

Journal Pre-proof

Comparison of 5-year survival and disease recurrence after trisegmentectomy or left upper lobectomy: a propensity score analysis of the national GEVATS database

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ORIGINAL ARTICLE

Comparison of 5-year survival and disease recurrence after
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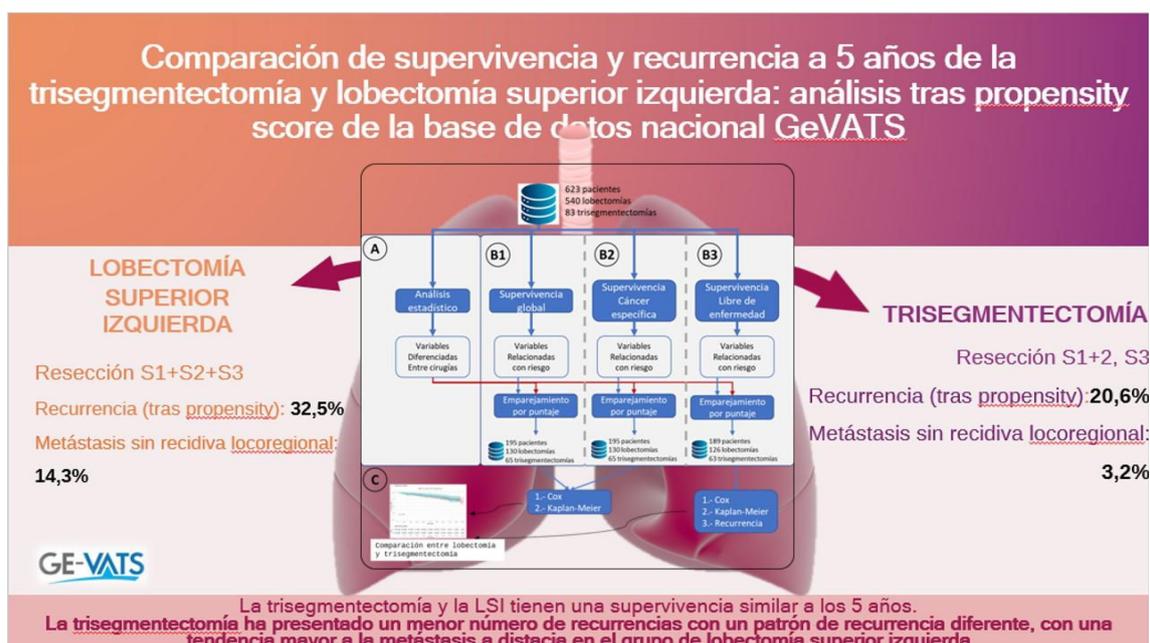
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Graphical abstract



INTRODUCTION

The extent of resections in lung tumors has been widely studied in recent years, and sublobar resection has been shown to to have similar survival rates to lobectomy in peripheral lesions measuring less than 2 cm with N0 status (1,2).

Lingula-sparing trisegmentectomy is a multisegmentary technique that lies midway between segmentectomy and lobectomy. It is considered by some authors to be equivalent to right upper lobectomy with preservation of the middle lobe (3). Studies suggest that this surgical approach achieves good oncological outcomes beyond the limits established in clinical trials for conventional segmentectomies (4,5,6,7,8,9). Although evidence in this area is limited by the lack of studies, no differences in terms of survival were observed in 2 studies in disease stages IA and IB (5,6), although the patient numbers in stage IB were low (9).

Our objective was to compare survival and recurrence after trisegmentectomy versus left upper lobectomy using propensity score techniques applied to the Spanish Video-Assisted Thoracic Surgery (GEVATS) database. Specifically,

nearest neighbor propensity score matching methods were used. Complications between both types of resection were also compared.

MATERIALS AND METHODS

Database: We analyzed data from the Spanish Society of Thoracic Surgery GEVATS database, which recruited patients undergoing anatomic pulmonary resections between December 20, 2016 and March 20, 2018 who were followed up until July 31, 2022 (10). This database prospectively included patients from 33 thoracic surgery units. The study was approved by the ethics committees of all participating centers. In this analysis, we included the 30 centers in which oncological follow-up for survival had been completed.

Of the 3533 patients included in the registry, patients with lung cancer (3085) were selected, and of these, individuals with a follow-up at least 90 days post-procedure (2726) were included in the study cohort. All left trisegmentectomies (anatomic resection S1-S3) and all left upper lobectomies in this group were selected, resulting in a total of 623 patients, comprising 540 lobectomies and 83 trisegmentectomies.

Statistical analysis: The following variables were compared for the 2 types of resection: age, smoking habit, tumor size, histological type, radiological density of the tumor, surgical access, forced expiratory volume in the first second (FEV1), diffusing capacity of the lungs for carbon monoxide (DLCO), hypertension, chronic heart failure, ischemic heart disease, arrhythmia, stroke, peripheral vascular disease, diabetes, cN status by positron emission tomography/computed tomography (PET/CT), pTNM, and postoperative N. Continuous variables were compared using a t-test, and categorical variables were compared using Fisher's exact test. A difference in any variable between both groups was considered significant if the p value was less than 0.05 (Figure 1A).

Survival analysis: A survival analysis of each variable was performed using the Cox regression model. Specifically, 3 separate survival analyses were performed: (I) overall survival, in which the event being studied was all-cause mortality; (II)

lung cancer-specific survival, in which the event being studied was cancer-specific mortality; and (III) disease-free survival, in which the event being studied was recurrence. A variable was considered to affect each of the analyses if the likelihood ratio test of the model had a p value less than 0.05 (Figure 1B).

Creation of comparable groups: Variables that were significant in the statistical analysis or survival analysis were used to perform propensity score matching using the 2:1 nearest neighbor technique (Matchit library). Once comparable groups had been created, group homogeneity was verified using the t-test (continuous variables) and the Fisher's exact test (discrete variables) for the aforementioned variables (Figure 1B).

Risk comparison between surgeries: Once the comparable groups had been created, overall survival, lung cancer-specific survival and disease-free survival were estimated using Kaplan-Meier curves, comparing both groups with the log-rank test. A Cox regression was also performed to compare the risk between both surgical approaches in all patients, using inverse probability of treatment weighting (IPTW) methodology (11). This method uses all patients, conferring to each one a weight according to the value obtained in the propensity score. These weights were calculated for each patient as $1/\text{propensity score}$ for patients with trisegmentectomy and $1/(1-\text{propensity score})$ for the remaining patients, where *propensity score* is the score obtained.

Recurrence type analysis: Finally, recurrence and the recurrence pattern were compared using Fisher's test.

Subgroup analysis of tumors measuring between 20 and 30 mm: the methodology described above and in Figure 1 was applied to a subgroup of patients with tumor size between 20 and 30 mm.

The statistical analysis was performed using R software and the Matchit library was used to calculate the propensity score.

