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Half the deaths after surgery for lung cancer occur after discharge

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ABSTRACT

Introduction: Mortality following surgery for lung cancer increases at 90 days. The objective of this study was to determine the rate, factors, time to death, hospital stay until discharge, time to death after discharge and causes of mortality at 90 days following surgery for lung cancer.

Methods: A prospective follow-up study was performed in a cohort of 378 patients who underwent surgery for lung cancer between January 2012 and December 2016. Data on preoperative status, postoperative complications, and mortality were collected.

Results: Rates of mortality were 1.6% vs. 3.2% at 30 and 90 days, respectively. Half of deaths occurred between 31 and 90 postoperative days following discharge.

The variables found to be related to mortality at 90 days were a Charlson Index > 3 ($p < 0.001$), a history of stroke ($p = 0.036$), postoperative pneumonia ($p = 0.001$), postoperative pulmonary or lobar collapse ($p = 0.001$), reintubation ($p < 0.001$) and postoperative arrhythmia ($p = 0.0029$). The risk of mortality was also observed to be associated with the type of surgical technique –being higher for thoracotomy as compared to video-assisted thoracoscopy (VATS) ($p = 0.011$) –, and hospital readmission after discharge ($p < 0.001$). Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. Multivariate analysis revealed that a Charlson Index > 3 ($p = 0.001$) OR 2.0 (1.55,2.78), a history of stroke ($p = 0.018$) OR 5.1 (1.81, 32.96) and postoperative pulmonary or lobar collapse ($p = 0.001$) OR 8.5 (2.41,30.22) were independent prognostic factors of mortality.

The most common causes of death were related to respiratory (58.3%) and cardiovascular (33.2%) complications.

Conclusions: Mortality at 90 days following surgery for lung cancer doubles 30-day mortality, which is a relevant finding of which both, patients and healthcare should be aware.

Half the deaths within 90 days after surgery for lung cancer occur after discharge.

Specific outpatient follow-up programs should be designed for patients at a higher risk of 90-day mortality.

1. Introduction

Traditional indicators of in-hospital mortality and 30-day mortality following pulmonary resection for lung cancer are not accurate in representing the actual risk of postoperative mortality.

Evidence has been consistently provided that 90-day mortality after pulmonary resection for lung cancer can exceed the double of 30-day mortality [1–6], with similar mortality rates reported for the first 30 postoperative days and the postoperative period from 31 to 90 days.

An explanation is that deaths that occur beyond 30 postoperative days may not be recorded. Some patients may die more than a month after surgery, as a result of severe postoperative complications that required prolonged hospitalization. On the other hand, death beyond 31 postoperative days may occur during readmission, or suddenly at home from complications [2]. Thus, surgery-related deaths may be underreported when only 30-day mortality is recorded [1–4].

Factors associated with 90-day mortality following pulmonary resection reportedly include age, male sex, comorbidity, pulmonary

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function, advanced stage, pneumonectomy, and a low number of pulmonary resections performed at the hospital or by the surgeon [1,3,5,7].

There is also evidence that hospital readmission is a risk factor for 90-day mortality after pulmonary resection [8]. Readmissions have a negative impact on 90-day survival after surgery for lung cancer. Evidence has been published that readmission is associated with a six-fold increase in 90-day mortality [8].

Reported causes of 90-day mortality included respiratory and cardiological complications and sepsis. The most frequent respiratory and cardiological causes are pneumonia or acute respiratory distress syndrome, and arrhythmia and acute myocardial infarction, respectively [2].

Mortality associated with lung cancer surgery should be assessed up to 90 postoperative days after lung resection [9–11]. Mortality after discharge should also be recorded.

The primary objective of this study was assessing the rate, cause, number of days until death, time to discharge, and death post-discharge. Secondary objectives included determining the relationship between the causes of readmission following pulmonary resection for lung cancer and 90-day mortality.

2. Methods

2.1. Design

A prospective, follow-up study was performed in a cohort of 378 patients who underwent surgery for lung cancer.

The study population was composed of patients with lung cancer who had surgery with curative intent at the Virgen de las Nieves hospital and Inmaculada hospital, Granada, Spain, between January 2012 and December 2016. Patients subjected to pulmonary resection for metastasis from other primary tumors or benign lesions were excluded from the study. Indication of surgery and preoperative functional status were assessed by a multidisciplinary hospital committee according to clinical practice guidelines [12,13].

The minimum duration of follow-up was 90 days. No loss to follow-up was reported. Data were prospectively extracted from electronic medical records kept by the Andalusian healthcare system and by telephone calls.

