



Perioperative outcome of lung cancer surgery in women: results from a Spanish nationwide prospective cohort study

Juan J. Fibla¹, Laureano Molins^{1,2}, Florencio Quero³, José Miguel Izquierdo⁴, David Sánchez², Jorge Hernández¹, Clara Bayarri³, Marc Boada², Ángela Guirao², Antonio Cueto³; on behalf of the Group of Postoperative Complications of the Spanish Society of Thoracic Surgeons (GCP-SECT)

¹Department of Thoracic Surgery, Hospital Universitari del Sagrat Cor, Barcelona, Spain; ²Department of Thoracic Surgery, Hospital Clinic, Barcelona, Spain; ³Department of Thoracic Surgery, Hospital Universitario Virgen de las Nieves, Granada, Spain; ⁴Department of Thoracic Surgery, Hospital Universitario Donostia, San Sebastián, Spain

Contributions: (I) Conception and design: JJ Fibla, L Molins, A Cueto; (II) Administrative support: L Molins, A Cueto; (III) Provision of study materials or patients: JM Izquierdo, D Sánchez, J Hernández, Á Guirao; (IV) Collection and assembly of data: F Quero, C Bayarri, M Boada, Á Guirao; (V) Data analysis and interpretation: JJ Fibla; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Juan J. Fibla, MD. Department of Thoracic Surgery, Hospital Universitari del Sagrat Cor, C/Viladomat 288, E-08029 Barcelona, Spain. Email: juanjofibla@yahoo.es.

Background: To assess possible differences in the perioperative profile between men and women in lung cancer surgery.

Methods: A prospective cohort multicenter study was design, in which consecutive patients undergoing curative intent surgery for lung cancer in 24 Thoracic Services throughout Spain were included. Clinical features, tumor- and surgery-related data, postoperative complications, and mortality were recorded.

Results: There were 2,566 men and 741 women. Women were younger than men [mean (SD) age, 61.8 (10.8) *vs.* 66.5 (9.1) years, $P<0.0001$] and showed a more favorable preoperative characteristics, with significantly higher percentages of ECOG grade 0 and lower percentages of active smokers (28.4% *vs.* 33.9%; pack-years 18.8 *vs.* 26.9) and comorbidities [chronic obstructive pulmonary disease (COPD), diabetes, hypertension, cardiac disorders]. There were significant differences ($P<0.001$) in histological types and TNM stages with adenocarcinoma (70.1% *vs.* 46.4%) and IA stage (41.5% *vs.* 33.6%) more frequent in women. The use of VATS or thoracotomy was similar. The rate of pneumonectomy was higher in men (10.9%) than in women (5.1%) ($P<0.001$) but the distributions of other procedures were similar. Postoperative complications (pneumonitis, atelectasis, air leak, hemorrhage, fistula, empyema, wound dehiscence, and need of reintubation) were lower in women. Significant differences ($P<0.0001$) in the severity of postoperative complications (Clavien-Dindo classification) were also found, with higher percentages of grades I (51.6% *vs.* 43%) and II (37.5% *vs.* 33%) and lower percentages of grades III and IV among women. The mean length of hospital stay was 7.8 (7.1) days in men versus 6.3 (5.0) days in women, and the 30-day mortality rate 0.3% in women versus 2.9% in men ($P<0.0001$). The percentage of readmissions within 30 days after surgery was also higher in men (8.6% *vs.* 2.8%).

Conclusions: This multicenter nationwide study of lung cancer surgery with curative intent shows that the perioperative profile is better in women than in men.

Keywords: Lung neoplasms/surgery; female; pneumonectomy; risk factors; sex factors; treatment outcome; tobacco smoking

Submitted Oct 14, 2018. Accepted for publication Mar 11, 2019.

doi: 10.21037/jtd.2019.03.30

View this article at: <http://dx.doi.org/10.21037/jtd.2019.03.30>

Introduction

The epidemiology of lung cancer is changing in many areas or the world in terms of incidence differences by gender (1). Tobacco smoking is the major cause, accounting for 80% of the worldwide lung cancer burden in males and at least 50% in females (2). However, in the last three decades, lung cancer incidence rates have decreased or leveled off among men, but have risen among women (1,3-5). This increase in women (by 600% in the last 50 years) has been defined as a 'contemporary epidemic' (6). Other factors rather than smoking and linked to sex may increase women's susceptibility to lung cancer, including genetic predisposition, exposure to sex hormones, tumor histology and molecular profile (7,8). In addition, several lifestyle and behavioral factors related to smoking habits or environmental and occupational exposures could account for some sex-specific differences (9).