RESULTS

Complete set analysis: In patients with a diagnosis of lung cancer and survival of more than 90 days, 540 left upper lobectomies and 83 trisegmentectomies were

retrieved. Statistical analysis was performed to compare the variables of interest between the lobectomy and trisegmentectomy subgroups. The results of this analysis are summarized in Table 1. The variables associated with significant differences (p value < 0.05) were: tumor size, tumor density, surgical access, cN, postoperative N and pTNM. Among these variables, tumor size is notable, with an average of 30 mm in lobectomies and 18.7 mm in trisegmentectomies. The differences in pTNM (p value = $5.32e-08$) between the 2 types of surgeries are also worth pointing out.

Complete set survival analysis: Table 2 shows the results for the 3 survival analyses (overall, cancer-specific, and disease-free survival). This table shows the p value of the Cox regression likelihood ratio test. See Supplementary Table 1 for the p value corresponding to each Cox regression coefficient.

In the overall survival analysis, the following variables were significant (p value < 0.05): tumor size, histological subtype, FEV1, DLCO, stroke, diabetes, cN, postoperative N, and pTNM.

In the analysis of cancer-specific survival, the following variables were significant: tumor size, histological subtype, surgical access, FEV1, DLCO, diabetes, cN, postoperative N and pTNM.

In the disease-free survival analysis, the following variables were significant: tumor size, histological subtype, surgical access, FEV1, DLCO, arrhythmia, diabetes, cN, postoperative N, and pTNM. In this analysis, 26 patients were excluded due to a lack of information on recurrence, leaving a total of 597 patients, with 517 lobectomies and 80 trisegmentectomies.

Creation of comparable groups using the complete set: Propensity score matching was performed with the variables that were significant in these analyses (Figure 1B). In total, 3 types of matching were conducted, 1 for each type of analysis. To be able to use all variables, patients with incomplete information were excluded. In this way, a group of 195 patients with 130 left upper lobectomies and 65 trisegmentectomies was obtained for the first 2 analyses and 1 group of 189 patients was obtained for the third analysis, consisting of 126 lobectomies and 63 trisegmentectomies. Table 3 shows the variables used for each of the 3 analyses, the number of patients with complete and incomplete

information, and finally the number of patients in each group after the propensity score procedure.

No differences were found between the 2 surgical groups for the 3 analyses in any of the technical aspects (fissureless lobectomy or the need for conversion to thoracotomy), or in postoperative complications or hospital stay. Table 4 provides information on complications after propensity scoring for overall survival. Supplementary Tables 2 and 3 show these results for the other 2 analyses.

The type of surgery does not affect the risk of survival or recurrence in the complete set: A Cox regression was performed to determine if trisegmentectomy increases the risk of survival, cancer-specific survival, and disease-free survival compared to lobectomy. This Cox regression was conducted with comparable groups obtained from propensity score matching for the 3 analyses. The Kaplan-Meier curve was also applied for the 3 analyses and compared with the log-rank test (Figure 2). Supplementary Tables 5, 6 and 7 show the 95% confidence interval for the risk in each case.

In the case of overall survival, the p value obtained is not significant ($p = 0.76$) showing that the type of surgery does not affect the risk of survival. Furthermore, the Kaplan-Meier curves corresponding to the types of surgery (Figure 2) show no significant differences (log-rank test, $p = 0.76$).

With regard to cancer-specific survival, the results are very similar, with a p value of 0.62 for the Cox regression and a p value of 0.62 in the log-rank test comparing the 2 Kaplan-Meier curves (Figure 2).

In the case of disease-free survival, the p value of the Cox regression is 0.15 and the p value for comparison of the 2 Kaplan-Meier curves (Figure 2) is 0.15. These results show that the type of surgery does not affect the risk of recurrence.

Comparable groups determined by propensity score matching were used in the 3 analyses: 291 patients were excluded out of 486 cases with complete data in the first 2 analyses; and 281 were excluded out of 470 cases with complete data in the third analysis. To avoid patient loss, a Cox regression was also performed with all patients using the IPTW method. The Cox regression p value for overall

survival was 0.23; for cancer-specific survival, it was 0.73; and for disease-free survival, it was 0.28. These results are consistent with previous reports suggesting that trisegmentectomy does not affect the risk of overall survival or disease-free survival compared to lobectomy.

Disease-free survival results for the complete set:

The analysis of disease-free survival using the set of patients with complete information (597 patients, 517 lobectomies and 80 trisegmentectomies) showed a recurrence rate of 37.52% for lobectomies and 28.75% for trisegmentectomies. This difference was not significant according to Fisher's exact test (p value = 0.1359).

In comparable groups (Table 5) comprising 189 patients (126 lobectomies and 63 trisegmentectomies), recurrence was 32.53% after lobectomy, compared to 20.63% after trisegmentectomy. This difference was not significant according to Fisher's exact test (p value = 0.12). It should be noted that, in the lobectomy group, 14.3% of patients had distant recurrence compared to 3.2% in the trisegmentectomy group (p = 0.02). If we combine these recurrences with mixed recurrence rates (locoregional + distant), a total of 19% of the patients in the lobectomy group had recurrence compared to 11% in the trisegmentectomy group (p = 0.21). Table 5 shows the recurrence rates in both groups after the creation of comparable groups.

Similar results in patients with tumors measuring 20-30 mm:

In this second analysis, patients with tumors measuring between 20 mm and 30 mm were studied, resulting in a total of 97 patients, of whom 82 underwent lobectomies and 15 trisegmentectomies.

The variables used for the propensity score for the 3 types of analyses are shown in Supplementary Table 4. After propensity score matching, a subset of 45 patients (30 left upper lobectomies and 15 trisegmentectomies) was obtained for the 3 analyses. For the disease-free survival analysis, 3 patients with incomplete data were excluded from the calculation of the propensity score.

For the overall survival analysis, there is no difference in risk between the 2 types of surgery (p value = 0.834 for the Cox regression and p value = 0.83 for the log-rank test). For the cancer-specific survival analysis, the Cox regression p value was 0.59, and also 0.59 for the log-rank test. Finally, for the disease-free survival analysis, the p value of the Cox regression was 0.646, and for the log-rank test, it was 0.65 (Figure 3).

The results obtained using the IPTW method are also consistent, with p values for the 3 analyses of 0.582, 0.743 and 0.611, respectively.

Table 6 summarizes the type of recurrence for each surgical approach. Differences are observed, but they are not statistically significant.

DISCUSSION

Lobectomy has been the mainstay of early-stage lung cancer treatment since Ginsberg et al. published their findings in 1995 (12). Two more recent clinical trials concluded that survival is similar in N0 patients with peripheral tumors measuring less than 2 cm undergoing sublobar resections.

