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ORIGINAL ARTICLE

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Perioperative outcomes of segmentectomies versus lobectomies in high-risk patients: an ESTS database analysis

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Key question

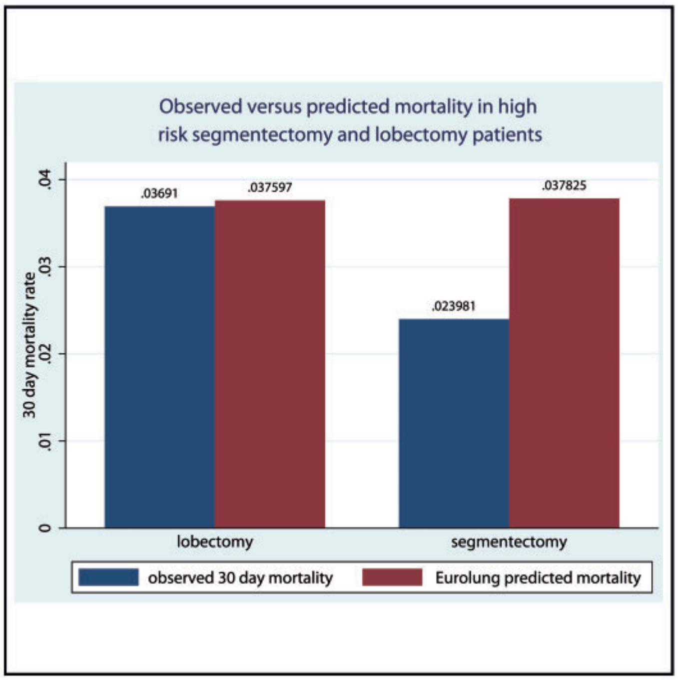
What is the 30-day mortality rate of high-risk patients undergoing segmentectomy compared to lobectomy?

Key finding(s)

In high-risk patients, the relative risk of 30-day mortality with segmentectomy is 0.65 compared to that with lobectomy.

Take-home message

This finding supports the use of a compromised segmentectomy for high-risk patients judged oncologically appropriate.



Abstract

OBJECTIVES: We queried the European Society of Thoracic Surgeons (ESTS) database with the aim to assess cardiopulmonary morbidity and 30-day mortality of segmentectomies and lobectomies in patients with a Eurolung-predicted mortality above the upper interquartile and classified as high risk.

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METHODS: A total of 61 492 patients registered in the ESTS database (2007–2018) and submitted to lobectomy (55 353) or segmentectomy (6139) were divided into high risk or low risk according to a Eurolung-predicted mortality cut-off of 2.5% (corresponding in our population to the upper interquartile). Predicted versus observed mortalities were compared within each type of operation by using binomial test of proportion. Observed morbidity and mortality rates were compared between the 2 procedures using the χ^2 test.

RESULTS: A total of 14 007 lobectomies and 1251 segmentectomies were classified as high risk. In the high-risk group, the cardiopulmonary morbidity and 30-day mortality rates observed in segmentectomies were lower than in lobectomies (morbidity: 12% vs 17%, $P < 0.0001$; mortality: 2.4% vs 3.7%, $P = 0.018$). In segmentectomy patients, the observed mortality rate was lower than the Eurolung-predicted one (2.4% vs 3.8%, $P = 0.009$), while in the lobectomy patients, there was no difference between observed and predicted mortality (3.7% vs 3.8%, $P = 0.9$). In the low-risk group, the cardiopulmonary morbidity and 30-day mortality rates observed in segmentectomies were lower than in lobectomies (morbidity: 4.5% vs 7.8%, $P < 0.0001$; mortality: 0.6% vs 1.0%, $P = 0.01$). In segmentectomy patients, the observed mortality rate was lower than the Eurolung-predicted one (0.6% vs 1.0%, $P = 0.0003$), while in the lobectomy patients, there was no difference between observed and predicted mortality (1.0% vs 1.1%, $P = 0.06$).

CONCLUSIONS: Segmentectomy was found associated with a 0.65 relative risk of mortality rate compared to lobectomy in patients deemed at higher surgical risk.

