14</sup> concluding that octogenarian patients can be submitted to lung resection. We ought not to forget that these patients are more fragile and we must always contemplate the sublobar surgery as an alternative, provided it is feasible, and by VATS since this approach is less aggressive.

In recent decades, the proportion of females diagnosed with BC has significantly increased in Spain<sup>1</sup> probably related to social smoking habits. As previously reported in literature,<sup>5</sup> in our series, females presented lower postoperative morbidity and mortality rates, probably due to lower comorbidity. As it is well-known, a high percentage of patients with BC present clinical COPD criteria, being it considered a risk for lung surgery.<sup>2</sup> In our sample, 28.4% of the patients had COPD, whose presence has been statistically related with both mortality and postoperative morbidity. The structural lesions that this pathology causes increase the dead space, imbalanced ventilation-perfusion quotients, hemodynamic changes in lung capillaries and altered diffusion, which increase the efforts made to breath and can lead to respiratory failure, which is the main cause of death during lung resection surgery.<sup>15</sup>

Low FEV1 values are associated with increased cardiorespiratory morbidity and mortality.<sup>16,17</sup> After performing a multivariate analysis in our sample, for which we dichotomised the FEV1 values into higher than or equal to 60% and into lower than 60% according to previous literature,<sup>18</sup> we observed that this variable did not act as an independent risk factor for morbidity and mortality. However, as we mentioned, COPD has been statistically related to morbidity and mortality, and we should not forget that FEV1 is one of the clinical criteria used to define obstructive lung disease.

Establishing a cut off of 60% for DLCO, we found that DLCO acted as a risk factor for morbidity, but not for mortality. Preoperative DLCO <60 have been associated with 25% mortality and 40% morbidity in patients who underwent lung resection surgery. Low predicted DLCO values act as a predictor of cardiorespiratory complications, and of mortality even in patients with FEV1 that fall within normality limits. Brunelli et al.<sup>19</sup> found a weak correlation between preoperative DLCO values and forced volume expired in the first second (FEV1%) values and systematic postoperative DLCO calculations, which improves predicting the lung resection risk. This is currently the reason why the guidelines of the American College of Chest Physicians<sup>8</sup> and those of the European Respiratory Society and the European Society of Thoracic Surgeons<sup>20</sup> recommend taking preoperative DLCO measure-

ments in all candidate patients for lung resection surgery. In our study we did not find DLCO as an independent risk factor for mortality but it should be taken into account that DLCO is other of the clinical criteria used to define COPD.

Ischemic cardiomyopathy is a high risk factor for lung resection surgery with an incidence ranging between 11% and 17%. Its presence implies a 3% risk for cardiac complications.<sup>21,22</sup> We obtained a similar incidence in our series. Those patients with a background of angina prior to surgery have a higher intraoperative morbidity probability. Similarly, those patients who have suffered MI before surgery present higher postoperative morbidity.

Video-assisted surgery appears to offer the similar results to conventional open approaches, and refers to the possibility of achieve optimal oncological resections.<sup>23,24</sup> Several studies<sup>13,25,26</sup> have suggested that performing lung resections by VATS in qualified centers is associated with lower morbidity. We coincide with these studies because in our series, the VATS surgical approach was statistically associated with lower morbidity. We also found lower postoperative mortality for those patients who underwent VATS, which also agrees with previous results.<sup>5,16</sup>

Sublobar resections have obtained excellent oncological results in tumors <2 cm, and have shown a lower perioperative morbidity risk.<sup>27</sup> The advantages of minor resections include maintaining lung function, a lower risk of perioperative morbidity and mortality, the possibility of patients tolerating future resections if a second primary lung tumor and/or recurring tumors appear/s, and a simple surgical procedure, plus the possibility of carrying it out by less invasive techniques. The current main disadvantage of such operations is the increased risk of loco-regional recurrence. It has been shown that 5-year survival rate for segmentectomy in tumors <3 cm is similar to lobectomy.<sup>28</sup> However wedge resection is correlated to worse survival.<sup>29</sup>

It is noteworthy that the pathological status of the patients in our series was also observed to act as a mortality predictor factor. Thus stages I and II patients presented a lower mortality probability. This may be due to the fact that surgical resection and surgery approach employed in early stages are less aggressive, and also because these patients received no neoadjuvant therapy, which could perhaps impact morbidity.

We acknowledge limitations to our analysis. From the different Hospitals that participated in the study, we are unable to assess the effects, if any, that the different surgeons, their work team or the hospital's volume have on the development of patients' complications. Furthermore, we analyzed complications altogether, rather than evaluating individual complications separately. Finally, other variables not contemplated in the study could have a role in patients' morbidity and mortality.

Despite these limitations, our study has several strengths. The large numbers of patients from different regions included in the study reflects the current practice patterns across the nation, and it may serve to guide surgeons in appropriate patient selection. Further, these findings may serve to stimulate the implementation of better perioperative protocols designed to reduce the incidence of postoperative complications among BC patients.

In summary, we found that MI, DLCO <60%, major resection, angina, COPD and lung disease are the comorbidities related to intraoperative and postoperative morbidity during BC surgery, causing mainly minor complications, being the most frequent air leaks, arrhythmia, pneumonitis and hypoxia. On the other hand, mortality appears to be related mainly to angina, prior stroke or ECOG  $\geq 1$ .

## Conclusions

We recorded a postoperative morbidity and mortality of 34.2% and 2.1%, respectively. Gender, MI, angina, ECOG  $\geq 1$ , COPD, DLCO <60%, tumoral pathological status, and surgical resection and surgery approach worked as predictor factors of morbidity and mortality in lung cancer surgery in our series.

## Conflict of Interest

None declared.

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