Trisegmentectomy is an intervention that lies midway between segmentectomy and lobectomy. Some authors believe that left upper lobe trisegmentectomy is similar to right upper lobectomy, as the lingula and the middle lobe maintain a similar anatomic relationship with their respective upper segments (3).

Some clear differences can be observed in the published literature on segmentectomies compared with trisegmentectomies. First, the quality of the studies on the indications for segmentectomy is high as it is based on 2 randomized clinical trials. In these reports, trisegmentectomies were included in the segmentectomy group, so the indication for tumors measuring less than 2 cm and N0 seems clear. In contrast, for studies conducted specifically to compare trisegmentectomy with left upper lobectomy, the literature is based on observational studies and, as such, is not of such high quality (4,5,6,7,8). In a recent meta-analysis (9) combining the 5 most important comparative studies on the subject (4,5,6,7,8), trisegmentectomy appeared to be equivalent to left upper lobectomy in terms of survival in disease up to and including stage IB tumors measuring up to 4 cm (5,7) or even 5 cm (6).

In our study, we compared overall, cancer-specific and disease-free survival between the 2 types of surgery. It should be noted that differences in survival between the groups may be due to cofactors such as tumor size, tumor density, pTNM, FEV1, DLCO, etc. If one of these cofactors differs significantly between the 2 surgical groups (e.g., tumor density, Table 1), the difference or lack of difference in survival between the 2 types of surgery may be due to the difference in that factor (e.g. tumor density) rather than to the different interventions. To avoid this effect, we applied the 2:1 nearest neighbor technique to create comparable groups. In this way, we ensured that the difference or the absence of difference in survival between the 2 types of surgery was due to the type of surgery and not to the cofactor. The results showed no differences in overall survival, cancer-specific survival and disease-free survival in comparable groups after propensity score matching. We should remember that patient data are lost when the 2:1 nearest neighbor technique is applied, so the results obtained are true for the subset of patients selected after the propensity score. To address this limitation, we completed the statistical analysis using the IPTW technique. This method reduces the possible bias that results from having non-comparable groups (13). Specifically, with the IPTW technique, the comparison of survival is made using all patients, weighing the importance of each patient according to the score obtained in the propensity score. With this analysis, we generated results consistent with those obtained with the 2:1 nearest neighbor technique.

A particularly interesting finding in our cohort was the pattern of recurrence: the lobectomy group showed a greater tendency to distant metastases than the trisegmentectomy group, with 18 patients (14.3%) vs 2 patients (3.2%), respectively ($p = 0.02$). If we add mixed dissemination to the distant dissemination observed in lobectomies versus trisegmentectomies (19% vs 11%; $p = 0.21$), the trend remains higher in the lobectomy group, although statistical significance is lost. Although this relationship and its causes are not known, after analyzing the variables used to obtain the propensity score, no errors were observed that might explain these findings. This difference is also seen in other studies. For example, Aprile et al. (7) reported that 20.2% of patients treated with lobectomy had distant metastases compared to 9.4% of patients treated with trisegmentectomy ($p = 0.067$). Zhou et al. (8) also identified this difference, but to a lesser degree due to

a lower rate of recurrences, probably associated with the histological characteristics of their Asian cohort. In fact, 96.7% of the lobectomy group and 96% of the trisegmentectomy group in Zhou's cohort were adenocarcinomas, compared to 50.4% and 62.6%, respectively, in our patients. Likewise, only 17% of Zhou's cohort had solid tumors compared to >80% of ours. This trend was also clearly observed in the above-mentioned meta-analysis (9), where statistical significance was not reached due to low case numbers. Significance may be reached if our data were added to the patient numbers. In our opinion, this finding is of the utmost importance, and we believe that it should be further evaluated in subsequent research on this type of surgery.

All studies on trisegmentectomies share the limitations of a retrospective design and a low number of patients in stage IB. Although the general conclusion is that this surgery is justified for tumors beyond stage IA, none of the authors included more than 20 cases in stage IB or higher. Our study is similarly limited, since we recruited only 45 patients with tumors measuring more than 2 cm (30 lobectomies and 15 trisegmentectomies). Nevertheless, the pattern of recurrence in these patients is surprisingly similar to that of the whole group.

Conclusions

Trisegmentectomy and left upper lobectomy show comparable 5-year survival rates. In our database, recurrence after trisegmentectomy was lower than after left upper lobectomy, while the pattern of recurrence was different for both surgical approaches, with a greater tendency to distant metastasis after left upper lobectomy.

The number of cases with tumors measuring 20-30 mm was low but the patterns of recurrence were similar.

For this reason, we believe that trisegmentectomy should be considered as the first surgical option in all these cases.

Conflicts of interest: The authors state that they have no conflict of interests.

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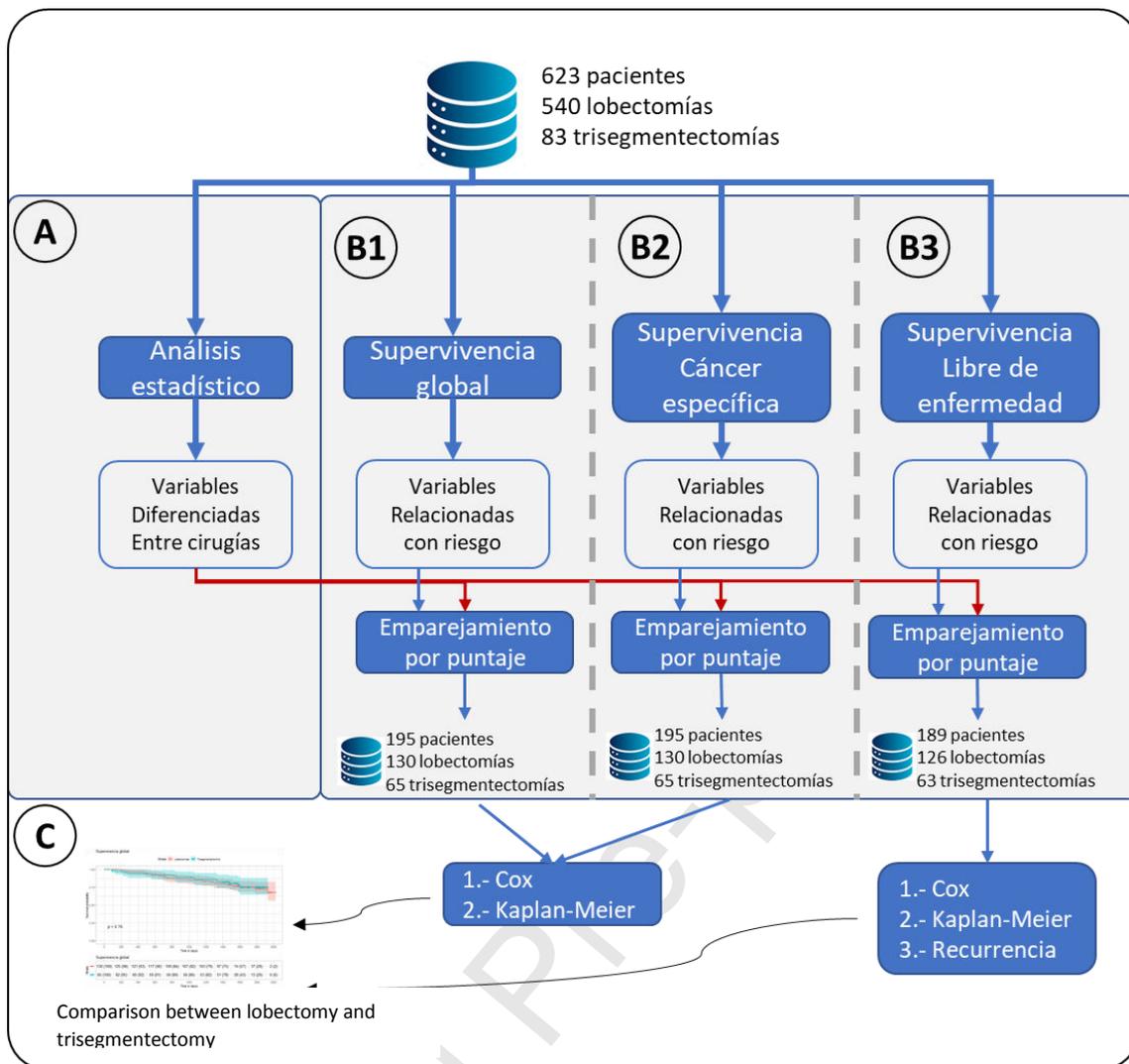