Keywords: Non-small-cell lung cancer • Lobectomy • Segmentectomy • Mortality • Surgical risk

ABBREVIATIONS

BMI	Body mass index
ESTS	European Society of Thoracic Surgeons
MITS	Minimally invasive thoracic surgery
ppoFEV1	Predicted postoperative forced expiratory volume in 1s

INTRODUCTION

Sublobar resections have become increasingly popular, especially for patients with early stage non-small-cell lung cancer deemed unfit for a lobectomy due to underlying comorbidities or compromised cardiorespiratory function.

In the most recent report of the European Society of Thoracic Surgeons (ESTS) database (http://www.ests.org/_userfiles/pages/files/database_reports/ESTS%202019%20Silver%20Book.pdf) inclu ding patients operated from 2007 to December 2018, the proportion of anatomic segmentectomies was 6.5% of all operations performed for primary lung cancer and 40% of them were performed by a minimally invasive approach.

The cardiopulmonary morbidity and mortality rates following segmentectomies were reported to be lower compared to those after lobectomies (10.5% vs 17.3% and 1.6% vs 2.0%, respectively) [1]. However, the exact quantification of the perioperative benefit of segmentectomy over lobectomy was not clearly defined in high-risk patients. In fact, the intentional or compromised nature of the sublobar resection is not reported in the ESTS database and the only way to extrapolate this information is an indirect measure of the patient estimate of risk using existing risk models.

For this reason, we queried the ESTS database with the aim to assess cardiopulmonary morbidity and 30-day mortality of segmentectomies and lobectomies in patients with a Eurolung-predicted mortality above the upper interquartile and classified as high risk.

METHODS

This is a retrospective analysis on 61 492 patients registered in the ESTS database (2007–2018) and submitted to lobectomy (55 353) or segmentectomy (6139). Pathological diagnosis was consistent with benign or non-neoplastic disease in 4251 patients, primary lung cancer in 53 543 and lung metastases in 3698 patients.

The study was reviewed by the Research and Innovation Department of the principal investigator hospital and classified as service evaluation not requiring review by a Research Ethics Committee.

The ESTS database is an online registry launched in 2007. It is free for members and voluntary. Its main purpose is to collect data for monitoring the thoracic surgical activity in Europe and develop risk-adjusting models to audit the quality of care across the Continent. Data can be input online through the database website or harvested yearly from existing institutional data sets after an automated variable matching process. Currently, the database includes information submitted by 270 European units from 25 countries. Only a minor portion of data in the ESTS database are audited and precisely for those units which participate in the ESTS Institutional Accreditation programme.

The variables and outcomes are defined and standardized according to the joint Society of Thoracic Surgeons (STS)-ESTS definitions [2].

For the purpose of this analysis, the patients were divided into high-risk or low-risk groups according to their Eurolung-predicted mortality rate. The cut-off value selected for categorizing the patients in the 2 groups was 2.5% corresponding to the upper interquartile of the Eurolung-predicted mortality rate in the entire population. To estimate the predicted mortality, the parsimonious Eurolung2 model was used [3]. Ninety-two per cent of patients included in this analysis were part of the sample used to develop the parsimonious Eurolung model. The parsimonious Eurolung2 model includes the following variables to estimate the risk of 30-day mortality following lung resection: age, sex, body mass index (BMI), predicted postoperative forced expiratory volume in 1 s (ppoFEV1), pneumonectomy (as opposed to lesser resections) and open approach (as opposed to minimally invasive surgery). The following logit [3] was used to estimate the risk: $-6.350 + 0.047 \times \text{Age} + 0.889 \times \text{Male} - 0.055 \times \text{BMI} - 0.010 \times \text{ppoFev1} + 0.892 \times \text{Thoracotomy} + 0.983 \times \text{Pneumonectomy}$. Due to the inclusion criteria of this study, the variable 'pneumonectomy' is always coded as 0 (absent).

All outcome variables in the patients included in the analysis were complete. Among the predictors, ppoFEV1 and BMI had

Table 1: Characteristics of all patients included in this study by type of operation