Lung cancer in women has been an increased focus of research, in particular prognosis and treatment outcomes as compared to men. It has been shown that women exhibit greater survival rates regardless of stage, histology, treatment modality or smoking status, even after adjusting for gender-specific life expectancy (10,11). Also, non-smoking status predicts better survival and possibly better response to therapy (12). The etiology behind these observations is theorized to be related to genetic and molecular differences (13) as well as to decreased DNA repair mechanisms, which is thought to lead to increased response to systemic chemotherapy (10). Moreover, better survival in older women may be related to higher prevalence of comorbidities among men of the same age (14).

Despite extensive evidence outlining gender differences in lung cancer, studies with special focus on differences by sex regarding perioperative outcomes are scarce. In an analysis of the Society of Thoracic Surgeon's General Thoracic Database for all patients undergoing resection for lung cancer between 2002 and 2010, in which a total of 34,188 patients (16,643 men and 17,545 women) were considered, significant differences in postoperative complications and in-hospital and 30-day mortality favoring women were found (15). Other studies have demonstrated that male sex is a predictor of prolonged hospital stay and postoperative pulmonary and cardiac complications following surgery (16,17).

To add further evidence of potential differences in the perioperative outcome between men and women undergoing lung cancer surgery, a nationwide prospective

cohort study was conducted. The objective of the study was to assess differential characteristics and postoperative complications of lung cancer surgery in women as compared to men, as well as to determine possible causal factors.

Methods

Study design

This was a retrospective analysis of data collected prospectively in the framework of a national registry set up by the Group of Postoperative Complications of the Spanish Society of Thoracic Surgeons (GCP-SECT). For the period of time between June 1, 2012 and November 30, 2014, data of 3,307 patients treated with some type of pulmonary resection due to bronchogenic carcinoma were systematically and prospectively collected in the GCP-SECT database. A total of 24 thoracic surgery departments each belonging to a different hospital throughout Spain participated in the study. The study was approved by the Ethics Committee of each participating hospitals. Patients provided written informed consent prior to study participation.

Patients

Patients with a histological diagnosis of bronchogenic carcinoma who had undergone surgery with curative intent at the Thoracic Surgery Departments of the participating hospitals in the GCP-SECT project were included in the study. Surgical procedures included wedge lung resection, segmentectomy, lobectomy, bilobectomy or pneumonectomy. Patients undergoing exploratory video-assisted thoracoscopies or thoracotomies, life-saving emergency surgeries and cases with synchronous tumors were excluded. The indication of extent of resection was decided by the primary surgeon.

Data collection

For each patient, data collected were grouped into (I) preoperative general characteristics; (II) tumor-related variables; (III) surgery data; and (IV) postoperative data. Preoperative general characteristics of patients included age, sex, ECOG performance status (18), medical history [smoking, chronic obstructive pulmonary disease (COPD), tuberculosis, obstructive sleep apnea (OSA), atelectasis, pneumonitis, ischemic heart disease, atrial fibrillation,

valve heart disease, hypertension, peripheral vascular disease, diabetes mellitus, obesity (body mass index, BMI >25 kg/m²), stroke, and results of lung function tests. Tumor-related variables included histological type and TNM stage (2009 TNM Classification, 7th edition). Surgery-related data were type of approach, side, type of resection, and intraoperative complications (hypoxia, hemorrhage, arrhythmia, and rib fracture). Postoperative data were length of hospital stay and postoperative complications. Postoperative complications included atelectasis, pneumonitis, hemoptysis, reintubation, pleural effusion, air leak, arrhythmias, pulmonary edema, myocardial infarction, hemorrhage, bronchopleural fistula, pleural empyema, surgical wound infection, and surgical wound dehiscence. Severity of complications was graded according to Clavien-Dindo classification (19). Ninety-day mortality was also recorded.

These data were compiled consecutively and anonymously in a computerized database with online internet access, and the information was recorded in an Excel file stored by the GCP-SECT. All the participating hospitals have followed the guidelines of the Patient Personal Data Protection Law.