Figure 1. Flowchart of the main methodology used. A) represents the statistical analysis performed comparing lobectomies and trisegmentectomies. This statistical analysis consisted of a t-test for continuous variables and Fisher's test for categorical variables. Statistical significance was set at a p value <0.05, obtaining a list of "variables that differed between surgeries". B) represents the 3 types of survival analyses performed: B1: overall survival in which the event was death; B2: cancer-specific survival, in which the event was cancer-specific mortality; and B3: disease-free survival. A Cox regression was performed for the 3 analyses, and a variable was considered to have an effect if the p value of the Cox regression likelihood ratio test was <0.05. For the 3 analyses, propensity score matching was performed in which the "variables that differed between surgeries" plus the variables related to risk were considered. C) Once the groups were obtained after propensity score matching, the effect of the type of surgery on the risk of overall survival, cancer-specific survival and disease-free survival was analyzed. Finally, for B3, the type of recurrence was analyzed using Fisher's test.

623 pacientes 540 lobectomías 83 trisegmentectomías	623 patients 540 lobectomies 83 trisegmentectomies
A	A
Análisis estadístico	Statistical analysis
Variables diferenciadas entre cirugías	Variables that differed between surgeries
B1	B1
Supervivencia global	Overall survival
Variables relacionadas con el riesgo	Risk-related variables
Emparejamiento por puntaje	Propensity score matching
195 pacientes 130 lobectomías 65 trisegmentectomías	195 patients 130 lobectomies 65 trisegmentectomies
B2	B2

Supervivencia cáncer específica	Cancer-specific survival
Variables relacionadas con el riesgo	Risk-related variables
Emparejamiento por puntaje	Propensity score matching
195 pacientes 130 lobectomías 65 trisegmentectomías	195 patients 130 lobectomies 65 trisegmentectomies
B3	B3
Supervivencia libre de enfermedad	Disease-free survival
Variables relacionadas con el riesgo	Risk-related variables
Emparejamiento por puntaje	Propensity score matching
189 pacientes 126 lobectomías 63 trisegmentectomías	189 patients 126 lobectomies 63 trisegmentectomies
C	C
1. Cox 2. Kaplan-Meier	1. Cox 2. Kaplan-Meier
1. Cox 2. Kaplan-Meier 3. Recurrencia	1. Cox 2. Kaplan-Meier 3. Recurrence
Comparación entre lobectomía y trisegmentectomía	Comparison between lobectomy and trisegmentectomy