	Lobectomy (*n* = 55 353)	Segmentectomy (*n* = 6139)
Age (years), mean (SD)	64.0 (10.5)	63.7 (11.3)
Male gender, *n* (%)	35 162 (64)	3570 (58)
BMI (kg/m^2), mean (SD)	25.8 (4.8)	26.0 (5.0)
ppoFEV1%, mean (SD)	75.3 (19.3)	78.6 (21.0)
CAD, *n* (%)	4895 (8.8)	421 (6.9)
CVD, *n* (%)	1829 (3.3)	194 (3.2)
Diabetes, *n* (%)	2472 (4.5)	314 (5.1)
Neoadjuvant chemotherapy, *n* (%)	4214 (7.6)	335 (5.5)
MITS, *n* (%)	15 493 (28)	2314 (38)
Pathological diagnosis, *n* (%)		
Primary lung cancer	49 434 (89)	4109 (67)
Benign	3243 (6)	1008 (16)
Metastases	2676 (5)	1022 (17)
Eurolung-predicted mortality risk, % (*SD*)	1.80 (1.4)	1.59 (1.3)

BMI: body mass index; CAD: coronary artery disease; CVD: cerebrovascular disease; MITS: minimally invasive thoracic surgery; ppoFEV1: predicted postoperative forced expiratory volume in 1 s; SD: standard deviation.

9% and 10% of missing data, respectively. These variables were estimated by multiple imputation technique using the variables with no missing values as predictors. 10 imputed data sets were used to apply the above Eurolung equation to estimate the risk.

Predicted versus observed mortalities were compared within each type of operation by using binomial test of proportion. Observed morbidity and mortality rates were compared between the 2 procedures using the χ^2 test.

Analyses were exploratory in nature and there was no prespecified plan to adjust for multiple comparisons.

A logistic regression analysis was also performed to test the independent association of the extent of resection with 30-day mortality adjusting for several baseline confounders included in the Eurolung model (age, sex, BMI, ppoFEV1, extent of resection, surgical access) and other covariates not already included in the Eurolung model (presence of coronary artery disease, cerebrovascular disease, diabetes, neoadjuvant chemotherapy and diagnosis).

All tests were performed on Stata 15.1 statistical software (Stata Corp., College Station, TX, USA).

RESULTS

The median Eurolung-predicted mortality rate in the entire population was 1.4% (interquartile range 0.7–2.5). Using the predicted mortality upper quartile (2.5%) to classify patients as high risk, 14 007 lobectomies and 1251 segmentectomies were classified as high risk.

Table 1 shows the characteristics of patients included in this study by type of operation.

In the high-risk group, 3.8% of the segmentectomies were performed using a minimally invasive approach compared to 2% of the lobectomies ($P < 0.0001$). This low proportion of operations performed by minimally invasive thoracic surgery (MITS) is the result of the surgical access being one of the factors compounding the Eurolung2 model used to classify the patients into high

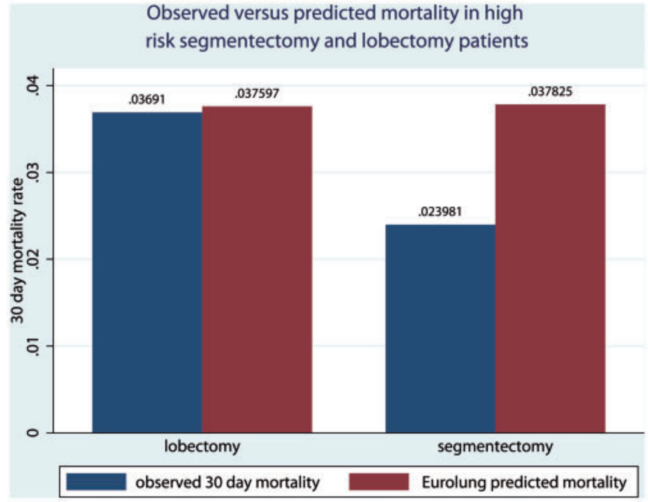

Figure 1: Observed versus Eurolung-predicted 30-day mortality after segmentectomy and lobectomy in high-risk patients.

risk. Sixty per cent of segmentectomy patients were older than 70 years of age compared to 56% of lobectomy ones ($P = 0.01$). Ninety-eight per cent of patients in both groups were male ($P = 0.9$) (Table 2).

The cardiopulmonary morbidity rate observed in segmentectomies was lower than in lobectomies (149/1251, 12% vs 2411/14 007, 17%, $P < 0.0001$). Likewise, the 30-day mortality rate observed in segmentectomies was lower than in lobectomies (30/1251, 2.4% vs 517/14 007, 3.7%, $P = 0.018$) (Fig. 1).

In segmentectomy patients, the observed mortality rate was lower than the Eurolung-predicted one (2.4% vs 3.8%, $P = 0.009$), while in the lobectomy patients, there was no difference between observed and predicted mortality rates (3.7% vs 3.8%, $P = 0.9$).