Statistical analysis

For the purpose of the present analysis, patients were stratified according to sex in order to examine differential characteristics between men and women. Categorical data are expressed as frequencies and percentages and quantitative data as mean and standard deviation (SD) or median with 95% confidence interval (CI). The Fisher's exact test was used for the comparison of categorical variables between men and women, and the Student's *t*-test for the comparison of continuous variables. In order to determine independent variables associated with lung cancer in women, variables that were found to be statistically significant in the bivariate analysis were included in a stepwise logistic regression model, in which gender (female *vs.* male) was the dependent variable. Statistical significance was set at *P*<0.05. Analyses were carried out using the Statistical Package for the Social Sciences (SPSS) version 9.4 for Windows.

Results

Of the 3,307 patients included in the GCP-SECT database during the study period, 2,566 (77.6%) were men and 741

(22.4%) women, with a mean (SD) age of 65.4 (9.8) years. Men were significantly older than women [66.5 (9.1) *vs.* 61.8 (10.8) years, *P*<0.0001]. The distribution of general preoperative characteristics in men and women is shown in *Table 1*. Women as compared with men showed a better ECOG performance status (e.g., grade 0, 72.1% *vs.* 59.3%); a lower percentage of current smokers (28.4% *vs.* 33.9%) and ex-smokers (34.9% *vs.* 60.7%) as well a higher percentage of never smokers (36.7% *vs.* 5.4%); a fewer number of associated comorbidities, including COPD, diabetes, overweight/obesity, hypertension, ischemic heart disease, myocardial infarction, peripheral vascular disease, and OSA; and higher forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), and carbon monoxide diffusing capacity (DLCO). All these differences were statistically significant.

TNM categories, pathologic tumor stages, and histological types are shown in *Table 2*. There were statistically significant differences between men and women in histological type of tumor (with fewer percentages of epidermoid carcinoma and higher percentages of adenocarcinoma in women), tumor size (higher percentage of T1A in women: 32.7% *vs.* 24.9% in men), nodal status (higher percentage of N0 in women: 78.7% *vs.* 74.5% in men), and TNM staging (higher percentage of stage IA in women: 41.5% *vs.* 33.6% in men).

In relation to surgical-related data, differences in surgical approach and the side of surgery were not found. Video-assisted thoracoscopy (VATS) procedure was used in 30.4% of men and in 34.3% of women, and thoracotomy in 68.5% of men and 65.1% in women. Details of type of lung resection and intraoperative complications are shown in *Table 3*. A significantly higher percentage of men underwent pneumonectomy as compared with women (10.9% *vs.* 5.1%, *P*<0.001). Differences in coverage of the bronchial stump, extended resections or intraoperative complications were not found.

Overall, postoperative complications were more frequent in men than in women, with statistically significant differences in the rates of pneumonitis, atelectasis, air leak, arrhythmia, hemorrhage, bronchopleural fistula, pleural empyema, wound dehiscence, and need of intubation (*Table 4*). Significant differences in the severity of postoperative complications classified according to the Clavien-Dindo score were also observed, with higher percentages of women having grade I, and lower percentages having grades III, IIIa, IIIb, IV, and V as compared with men (*P*<0.001) (*Figure 1*).