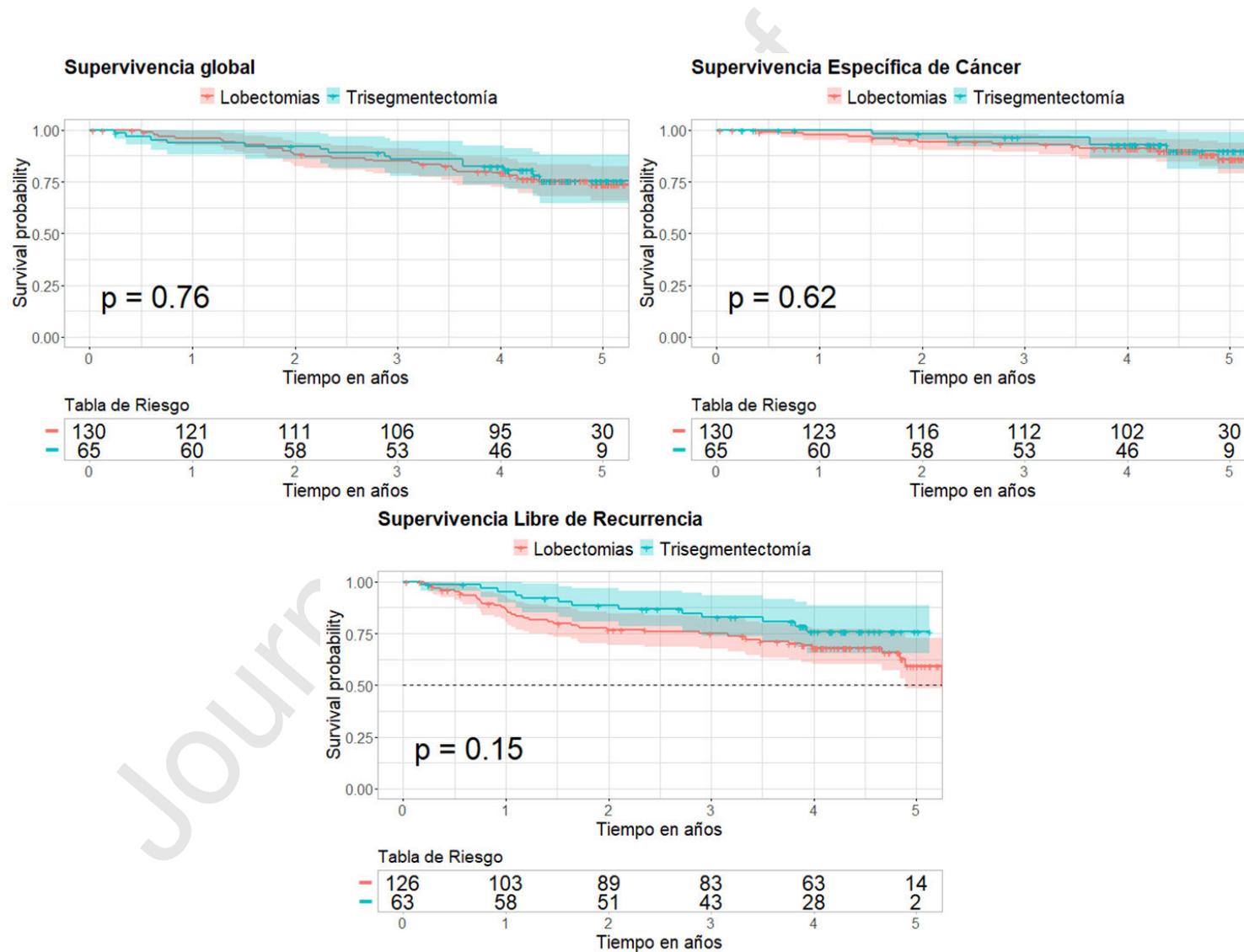


Figure 2. Kaplan-Meier curves after propensity score matching for overall survival, cancer-specific survival, and disease-free survival analyses. The 95% confidence interval and the p value corresponding to the log-rank test are shown for the 3 analyses.

Supervivencia global Lobectomías Trisegmentectomía	Overall survival Lobectomies Trisegmentectomy
Tiempo en años	Time in years
Supervivencia específica de cáncer Lobectomías Trisegmentectomía	Cancer-specific survival Lobectomies Trisegmentectomy
Tiempo en años	Time in years
Tabla de Riesgo	Risk table
Supervivencia libre de recurrencia Lobectomías Trisegmentectomía	Disease-free survival Lobectomies Trisegmentectomy

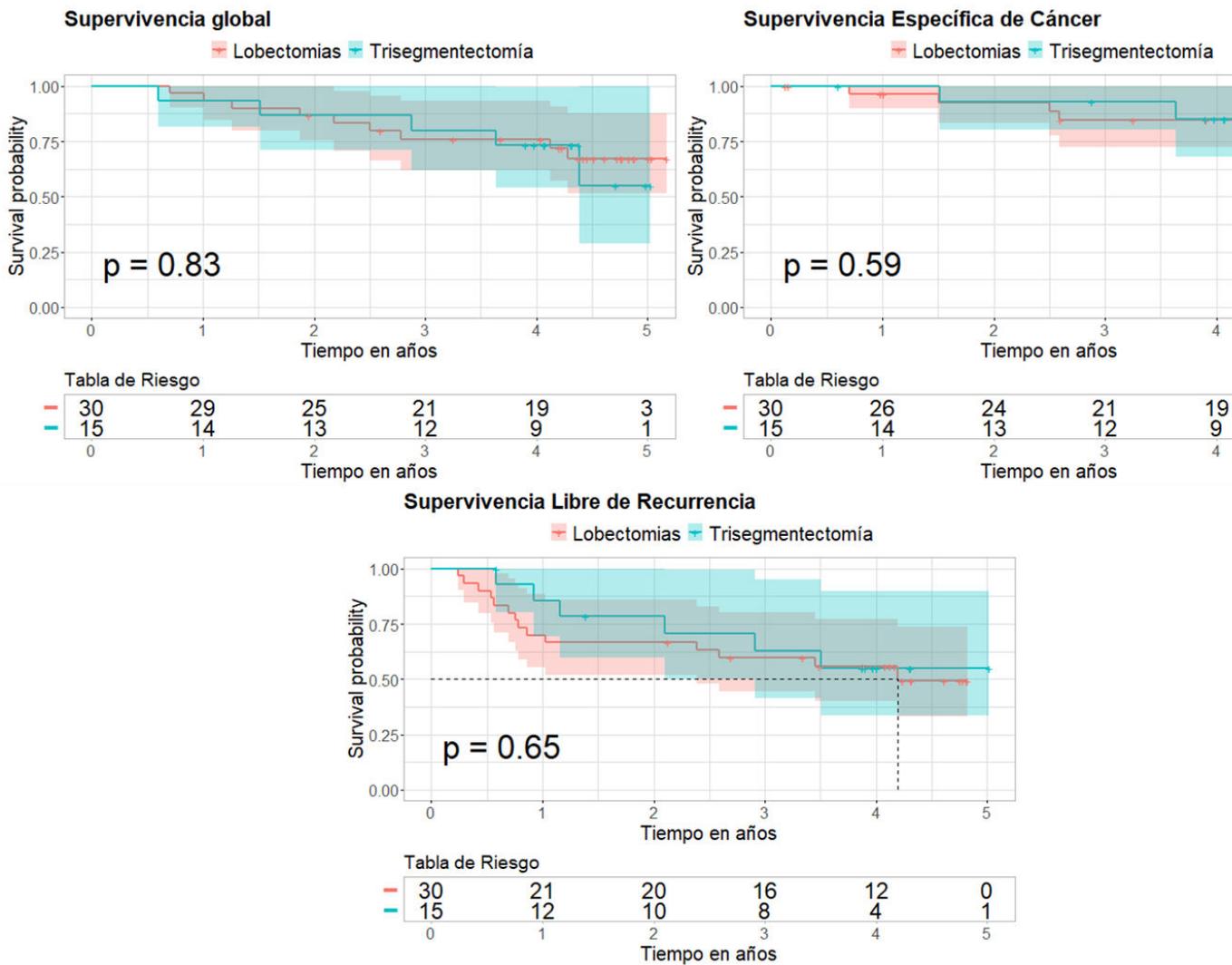


Figure 3. Kaplan-Meier curves after propensity score matching for overall survival, cancer-specific survival, and disease-free survival analyses in the subgroup of patients with tumors measuring 20-30 mm. The 95% confidence interval and the p value corresponding to the log-rank test are shown for the 3 analyses.

Supervivencia global	Overall survival
Lobectomías Trisegmentectomía	Lobectomies Trisegmentectomy
Tiempo en años	Time in years
Supervivencia específica de cáncer	Cancer-specific survival
Lobectomías Trisegmentectomía	Lobectomies Trisegmentectomy
Tiempo en años	Time in years
Tabla de Riesgo	Risk table
Supervivencia libre de recurrencia	Disease-free survival
Lobectomías Trisegmentectomía	Lobectomies Trisegmentectomy

Table 1: Baseline characteristics of both groups (lobectomies and segmentectomies) prior to propensity score matching. The p value was calculated from the t-test for continuous variables and the Fisher's exact test for categorical variables. The lobectomy and trisegmentectomy columns are presented as mean for continuous variables and percentage for categorical variables.