Table 3 shows the breakdown of complications by type of operation in the high-risk group. Compared to high-risk lobectomies, segmentectomies had significantly lower rate of both respiratory (14% vs 17%, $P = 0.003$) and cardiovascular complications (5.6% vs 9.1%, $P < 0.0001$).

In the low-risk group, there were 41 346 lobectomies and 4888 segmentectomies. The cardiopulmonary morbidity rate observed in segmentectomies was lower than in lobectomies (221/4888, 4.5% vs 3205/41 346, 7.8%, $P < 0.0001$). Similarly, the 30-day mortality rate was significantly lower in the segmentectomy patients (32/4888, 0.6% vs 431/41 346, 1.0%, $P = 0.01$). In this group, 46% of segmentectomies were performed by MITS compared to 37% of lobectomies ($P < 0.0001$).

In segmentectomy patients, the observed mortality rate was lower than the Eurolung-predicted one (0.6% vs 1.0%, $P = 0.0003$), while in the lobectomy patients, there was no difference between observed and predicted mortality (1.0% vs 1.1%, $P = 0.06$).

When the analysis was restricted to operation performed by MITS only, mortality rates were similar in the 2 groups (120/15 214, 0.8% vs 12/2266, 0.5%, $P = 0.18$).

In order to verify the independent association of the extent of operation with the outcome, the analysis was adjusted for several patient- and disease-related characteristics and the surgical approach by using logistic regression analysis. The analysis showed that lobectomy remained an independent significant factor associated with increased risk of mortality (Table 4). Patients undergoing to lobectomy had a 1.5-fold higher risk of 30-day mortality compared to those after segmentectomy after risk adjustment.

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Table 2: Characteristics of 'high-risk' patients by type of operation

	Lobectomy (*n* = 14 007)	Segmentectomy (*n* = 1251)
Age (years), mean (SD)	71.4 (6.6)	71.9 (6.4)
Male gender, *n* (%)	13 665 (98)	1221 (98)
BMI (kg/m^2), mean (SD)	24.7 (3.6)	24.7 (3.6)
ppoFEV1%, mean (SD)	67.2 (17.3)	67.1 (19.2)
CAD, *n* (%)	1773 (13)	149 (12)
CVD, *n* (%)	664 (4.7)	52 (4.1)
Diabetes, *n* (%)	658 (4.7)	62 (5.0)
Neoadjuvant chemotherapy, *n* (%)	1067 (7.6)	69 (5.5)
Pathological diagnosis, *n* (%)		
Primary lung cancer	13 006 (93)	1007 (80)
Benign	483 (3)	82 (7)
Metastases	518 (4)	162 (13)
Eurolung-predicted mortality risk, % (*SD*)	3.8 (1.1)	3.8 (1.1)
Observed cardiopulmonary morbidity, *n* (%)	2411 (17)	149 (12)
Observed 30-day mortality, *n* (%)	517 (3.7)	30 (2.4)

BMI: body mass index; CAD: coronary artery disease; CVD: cerebrovascular disease; ppoFEV1: predicted postoperative forced expiratory volume in 1 s; SD: standard deviation.

Table 3: Incidence of different types of complications in the high-risk patients by type of operation

Complication	Lobectomy (*n* = 14 007), *n* (%)	Segmentectomy (*n* = 1251), *n* (%)	*P*-value
Pneumonia	1313 (9.4)	116 (9.3)	0.95
Respiratory failure	339 (2.4)	20 (1.6)	0.079
ARDS	192 (1.4)	10 (0.08)	0.094
Atelectasis	1066 (7.6)	45 (3.6)	<0.001
Pulmonary oedema	15 (0.01)	3 (0.02)	0.18
Pulmonary embolism	56 (0.4)	12 (1.0)	0.004
MI	69 (0.05)	5 (0.04)	1
AF	1044 (7.5)	52 (4.2)	<0.001
Cardiac failure	103 (0.7)	7 (0.6)	0.60
Stroke	165 (1.2)	12 (1.0)	0.49
ICU admission	397 (2.8)	25 (2.0)	0.084
MOF	77 (0.5)	3 (0.02)	0.22
Total cardiovascular complications	1277 (9.1)	70 (5.6)	<0.001
Total respiratory complications	2393 (17)	172 (14)	0.003

AF: atrial fibrillation; ARDS: acute respiratory distress syndrome; ICU: intensive care unit; MI: myocardial ischaemia; MOF: multiorgan failure.