The mean length of hospital stay was 7.8 (7.1) days in

Table 1 Preoperative clinical characteristics of patients according to sex

Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Age, years, mean \pm SD	65.4 \pm 9.8	66.5 \pm 9.1	61.8 \pm 10.8	<0.0001
ECOG performance status, n (%)				
0	1,988 (62.2)	1,473 (59.3)	515 (72.1)	<0.0001
1	1,090 (34.1)	908 (36.6)	182 (25.5)	
2	109 (3.4)	92 (3.7)	17 (2.4)	
3	8 (0.3)	8 (0.3)	0	
4	2 (0.1)	2 (0.1)	0	
Smoking status, n (%)				
Smoker	1,042 (32.7)	841 (33.9)	201 (28.4)	<0.0001
Ex-smoker	1,751 (55.0)	1,504 (60.7)	247 (34.9)	
Never smoker	393 (12.3)	133 (5.4)	260 (36.7)	
Smoking pack years, mean \pm SD	50.5 (26.3)	53.7 (26.9)	37.5 (18.8)	<0.0001
Comorbidities, n (%)				
COPD	940 (28.4)	859 (33.5)	81 (10.9)	<0.0001
Atelectasis	25 (0.8)	20 (0.8)	5 (0.7)	1.0
Pneumonitis	68 (2.1)	56 (2.2)	12 (1.6)	0.381
Tuberculosis	93 (2.8)	83 (3.2)	10 (1.3)	0.005
Diabetes mellitus	614 (18.6)	564 (22.0)	68 (9.2)	<0.0001
Overweight/obesity, BMI >25 kg/m ²	187 (5.7)	142 (5.5)	45 (6.1)	0.588
Hypertension	1,479 (44.7)	1,216 (47.4)	263 (35.5)	<0.0001
Ischemic heart disease	304 (9.2)	282 (11.0)	22 (3.0)	<0.0001
Myocardial infarction	128 (3.9)	122 (4.8)	6 (0.8)	<0.0001
Atrial fibrillation	221 (6.7)	188 (7.3)	33 (4.5)	0.005
Valve heart disease	69 (2.1)	54 (2.1)	15 (2.0)	1.0
Peripheral vascular disease	267 (8.1)	250 (9.7)	17 (2.3)	<0.0001
Obstructive sleep apnea	153 (4.6)	135 (5.3)	18 (2.4)	<0.001
Lung function tests, mean \pm SD				
FVC, % predicted	91.5 \pm 23.0	89.3 \pm 23.1	99.5 \pm 20.8	<0.0001
FEV ₁ , % predicted	83.9 \pm 36.7	81.1 \pm 37.0	83.7 \pm 34.1	<0.0001
DLCO, % predicted	78.7 \pm 38.7	78.7 \pm 38.6	78.4 \pm 38.8	0.868
pO ₂ , mmHg	82.3 \pm 33.5	80.2 \pm 13.4	90.3 \pm 68.4	0.001
pCO ₂ , mmHg	41.0 \pm 25.7	40.2 \pm 20.0	44.1 \pm 40.5	0.097
SpO ₂ , %	95.6 \pm 3.2	95.6 \pm 3.3	95.7 \pm 2.8	0.606
FEV ₁ ppo, % predicted	62.4 \pm 16.9	60.3 \pm 16.2	70.1 \pm 17.4	<0.0001
DLCO ppo, % predicted	56.8 \pm 17.2	56.6 \pm 17.2	57.5 \pm 17.2	0.519
Exercise stress test, METS	18.4 \pm 5.7	18.5 \pm 5.6	17.7 \pm 6.7	0.428

ECOG, Eastern Cooperative Oncology Group; SD, standard deviation; COPD, chronic obstructive pulmonary disease; BMI, body mass index; FVC, forced vital capacity; FEV₁, forced expiratory volume in one second; DLCO, carbon monoxide diffusing capacity; pO₂, partial oxygen pressure; pCO₂, partial carbon monoxide pressure; SpO₂, peripheral capillary oxygen saturation; ppo, postoperative; METS, metabolic equivalents.