	Lobectomy	Trisegmentectomy	P value
Age (years)	66.1	66.9	0.47
Smoking habit			
Active smoker (%)	31	33.7	
Former smoker >12 months (%)	15.6	10.9	
Former smoker <12 months (%)	41.5	41	
Never smoker (%)	11	3.6	0.35
Tumor size (mm)	30.1	18.7	< 0.01
Histological subtype			
Adenocarcinoma (%)	50.4	62.6	
Squamous cell carcinoma (%)	37.8	25.3	
Large cell neuroendocrine carcinoma (%)	3.9	3.6	
Atypical carcinoid (%)	0.9	0	
Small cell (%)	1.3	1.2	
Other histologies (%)	1.11	2.41	
Typical carcinoid (%)	2.78	4.82	0.18
Large cell carcinoid carcinoma (%)	1.85	0	
Tumor density			
Ground-glass (%)	1.7	6	
Mixed (%)	12.8	14.4	
Solid (%)	85.5	79.6	0.04
Surgical access			
Open (%)	45.7	28.9	
VATS (%)	54.3	71.1	<0.01
FEV1 (%)	87.1	83.3	0.14
DLCO (%)	82	80.8	0.7
High blood pressure (%)	47	51.8	0.48
Heart failure (%)	2.2	3.6	0.44
Myocardial ischemia (%)	8.9	8.4	1
Arrhythmia (%)	7.8	7.2	1
Stroke (%)	4.4	9.6	0.06
Peripheral vascular disease (%)	9	9.6	0.84
Diabetes (%)	21.5	15.7	0.25
cN_PET/CT			
N0 (%)	74.6	93.6	
N1 (%)	9.8	1.3	
N2 (%)	13.5	2.6	
N3 (%)	2.1	2.6	<0.01
Postoperative N			
N0 (%)	76.82	90.13	
N1 (%)	14.39	3.70	
N2 (%)	8.60	6.17	
N3 (%)	0.19	0	0.02
pTNM			
0 (%)	0.57	4.94	
Occult carcinoma (%)	0.18	0	
I (%)	54.92	80.25	
II (%)	27.27	6.18	
III (%)	15.15	4.94	
IV (%)	1.89	3.7	<0.01

Table 2: Cox regression survival analysis for each variable selected separately, prior to propensity score matching. The first column shows the p value of the overall survival analysis. The second column shows cancer-specific survival analysis and the last column shows disease-free survival. The p value is that of the Cox regression likelihood ratio test.

	P value (I)	P value (II)	P value (III)
Age (years)	0.31	0.81	0.71
Smoking habit	0.611	0.54	0.9
Tumor size	<0.01	<0.01	<0.01
Histological subtype	0.04	0.02	0.15
Tumor density	0.26	0.12	0.06
Surgical access	0.07	<0.01	<0.01
FEV1	0.01	0.02	0.02
DLCO	0.01	0.03	0.03
Hypertension	0.50	0.83	0.82
Heart failure	0.29	0.85	0.86
Myocardial ischemia	0.45	0.49	0.09
Arrhythmia	0.77	0.13	<0.01
Stroke	0.03	0.4	0.52
Peripheral vascular disease	0.12	0.34	0.6
Diabetes	<0.01	<0.01	<0.01
cN_PET/CT	<0.01	<0.01	<0.01
Postoperative N	<0.01	<0.01	<0.01
pTNM	<0.01	<0.01	<0.01

Table 3: Variables used for propensity score matching for each type of survival analysis.

	Overall survival		Cancer-specific survival		Disease-free survival	
	Tumor size Tumor density Surgical access cN PET/CT Postoperative N pTNM Histological subtype FEV1 DLCO Stroke Diabetes		Tumor size Tumor density Surgical access cN PET/CT Postoperative N pTNM Histological subtype FEV1 DLCO Diabetes		Tumor size Histological subtype Surgical access cN PET/CT Postoperative N pTNM FEV1 DLCO Arrhythmia Diabetes	
	Lobectomy	Trisegment- ectomy	Lobectomy	Trisegment- ectomy	Lobectomy	Trisegment- ectomy
Incomplete	119	18	119	18	110	17
Complete	421	65	421	65	407	63
After propensity score matching	130	65	130	65	126	63

Table 4: Technical factors, complications and hospital stay of overall survival analysis after propensity score matching.

	Lobectomy	Trisegmentectomy	p value
Conversion	14.42% Yes	15.38% Yes	1
Fissureless technique	42.31% Yes	49.23% Yes	0.36
Unplanned admission to intensive care	3.08% Yes	4.62% Yes	0.69
Reintervention	3.85% Yes	1.54% Yes	0.669
Air leak >5 days	14.62% Yes	9.23% Yes	0.37
Atelectasis	6.15% Yes	6.15% Yes	1
Pneumothorax or pleural effusion	1.54% Yes	1.54% Yes	1
Pneumonia	3.08% Yes	6.15% Yes	0.44
Respiratory distress	1.54% Yes	0% Yes	0.55
Bronchopleural fistula	0% Yes	0% Yes	1
Empyema	0.77% Yes	0% Yes	1
Pulmonary thromboembolism	0% Yes	0% Yes	1
Arrhythmia	6.15% Yes	9.23% Yes	0.56
Hospital stay	7.769	6.092	0.08
Death at 90 days	0% Dead	0% Dead	1

Table 5. Type of recurrence in 189 patients (126 lobectomies and 63 trisegmentectomies) included in the disease-free survival analysis after propensity score matching. Number of cases of each type of recurrence and percentage of the total number of cases in each group are shown. The p value is that of the Fisher's exact test result.

	Lobectomy (126)	Trisegmentectomy (63)	P value
Locoregional	17 (13.5%)	6 (9.5%)	0.06
Distant	18 (14.3%)	2 (3.2%)	
Mixed	6 (4.8%)	5 (7.9%)	
Total recurrence	41 (32.5%)	13 (20.7%)	

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Table 6. Pattern of recurrence in 45 patients (30 lobectomies and 15 trisegmentectomies) included in the disease-free survival analysis after propensity score matching in subgroup of patients with tumors measuring 20-30 mm. Number of cases of each type of recurrence and percentage of the total number of cases in each group are shown. The *p* value is that of the Fisher's exact test result.

	Lobectomy (30)	Trisegmentectomy (15)	<i>P</i> value
Locoregional	5 (16.6%)	4 (26.6%)	
Distant	6 (20%)	0%	
Mixed	3 (10%)	2 (13.3%)	
Total recurrence	14 (46.6%)	6 (40%)	<i>p</i> = 0.28

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Tabla S1. P.value correspondiente a los coeficientes de la regresión de COX previa al puntaje de propensión. La primera columna corresponde al p.value del análisis de supervivencia global. La segunda columna al análisis de supervivencia específico de cáncer y la última columna a la supervivencia libre de enfermedad.