DISCUSSION

Rationale

One of the most important classifications of segmentectomies is whether they are performed intentionally or for compromised patients (i.e. deemed unfit for a lobectomy). Long-term outcome has been reported to be worse following compromise segmentectomies [4]. The rationale to perform a compromise segmentectomy stems from the assumption that sublobar resection is safer in the immediate postoperative period compared to a larger resection. A report from the ESTS database showed that unadjusted perioperative outcome was better after segmentectomies compared to lobectomies [1]. In this regard, the guidelines on lung cancer management of the American College of Chest Physicians (ACCP) recommend a sublobar resection over a non-surgical treatment in patients who may tolerate an operation but not a lobectomy due to reduced cardiopulmonary reserve or increased underlying comorbidities. They also stated that a sublobar resection should involve an anatomic segmentectomy whenever possible [5]. Similarly, the joint European Respiratory Society (ERS) and ESTS functional guidelines recommend to consider sublobar resections in patients deemed at high risk for a lobectomy whenever technically and oncologically appropriate [6]. However, the amount of benefit provided by segmentectomy over lobectomy in terms of morbidity and mortality for high-risk patients is difficult to quantify accurately.

The ongoing randomized trials comparing sublobar resections versus lobectomies were not able to find significant differences in cardiopulmonary complications and mortality between the groups [7, 8]. However, those studies included intentional segmentectomies in patients fit for lobectomies and therefore do not contribute much to understand the problem related to high-risk patients. In the latter category, it is critical to appraise the reduced surgical risk in light of a compromised oncological outcome to accurately inform the shared decision-making process and the multidisciplinary discussion.

In this context, one of the major challenges is the definition of high-risk patients, which may be variable in different practices and dependent on objective and subjective factors, which may be difficult to capture in a database. In the attempt to gather more information about this topic, we queried the ESTS database to assess the early outcome of patients undergoing segmentectomies or lobectomies grouped by surgical risk. In order to estimate the risk in this retrospective population, we used the Eurolung-predicted mortality [3] choosing as cut-off value the upper interquartile of the predicted mortality in the entire population. Accordingly, 25% of lobectomies and 20% of segmentectomies were classified as high-risk.

Main finding

We found that in high-risk patients, the 30-day mortality rate after segmentectomy was 35% lower than after lobectomy. In addition, whereas the observed and predicted mortality rates were similar after lobectomy, the observed mortality rate after segmentectomy was significantly lower than the predicted one. This is not explained by a reduction in the failure to rescue rate (the proportion of dead among the complicated patients), which is similar in segmentectomy and lobectomy high-risk patients (∼20%). It seems more linked to an absolute reduction in the incidence of cardiopulmonary complications of ∼20% in the segmentectomy patients. The better preservation of pulmonary function after sublobar resections may play a role in the reduction of postoperative morbidity. Several studies, in fact, have demonstrated [9, 10] a better preservation of the whole lung function after segmentectomy compared to lobectomy, by sparing the operated lobe and also increasing the residual function of the non-operated lobe [10]. It is noteworthy that a similar benefit in terms of early mortality was found in the low-risk patients. Although the mortality rates are much lower than in high-risk patients, low-risk segmentectomy patients had a 40% lower mortality rate than lobectomy patients. The protective effect of sublobar resections seems to apply for both high- and lower risk

Table 4: Results of the logistic regression analysis (dependent variable: 30-day mortality)

	OR	SE	P-value	95% CI
Age	1.05	0.04	<0.001	1.04–1.06
Male gender	2.6	0.22	<0.001	2.1–3.0
BMI	0.93	0.01	<0.001	0.92–0.95
ppoFEV1	0.98	0.01	<0.001	0.98–0.99
Thoracotomy (as opposed to MITS)	2.3	0.20	<0.001	1.9–2.7
Lobectomy	1.5	0.20	0.002	1.2–2.0
CAD	1.2	0.12	0.07	0.99–1.4
CVD	1.8	0.23	<0.001	1.4–2.3
Diabetes	1.1	0.16	0.56	0.8–1.5
Neoadjuvant chemotherapy	0.84	0.11	0.19	0.7–1.1
Diagnosis of lung cancer (as opposed to benign disease or metastases)	0.95	0.11	0.67	0.8–1.2

BMI: body mass index; CAD: coronary artery disease; CI: confidence interval; CVD: cerebrovascular disease; MITS: minimally invasive thoracic surgery; OR: odds ratio; ppoFEV1: predicted postoperative forced expiratory volume in 1 s; SE: standard error.

populations. For instance, in elderly patients, previous investigators demonstrated that lobectomy was an independent predictive factor for severe postoperative complications when compared to segmentectomies [11].