Table 2 Tumor-related characteristics in men and women with lung cancer

Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Histological type, n=3,272 (%)				
Epidermoid	1,212 (36.8)	1,098 (43.0)	114 (15.4)	<0.0001
Adenocarcinoma	1,704 (51.7)	1,185 (46.4)	519 (70.1)	
Undifferentiated large-cell	96 (2.9)	81 (3.2)	15 (2.0)	
Undifferentiated small-cell	28 (0.9)	22 (0.9)	6 (0.8)	
Adenosquamous	55 (1.7)	48 (1.9)	7 (0.9)	
Poorly-differentiated	23 (0.7)	16 (0.6)	7 (0.9)	
Other	175 (5.3)	103 (4.0)	72 (9.7)	
T (tumor size), n=3,272 (%)				
T1A	871 (26.6)	632 (24.9)	239 (32.7)	<0.001
T1B	533 (16.3)	415 (16.3)	118 (16.1)	
T2A	999 (30.5)	780 (30.7)	219 (29.9)	
T2B	272 (8.3)	233 (9.2)	39 (5.3)	
T3	451 (13.8)	366 (14.4)	85 (11.6)	
T4	103 (3.1)	79 (3.1)	24 (3.3)	
Tx	43 (1.3)	35 (1.4)	8 (1.1)	
N (regional lymph nodes), n=2,345 (%)				
N0	2,449 (75.5)	1,876 (74.5)	573 (78.7)	<0.001
N1	456 (14.0)	384 (15.3)	72 (9.9)	
N2	337 (10.4)	255 (10.1)	82 (11.3)	
N3	3 (0.1)	2 (0.1)	1 (0.1)	
M (distant metastasis), n=3,156 (%)				
M0	3,089 (97.9)	2,396 (98.0)	693 (97.5)	0.615
M1A	31 (1.0)	23 (0.9)	8 (1.1)	
M1B	36 (1.1)	26 (1.1)	10 (1.4)	
TNM stage, n=3,200 (%)				
IA	1,133 (35.5)	832 (33.6)	301 (41.5)	<0.001
IB	688 (21.6)	541 (21.9)	147 (20.3)	
IIA	454 (14.2)	369 (14.9)	85 (11.7)	
IIB	371 (11.6)	309 (12.5)	62 (8.6)	
IIIA	426 (13.3)	328 (13.3)	98 (13.5)	
IIIB	37 (1.2)	27 (1.1)	10 (1.4)	
IV	63 (2.0)	45 (1.8)	18 (2.5)	
Complete response	28 (0.9)	24 (1.0)	4 (0.6)	

TNM stage refers to pathologic staging.

Table 3 Surgical-related data in men and women with lung cancer

Variables	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Type of resection, n=3,268 (%)				
Sublobar resection	409 (12.5)	324 (12.7)	85 (11.6)	0.447
Segmentectomy	106 (3.2)	78 (3.1)	28 (3.8)	0.342
Wedge resection	303 (9.3)	246 (9.7)	57 (7.8)	0.128
Lobar resection				
Right upper lobe	857 (26.2)	661 (26.0)	196 (26.8)	0.702
Left upper lobe	648 (19.8)	503 (19.8)	145 (19.8)	0.013
Middle lobe	112 (3.4)	84 (3.3)	28 (3.8)	0.489
Right lower lobe	373 (11.4)	277 (10.9)	96 (13.1)	0.099
Left lower lobe	386 (11.8)	280 (11.0)	106 (14.5)	0.013
Bilobectomy				
Right upper and middle lobes	67 (2.1)	51 (2.0)	16 (2.2)	0.767
Right lower and middle lobes	102 (3.1)	80 (3.1)	22 (3.0)	0.904
Pneumonectomy				
Right lung	119 (3.6)	110 (4.3)	9 (1.2)	<0.001
Left lung	195 (6.0)	167 (6.6)	28 (3.8)	0.004
Bronchial stump coverage, n=264 (%)				
Muscle	57 (21.6)	50 (21.3)	7 (24.1)	0.810
Pleura	69 (26.1)	61 (25.9)	8 (27.6)	0.825
Pericardial fat pad	58 (22.0)	54 (23.0)	4 (13.8)	0.489
Other	18 (6.8)	14 (6.0)	4 (13.8)	0.344
No coverage	26 (23.5)	56 (23.8)	6 (20.7)	0.819
Intraoperative complications, n=3,307 (%)				
Arrhythmia	39 (1.2)	32 (1.2)	7 (0.9)	0.698
Hypoxia	89 (2.7)	61 (2.4)	28 (3.8)	0.052
Hemorrhage	61 (1.8)	51 (2.0)	10 (1.3)	0.282
Rib fracture	55 (1.7)	47 (1.8)	8 (1.1)	0.192
Other	35 (1.1)	26 (1.0)	9 (1.2)	0.683

Percentages calculated excluding missing data.

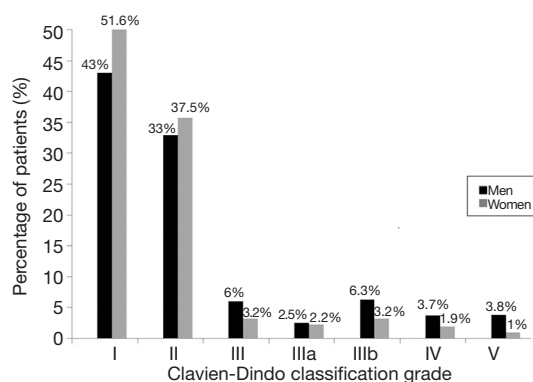
men and 6.3 (5.0) days in women ($P<0.0001$). This longer length of stay was mainly related to air leaks. The 90-day mortality rate was significantly lower in women as compared with men (0.3% *vs.* 2.5%, $P<0.0001$). A total of 109 patients (8.6% men *vs.* 2.8% women, $P<0.001$) were readmitted to the hospital within 30 days of primary surgery, with a mean length of stay of 9.2 (7.8) days for men and 5.6 (4.1) for

women ($P=0.158$).