	P value (I)	P value (II)	P value (III)
Edad (años)	0.31	0.80	0.71
Hábito tabáquico			
Fumador activo (%)	0.38	0.30	0.43
Ex fumador > 12meses (%)	0.22	0.50	0.51
Ex fumador <12meses (%)	0.72	0.52	0.65
Nunca fumador (%)	Referencia	Referencia	Referencia
Tamaño tumoral (mm)	6.82E-09	2.32E-10	4.83E-05
Subtipo histológico			
Adenocarcinoma (%)	Referencia	Referencia	Referencia
Carcinoma escamoso (%)	0.38	0.48	0.60
Neuroendocrino de cél. grandes (%)	0.03	0.01	0.09
Carcinoide atípico (%)	0.71	0.99	0.87
Células pequeñas (%)	0.01	0.01	0.23
Otras histologías (%)	0.42	0.56	0.87
Carcinoide típico (%)	0.15	0.99	0.05
Carcinoide de cél. Grandes (%)	0.84	0.87	0.82
Densidad tumoral			
Vidrio deslustrado (%)	Referencia	Referencia	Referencia
Mixto (%)	0.49	0.99	0.41
Sólido (%)	0.26	0.99	0.14
Acceso quirúrgico			
Abierta (%)	Referencia	Referencia	Referencia
VATS (%)	0.07	0.007	0.009
FEV1 (%)	0.01	0.018	0.016
DLCO (%)	0.01	0.027	0.026

HTA (%)	0.5	0.826	0.825
Fallo cardíaco (%)	0.3	0.853	0.857
Isquemia cardiaca (%)	0.45	0.491	0.090
Arritmia (%)	0.77	0.141	0.040
ICTUS (%)	0.03	0.395	0.523
Vasculopatía periférica (%)	0.13	0.340	0.603
Diabetes (%)	0.002	0.048	0.021
cN_PET/CT			
N0 (%)	Referencia	Referencia	Referencia
N1 (%)	0.001	2.97E-05	1.43E-06
N2 (%)	0.08	0.243	0.644
N3 (%)	0.62	0.716	0.483
N postoperatoria			
N0	Referencia	Referencia	Referencia
N1	1.80E-05	7.14E-10	1.19E-05
N2	0.00719	0.00311	1.98e-0.5
PTNM			
0	Referencia	No hay casos	Referencia
I	0.598	Referencia	0.599
II	0.669	1.04E-07	0.2705
III	0.491	5.35E-08	0.1122
IV	0.436	0.00172	0.0378

Tabla S2. Aspectos técnicos, complicaciones y estancia hospitalaria tras puntaje por propensión con análisis de supervivencia específica de cáncer.

	Lobectomía	Trisegmentectomía	Valor p
Conversión	12.38% Yes	15.38% Yes	0.624
Técnica fissure-less	37.69% Yes	49.23% Yes	0.127
Admisión no planeada en cuidados intensivos	3.08% Yes	4.62% Yes	0.688
Reintervención	2.31% Yes	1.54% Yes	1
Fuga aérea >5días	13.08% Yes	9.23% Yes	0.489
Atelectasia	5.38% Yes	6.15% Yes	1
Neumotórax o derrame pleural	1.54% Yes	1.54% Yes	1
Neumonía	3.85% Yes	6.15% Yes	0.484
Distress respiratorio	0.77% Yes	0% Yes	1
Fístula broncopleurales	0% Yes	0% Yes	1
Empiema	0% Yes	0% Yes	1
Tromboembolismo pulmonar	0% Yes	0% Yes	1
Arritmia	6.15% Yes	9.23% Yes	0.557
Estancia hospitalaria	6.9	6.092	0.347
Mortalidad a los 90 días	0% Dead	0% Dead	1

Tabla S3. Aspectos técnicos, complicaciones y estancia hospitalaria tras puntaje por propensión con análisis de supervivencia libre de recurrencia.

	Lobectomía	Trisegmentectomía	Valor p
Conversión	13.13% Yes	16% Yes	0.627
Técnica fissure-less	38.1% Yes	47.62% Yes	0.215
Admisión no planeada en cuidados intensivos	0.79% Yes	4.76% Yes	0.109
Reintervención	2.38% Yes	1.59% Yes	1
Fuga aérea >5días	16.67% Yes	9.52% Yes	0.270
Atelectasia	3.17% Yes	4.76% Yes	0.688
Neumotórax o derrame pleural	1.59% Yes	1.59% Yes	1
Neumonía	2.38% Yes	6.35% Yes	0.224
Distress respiratorio	0% Yes	0% Yes	1
Fístula broncopleurales	0.79% Yes	0% Yes	1
Empiema	0.79% Yes	0% Yes	1
Tromboembolismo pulmonar	0% Yes	0% Yes	1
Arritmia	7.14% Yes	7.94% Yes	1
Estancia hospitalaria	6.706349206	6.048	0.447
Mortalidad a los 90 días	100% Alive	100% Alive	1

Tabla S4. Variables utilizadas para el puntaje por propensión para cada tipo de análisis de supervivencia para el subgrupo de tamaño de tumor entre 20 y 30 mm.

Supervivencia Global	Supervivencia específica de cáncer	Supervivencia libre de recurrencia
Hábito tabático FEV1 cardiopatía isquémica	cardiopatía isquémica PTNM	Acceso quirúrgico FEV1 cardiopatía isquémica

	Lobectomías	Trisegmen tectomy	Lobectomías	Trisegmen tectomy	Lobectomías	Trisegmen tectomy
Incompleta	0	0	1	0	0	0
Completa	82	15	81	15	79	15
Después del puntaje de propensión	30	15	30	15	30	15

Tabla S7. Intervalo de confianza del 95% para el curva de supervencia global después del puntaje de propensión. La primera tabla corresponde a los pacientes con lobectomía y la tabla inferior a los pacientes con trisegmentectomía.

Lobectomia						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
0.501	127	1	0.992	0.00784	0.977	1
0.616	125	1	0.984	0.01109	0.963	1
0.621	124	1	0.976	0.01355	0.95	1
0.674	123	1	0.968	0.01559	0.938	0.999
0.832	122	1	0.96	0.01737	0.927	0.995
1.279	121	1	0.952	0.01895	0.916	0.99
1.309	120	1	0.945	0.02039	0.905	0.985
1.418	119	1	0.937	0.0217	0.895	0.98
1.503	118	1	0.929	0.02293	0.885	0.975
1.708	117	1	0.921	0.02406	0.875	0.969
1.736	116	1	0.913	0.02513	0.865	0.963
1.881	115	1	0.905	0.02614	0.855	0.958
1.884	114	1	0.897	0.02709	0.845	0.952
1.963	113	1	0.889	0.02799	0.836	0.946
1.985	112	1	0.881	0.02884	0.826	0.939
2.092	110	1	0.873	0.02967	0.817	0.933
2.357	109	1	0.865	0.03046	0.807	0.927
2.689	108	1	0.857	0.03121	0.798	0.92
2.762	107	1	0.849	0.03193	0.789	0.914
3.14	106	1	0.841	0.03262	0.779	0.907
3.209	105	1	0.833	0.03328	0.77	0.901
3.431	103	1	0.825	0.03392	0.761	0.894