The study was approved by the ethics committee of University Hospital Virgen de las Nieves of Granada (CEI 080615). Written informed consent was obtained from all patients.

2.2. Definition of primary endpoints

Mortality at 90 days, was defined as all-cause mortality within 30 days following surgery.

Mortality at 30 days was defined as all-cause mortality within 30 days following surgery.

Mortality during first admission was defined as all-cause mortality during first admission following surgery regardless of the length of stay.

Prolonged air leak, was defined as air leakages occurred post-operatively for more than 5 days.

The *Charlson index* contains 19 categories of comorbidity which are assigned with a score of 1,2,3 or 6 based on the risk of dying associated with each condition and age [14].

Postoperative pulmonary or lobar collapse was defined as radiologically confirmed pulmonary or lobe collapse following pulmonary resection surgery.

Postoperative hemothorax, defined as a patient requiring surgical reintervention for 150–200 cc/hour bleeding for 2–4 h or haemodynamic instability.

Intraoperative hemorrhage, defined as any bleeding during surgery that causes hemodynamic instability and requires transfusion.

Performance status was evaluated using ECOG scale [15].

Obesity was defined as a body mass index (BMI) > 30.

The variable "surgical approach" was classified as video-assisted thoracoscopy (VATS) or thoracotomy.

Types of resection included lobectomy, enlarged lobectomy (to the thoracic wall, vertebra or diaphragm), pneumonectomy, bilobectomy, segmentectomy and atypical.

Other variables were age, sex, hemoglobin, albumin, TNM and stage [16,17], tobacco use, number of packs/year, induction or neoadjuvant treatment, adjuvant treatment, comorbidities such as hypertension, atrial fibrillation, ischemic heart disease, acute myocardial infarction, cardiac valve disease, peripheral arterial vasculopathy, renal failure, history of stroke, chronic obstructive pulmonary disease (COPD), forced expiratory volume in the 1st second (FEV1), forced vital capacity (FVC), lung diffusion capacity for carbon monoxide (DLCO)), predicted FEV1%, predicted DLCO%, maximum oxygen uptake (VO2 max), readmission at 30 days and postoperative complications.

2.3. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 19 package. A univariate analysis was performed to identify preoperative and postoperative differences between the cohort of patients who remained alive and the cohort of patients who died at 30 or 90 days.

Univariate anaysis included Chi-square test or Fisher's test when applicability criteria were not met. Multivariate logistic regression was used to identify risk factors of 90-day mortality.

3. Results

The overall 30-day mortality rate was 1.6% vs. 3.2% for 90-day mortality. Six patients died during first admission (1.6%), while another six patients died after discharge at 31 to 90 postoperative days. The mean number of postoperative days until death was 39 ± 24.12, with a median of 38 and a (13–62) day range.

The mean age of the patients who died early within the first 90 postoperative days was 67.91 ± 7.2 years vs. 65.21 ± 9.4 in patients who survived ($p = 0.371$). In total, 16.7% of patients were female and 83.3% were male, without any gender-based differences observed between the patients who survived and those who did not survive surgery.

The mean length of hospital stay was higher in patients who died within the first 90 postoperative days (14.7 vs. 7.2 days ($p = 0.002$) in the group of survivors).

The rates of mortality at 30 and 90 days by type of resection were 3.7% and 7.4% for pneumonectomy, and 1.6% and 3.6% for lobectomy, respectively. Mortality by type of resection and period (30-day vs 90-day) is shown in Table 1.

Univariate analysis of 30-day mortality revealed that significant differences existed in patients with a history of peripheral vascular disease ($p = 0.033$), postoperative pneumony ($p = 0.029$), postoperative pulmonary or lobar collapse ($p = 0.031$), postoperative arrhythmia ($p < 0.001$), reintubation ($p < 0.001$) and patients how underwent a pneumonectomy as compared to other types of resections ($p = 0.027$). No significant differences were observed in the other variables studied. Table 2 displays the results of univariate analysis

Table 1
Mortality by type of pulmonary resection and by postoperative period.

	n	Period 0–30 days	Period 31–90 days	Global Mortality 90 days
Pneumonectomy	27	1 (3.7%)	1 (3.7%)	2 (7.4%)
Bilobectomy	13	0 (0%)	0 (0%)	0 (0%)
Extended lobectomy	35	1 (2.8%)	0 (0%)	1 (2.8%)
Lobectomy	249	4 (1.6%)	5 (2.0%)	9 (3.6%)
Segmentectomy	23	0 (0%)	0 (0%)	0 (0%)
Wedge resection	31	0 (0%)	0 (0%)	0 (0%)