Results of the logistic regression analysis are shown in *Table 5*. It was found that women were younger than men, were more likely to be non-smokers, had better FVC values, more stage T1A tumors, and lower incidence of COPD, diabetes mellitus, ischemic heart disease, and peripheral vascular disease as well as epidermoid tumors,

Table 4 Postoperative complications of lung cancer surgery in men and women

Complication	Total (n=3,307)	Men (n=2,566)	Women (n=741)	P value
Postoperative complication, n (%)				
Pneumonia	204 (6.2)	177 (6.9)	7 (0.9)	<0.001
Hemoptysis	6 (0.2)	6 (0.2)	0	0.348
Atelectasis	191 (5.8)	166 (6.5)	25 (3.4)	0.001
Pleural effusion	70 (2.1)	56 (2.2)	14 (1.9)	0.771
Air leak	355 (10.7)	311 (12.1)	44 (5.9)	<0.0001
Arrhythmia	208 (6.3)	183 (7.1)	25 (3.4)	0.0001
Hemorrhage	121 (3.7)	110 (4.3)	11 (1.5)	<0.001
Bronchopleural fistula	38 (1.1)	35 (1.4)	3 (0.4)	0.03
Pleural empyema	31 (0.9)	29 (1.1)	2 (0.3)	0.02
Wound dehiscence	12 (0.4)	12 (0.5)	0	0.05
Wound infection	20 (0.6)	19 (0.7)	1 (0.1)	0.062
Myocardial infection	5 (0.2)	4 (0.2)	1 (0.1)	1.0
Need of intubation	57 (1.7)	55 (2.1)	2 (0.3)	<0.001
Other	133 (4.0)	99 (3.9)	34 (4.6)	0.395
Hospital stay, days, mean \pm SD	7.5 \pm 6.7	7.8 \pm 7.1	6.3 \pm 5.0	<0.0001
90-day mortality rate, n (%)	66 (2.0)	64 (2.5)	2 (0.3)	<0.0001

**Figure 1** Distribution of postoperative complications according to severity in men and women with lung cancer.

right pneumonectomy, and air leaks. Other variables were not significant in the multivariable analysis.

Discussion

This multicenter nationwide prospective cohort study of a large sample of patients with lung cancer undergoing

surgical treatment with curative intent shows that the perioperative profile is better in women than in men. Notably, women were younger and had a lower rate of concomitant chronic diseases as compared with men. Also there were more women non-smokers than men. Differences in histology, with adenocarcinoma as the most common tumor in women were also remarkable. Postoperative complications and 30-day mortality were lower in women too.

The more favorable perioperative profile in women might be related to the consistent evidence of superior response to lung cancer treatment and survival benefit in women reported in numerous studies, including systematic reviews and meta-analysis (4,11,20-25). Also, longer survival duration and response to chemotherapy in patients with untreated early-stage lung cancer have been reported (26), suggesting that lung cancer has a different natural history among women. This survival advantage appears to be multifactorial, with hormonal influences, genetic, metabolic, lifestyle and environmental factors (27,28) other than smoking playing a role. However, although cancer mortality predictions for 2015 in the EU

Table 5 Results of multivariable analysis

Variables	Odds ratio (95% confidence interval)	P value
Age	0.96 (0.947 to 0.972)	<0.001
Current smoking (yes vs. no)	7.05 (5.162 to 9.605)	<0.001
COPD (yes vs. no)	0.45 (0.323 to 0.620)	<0.001
Diabetes mellitus (yes vs. no)	0.52 (0.362 to 0.758)	0.0006
Ischemic heart disease (yes vs. no)	0.48 (0.274 to 0.825)	0.008
Peripheral vascular disease (yes vs. no)	0.41 (0.215 to 0.785)	0.007
FVC	1.01 (1.007 to 1.019)	<0.001
Epidermoid histological type (yes vs. no)	0.46 (0.342 to 0.608)	<0.001
T1A stage (yes vs. no)	1.40 (1.091 to 1.806)	0.008
Right pneumonectomy (yes vs. no)	0.22 (0.077 to 0.650)	0.006
Air leak (yes vs. no)	0.50 (0.324 to 0.776)	0.001

COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity.

showed an overall favorable trend, with an estimated 26% fall in men and 31% in women since 1988, a 9% rise in lung cancer rates were expected, becoming the cancer with the highest rate, reaching and possibly overtaking breast cancer was predicted (29). In a comprehensive global analysis of lung mortality in women using the World Health Organization's Cancer Mortality Database covering 65 populations on six continents, rates among young women (30–49 years) were stable or declining in 47 of 52 populations examined, whereas in older women (50–74 years) rates were increasing for more than half of populations examined, including most countries in Southern, Eastern, and Western Europe and South America (30). In this line, changes in aging of the population the risk factors for cancer could contribute 37.9% to the burden of lung cancer mortality expected to be observed among Spanish women during 2018–2022 (31). Interestingly, according to Bayesian prediction of lung cancer mortality among women in Spain, by 2020 lung cancer mortality rates may exceed those of breast cancer for ages 55–74 years, possibly because of the prevalence of smoking among women, and the screening for and more effective treatment of breast cancer (32).

In our study, women presenting with lung cancer were significantly younger than men even though the rate of active smokers was lower and they had smoked fewer cigarettes. Women appear to have an increased susceptibility cancer-causing chemicals or carcinogens in

tobacco than men (33,34). Nicotine appears to trigger the gastrin releasing peptide receptor gene, which is also more active in women (35).

Chronic concomitant diseases were less frequently present in women than in men, but comorbidity does not appear to have an independent prognostic effect in patients with non-small cell lung cancer (36). Other findings of our study, such as a better performance status on diagnosis, higher percentage of women with IA stage (N0 78.7% in women *vs.* 74.5% in men, $P<0.001$) and adenocarcinoma as the most common histological type are consistent with previous studies (5,9,15). It is unclear why women are more predisposed to adenocarcinoma than men. Given that small-cell cancer cases are related to heavier smoking history, low exposure to cigarettes but increased sensitivity to their carcinogens may explain why the incidence of adenocarcinoma is higher among women (20). Also, estrogen may affect molecular and histological features of lung cancer, and it may explain some of the differences between genders (4,6,7).

The higher rate of pneumonectomies in men as compared with women found in the present study is consistent with data of other clinical series (37,38). A high rate of pneumonectomies worsens postoperative outcome with an increased risk of complications and negative impact on the quality of life. Indeed, in our study, women were less likely to develop postoperative complications as compared with men. The most frequent complication was air leak,

which was observed in 12.1% of men and 5.9% of women. Postsurgical atelectasis occurred in 6.5% of men and 3.4% of women. It has been reported that these complications are associated with patient age, being more frequent over 70 years of age than in yours age groups (39). This lower rate of postoperative complications among women was associated with a shorter duration of hospitalization. The mortality rate at 30 days was also significantly lower in women.

Conclusions

The results of this multicenter nationwide study of lung cancer surgery with curative intent show that the perioperative profile is better in women than in men. Further studies focused on the epidemiology and biology of lung cancer may lead to improvement of patient-specific management according to gender in the future.

Acknowledgements

The authors thank all members of the Group of Postoperative Complications of the Spanish Society of Thoracic Surgeons (GCP-SECT) for their contribution to the study and Marta Pulido, MD, PhD, for editing the manuscript and editorial assistance.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study protocol was approved by the participating centers involved in the Postoperative Complications Study Group of the Spanish Society of Thoracic Surgery (GCP-SECT). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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Cite this article as: Fibla JJ, Molins L, Quero F, Izquierdo JM, Sánchez D, Hernández J, Bayarri C, Boada M, Guirao Á, Cueto A; on behalf of the Group of Postoperative Complications of the Spanish Society of Thoracic Surgeons (GCP-SECT). Perioperative outcome of lung cancer surgery in women: results from a Spanish nationwide prospective cohort study. *J Thorac Dis* 2019;11(4):1475-1484. doi: 10.21037/jtd.2019.03.30