3.535	101	1	0.817	0.03455	0.752	0.887
3.54	100	1	0.809	0.03516	0.742	0.88
3.573	99	1	0.8	0.03574	0.733	0.874
3.915	96	1	0.792	0.03633	0.724	0.867
4.085	88	1	0.783	0.03701	0.714	0.859
4.167	86	1	0.774	0.03769	0.703	0.851
4.178	84	1	0.765	0.03835	0.693	0.844
4.361	75	1	0.755	0.03917	0.682	0.835
4.884	41	1	0.736	0.04232	0.658	0.824
5.284	13	1	0.679	0.06697	0.56	0.824

Trisegmentectomía						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
0.238	65	1	0.985	0.0153	0.955	1
0.356	63	1	0.969	0.0216	0.928	1
0.597	62	1	0.953	0.0263	0.903	1
0.753	61	1	0.938	0.0302	0.88	0.999
1.514	60	1	0.922	0.0335	0.859	0.99
2.245	58	1	0.906	0.0365	0.837	0.981
2.33	57	1	0.89	0.0391	0.817	0.97
2.875	55	1	0.874	0.0416	0.796	0.96
2.932	54	1	0.858	0.0439	0.776	0.948
3.636	53	1	0.842	0.046	0.756	0.937
3.639	52	1	0.826	0.0478	0.737	0.925
4.041	45	1	0.807	0.0502	0.715	0.912
4.32	31	1	0.781	0.0549	0.681	0.897
4.383	28	1	0.753	0.0596	0.645	0.88

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Tabla S7. Intervalo de confianza del 95% para el curva de supervencia específica de cáncer después del puntaje de propensión. La primera tabla corresponde a los pacientes con lobectomía y la tabla inferior a los pacientes con trisegmentectomía.

Lobectomia						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
0.405	127	1	0.992	0.00784	0.977	1
0.621	125	1	0.984	0.01109	0.963	1
0.841	124	1	0.976	0.01355	0.95	1
1.279	123	1	0.968	0.01559	0.938	0.999
1.503	122	1	0.96	0.01737	0.927	0.995
1.771	119	1	0.952	0.019	0.916	0.99
1.963	117	1	0.944	0.02051	0.905	0.985
2.689	114	1	0.936	0.02194	0.894	0.98
3.14	112	1	0.928	0.02328	0.883	0.974
3.455	110	1	0.919	0.02455	0.872	0.968
3.535	108	1	0.911	0.02575	0.861	0.962
4.279	88	1	0.9	0.02746	0.848	0.956
4.701	53	1	0.883	0.03176	0.823	0.948
4.884	39	1	0.861	0.03818	0.789	0.939

Trisegmentectomía						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
1.51	60	1	0.983	0.0165	0.951	1
2.25	58	1	0.966	0.0234	0.922	1
3.64	53	1	0.948	0.0292	0.893	1
3.64	52	1	0.93	0.0338	0.866	0.999
4.38	28	1	0.897	0.0461	0.811	0.992

Tabla S7. Intervalo de confianza del 95% para el curva de supervencia libre de recurrencia después del puntaje de propensión. La primera tabla corresponde a los pacientes con lobectomía y la tabla inferior a los pacientes con trisegmentectomía.

Lobectomia						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
0.203	124	1	0.992	0.00803	0.976	1
0.238	123	1	0.984	0.01131	0.962	1
0.244	122	1	0.976	0.0138	0.949	1
0.296	120	1	0.968	0.0159	0.937	0.999
0.364	119	1	0.96	0.01772	0.925	0.995
0.504	116	1	0.951	0.01941	0.914	0.99
0.553	115	1	0.943	0.02093	0.903	0.985
0.578	113	1	0.935	0.02234	0.892	0.979
0.709	112	1	0.926	0.02365	0.881	0.974
0.72	111	1	0.918	0.02487	0.87	0.968
0.75	110	1	0.91	0.026	0.86	0.962
0.756	109	1	0.901	0.02707	0.85	0.956
0.769	108	1	0.893	0.02808	0.84	0.95
0.884	106	1	0.885	0.02905	0.829	0.943
0.961	105	1	0.876	0.02997	0.819	0.937
0.994	104	1	0.868	0.03084	0.809	0.93
1.013	103	1	0.859	0.03167	0.799	0.924
1.016	102	1	0.851	0.03246	0.79	0.917
1.057	101	1	0.842	0.03322	0.78	0.91
1.092	100	1	0.834	0.03393	0.77	0.903
1.177	99	1	0.826	0.03462	0.76	0.896
1.224	98	1	0.817	0.03528	0.751	0.889

1.41	97	1	0.809	0.03591	0.741	0.882
1.459	96	1	0.8	0.03651	0.732	0.875
1.634	94	1	0.792	0.0371	0.722	0.868
1.7	93	1	0.783	0.03766	0.713	0.861
1.717	92	1	0.775	0.0382	0.703	0.853
1.99	91	1	0.766	0.03872	0.694	0.846
2.357	86	1	0.757	0.03928	0.684	0.838
2.888	85	1	0.748	0.03982	0.674	0.831
3.162	83	1	0.739	0.04035	0.664	0.823
3.326	80	1	0.73	0.04089	0.654	0.815
3.343	78	1	0.721	0.04142	0.644	0.807
3.474	77	1	0.711	0.04193	0.634	0.799
3.759	74	1	0.702	0.04245	0.623	0.79
3.882	71	1	0.692	0.04299	0.613	0.782
3.986	65	1	0.681	0.04362	0.601	0.772
4.665	30	1	0.659	0.04771	0.571	0.759
4.841	22	1	0.629	0.05413	0.531	0.744
4.89	18	1	0.594	0.06136	0.485	0.727
5.248	6	1	0.495	0.1038	0.328	0.746

Trisegmentectomía						
Time	n.risk	n.event	Survival rate	std.err	lower 95% IC	upper 95% IC
0.175	63	1	0.984	0.0157	0.954	1
0.753	60	1	0.968	0.0225	0.925	1
0.92	59	1	0.951	0.0274	0.899	1
1.095	58	1	0.935	0.0315	0.875	0.999
1.155	57	1	0.919	0.0349	0.853	0.99
1.517	54	1	0.902	0.0382	0.83	0.98

1.643	53	1	0.884	0.0411	0.808	0.969
2.103	51	1	0.867	0.0438	0.785	0.957
2.716	45	1	0.848	0.0469	0.761	0.945
2.916	44	1	0.829	0.0496	0.737	0.932
3.502	40	1	0.808	0.0525	0.711	0.918
3.819	37	1	0.786	0.0555	0.685	0.903
3.932	31	1	0.761	0.0592	0.653	0.886

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