Another interesting finding is the very low rate of procedures performed using a minimally invasive approach in the high-risk group, which may be explained by the method of classifying the patients into a high-risk group. In fact, one of the factors compounding the Eurolung is the surgical approach (with the open approach having a positive coefficient in the regression equation). This mathematical artefact further underscores the benefits of sublobar resection (even when performed through an open approach). As previous investigations have shown that video-assisted thoracoscopic surgery is particularly advantageous in lobectomy patients with prohibitive pulmonary function [12], other classes of high-risk patients [13] and specifically for segmentectomies patients [14], we can speculate that the application of a minimally invasive approach in high-risk candidates to segmentectomy would enhance the benefits of this procedure on the early postoperative outcome.

This assumption is supported by the results of the multivariable regression which found segmentectomy and a minimally invasive approach to be independently associated with a more favourable outcome.

Limitations

This study has potential limitations.

First, the selection bias inherent to the retrospective big data analysis including patients operated on in multiple centres should be taken into account when interpreting the results. In particular, the choice of performing a sublobar resection may have been driven by subjective and objective factors not captured in the database or in the model used to classify high-risk patients. In fact, the voluntary nature of the data set may not demonstrate aspects of the decision-making (patient-related, disease-related and surgeon-related) that went into the approach to each case.

Second, we used the Eurolung2-predicted mortality to classify patients into high-risk group. Eurolung does not include important variables such as carbon monoxide lung diffusion capacity, maximum oxygen consumption measured during exercise test, cardiovascular comorbidities and other important comorbidities that may influence the decision to perform a compromise segmentectomy instead of lobectomy. However, in a retrospective multicentre setting and in the absence of a specific variable defining segmentectomies as intentional or compromise, the use of an objective model to stratify the surgical risk seems probably the most reliable method to categorize patients.

In addition, the surgical access is one of the components of the Eurolung model and this explains the fact a minimal number of resections are performed by MITS in the high-risk group. To obviate this mathematical artefact, we performed a logistic regression analysis including the individual factors compounding the Eurolung and the extent of resection, showing an independent association of segmentectomy with favourable outcome independent of surgical access.

We cannot completely rule out the fact that differences in predicted versus observed mortality rates between types of operation depend on a more accurate discrimination of Eurolung for lobectomies, as they represented 77% of the population used to develop the original model and the majority of patients in this study were in common with the sample from which the Eurolung was developed [3].

The ESTS does not collect long-term follow-up data. This information would have been extremely useful to assess the real efficacy of segmentectomies when compared to lobectomies. In this regard, recent meta-analyses have shown encouraging results in favour of segmentectomies [8, 15, 16].

The choice of intentionally performing a segmentectomy should depend on the balance between the long-term prognosis and the short-term morbidity. This balance may be altered by future evidence and influenced by the patient preferences and risk acceptance during the shared decision-making process.

Similarly, other important outcomes are not currently recorded in the ESTS database such as patient-reported outcomes and postoperative pulmonary function. The analysis of these outcomes would add to the critical appraisal of the relative merits of one or the other operation.

CONCLUSIONS

In patients deemed at higher surgical risk, the relative risks of cardiopulmonary morbidity and 30-day mortality in segmentectomy were 0.71 and 0.65 compared to lobectomy. Taking into account the high-risk classification used in this analysis, our finding may represent additional information in support of performing a compromise segmentectomy if deemed technically and oncologically feasible.

Conflict of interest: none declared.

Author contributions

Alessandro Brunelli: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing—original draft. **Herbert Decaluwe:** Conceptualization; Writing—review & editing. **Dominique Gossot:** Conceptualization; Writing—review & editing. **Francesco Guerrera:** Writing—review & editing. **Zalan Szanto:** Writing—review & editing. **Pierre Emmanuel Falcoz:** Conceptualization; Data curation; Writing—review & editing.

Reviewer information

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