

Original Article

[Translated article] Surgical Risk Following Anatomic Lung Resection in Thoracic Surgery: A Prediction Model Derived From a Spanish Multicenter Database



David Gómez de Antonio^{a,*}, Silvana Crowley Carrasco^a, Alejandra Romero Román^a, Ana Royuela^b, Álvaro Sánchez Calle^a, Carme Obiols Fornell^c, Sergi Call Caja^c, Raúl Embún^d, Íñigo Royo^d, José Luis Recuero^d, Alberto Cabañero^e, Nicolás Moreno^e, Sergio Bolufer^f, Miguel Congregado^g, Marcelo F. Jimenez^h, Borja Aguinagaldeⁱ, Sergio Amor-Alonso^j, Miguel Jesús Arrarás^k, Ana Isabel Blanco Orozco^l, Marc Boada^m, Isabel Calⁿ, Ángel Cilleruelo Ramosⁿ, Elena Fernández-Martín^o, Santiago García-Barajas^p, María Dolores García-Jiménez^q, Jose María García-Prim^r, José Alberto Garcia-Salcedo^s, Juan José Gelbenzu-Zazpe^t, Carlos Fernando Giraldo-Ospina^u, María Teresa Gómez Hernández^h, Jorge Hernández^v, Jennifer D. Illana Wolf^w, Alberto Jáuregui Abularach^x, Unai Jiménez^y, Iker López Sanzⁱ, Néstor J. Martínez-Hernández^z, Elisabeth Martínez-Téllez^{aa}, Lucía Milla Collado^{ab}, Roberto Mongil Poce^u, Francisco Javier Moradiellos-Díez^j, Ramón Moreno-Basalobreⁿ, Sergio B. Moreno Merino^g, Florencio Quero-Valenzuela^{ac}, María Elena Ramírez-Gil^t, Ricard Ramos-Izquierdo^{ad}, Eduardo Rivo^r, Alberto Rodríguez-Fuster^{ae}, Rafael Rojo-Marcos^y, David Sanchez-Lorente^m, Laura Sánchez Moreno^{af}, Carlos Simón^{ag}, Juan Carlos Trujillo-Reyes^{aa}, Cipriano López García^p, Juan José Fibla Alfara^v, Julio Sesma Romero^f, Florentino Hernando Trancho^o

^a Servicio de Cirugía Torácica, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain

^b Unidad de Bioestadística, Instituto de Investigación Biomédica Puerta de Hierro (IDIPHISA), CIBERESP, Madrid, Spain

^c Servicio de Cirugía Torácica, Hospital Universitari Mútua Terrassa, Universidad de Barcelona, Terrassa, Barcelona, Spain

^d Servicio de Cirugía Torácica, Hospital Universitario Miguel Servet y Hospital Clínico Universitario Lozano Blesa, IIS Aragón, Zaragoza, Spain

^e Servicio de Cirugía Torácica, Hospital Universitario Ramón y Cajal, Madrid, Spain

^f Servicio de Cirugía Torácica, Hospital General Universitario de Alicante, Alicante, Spain

^g Servicio de Cirugía Torácica, Hospital Universitario Virgen Macarena, Sevilla, Spain

^h Servicio de Cirugía Torácica, Hospital Universitario de Salamanca, Universidad de Salamanca, IBSAL, Salamanca, Spain

ⁱ Servicio de Cirugía Torácica, Hospital Universitario de Donostia, San Sebastián-Donostia, Spain

^j Servicio de Cirugía Torácica, Hospital Universitario Quironsalud Madrid, Madrid, Spain

^k Servicio de Cirugía Torácica, Fundación Instituto Valenciano de Oncología, Valencia, Spain

^l Servicio de Cirugía Torácica, Hospital Universitario Virgen del Rocío, Sevilla, Spain

^m Servicio de Cirugía Torácica, Hospital Clínic de Barcelona, Instituto Respiratorio, Universidad de Barcelona, Barcelona, Spain

ⁿ Servicio de Cirugía Torácica, Hospital Universitario La Princesa, Madrid, Spain

ⁿ Servicio de Cirugía Torácica, Hospital Clínico Universitario, Valladolid, Spain

^o Servicio de Cirugía Torácica, Hospital Clínico San Carlos, Madrid, Spain

^p Servicio de Cirugía Torácica, Hospital Universitario de Badajoz, Badajoz, Spain

^q Servicio de Cirugía Torácica, Hospital Universitario de Albacete, Albacete, Spain

^r Servicio de Cirugía Torácica, Hospital Universitario Santiago de Compostela, Santiago de Compostela, Spain

^s Servicio de Cirugía Torácica, Hospital Universitario 12 de Octubre, Madrid, Spain

^t Servicio de Cirugía Torácica, Complejo Hospitalario de Navarra, Pamplona, Spain

^u Servicio de Cirugía Torácica, Hospital Regional Universitario, Málaga, Spain

^v Servicio de Cirugía Torácica, Hospital Universitario Sagrat Cor, Barcelona, Spain

^w Servicio de Cirugía Torácica, Hospital Puerta del Mar, Cádiz, Spain

^x Servicio de Cirugía Torácica, Hospital Universitario Vall d'Hebron, Barcelona, Spain

^y Servicio de Cirugía Torácica, Hospital Universitario Cruces, Bilbao, Spain

^z Servicio de Cirugía Torácica, Hospital Universitario La Ribera, Alcira, Valencia, Spain

DOI of original article: <https://doi.org/10.1016/j.arbres.2021.01.037>

* Corresponding author.

E-mail address: dgavm@yahoo.es (D. Gómez de Antonio).

<https://doi.org/10.1016/j.arbres.2021.01.039>

0300-2896/© 2021 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

^{aa} Servicio de Cirugía Torácica, Hospital Santa Creu y Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain

^{ab} Servicio de Cirugía Torácica, Hospital Arnau de Vilanova, Lleida, Spain

^{ac} Servicio de Cirugía Torácica, Hospital Virgen de las Nieves, Granada, Spain

^{ad} Servicio de Cirugía Torácica, Hospital Universitario de Bellvitge, Hospitalet de Llobregat, Barcelona, Spain

^{ae} Servicio de Cirugía Torácica, Hospital del Mar, IMIM (Instituto de Investigación Médica Hospital del Mar), Barcelona, Spain

^{af} Servicio de Cirugía Torácica, Hospital Universitario Marqués de Valdecilla, Santander, Spain

^{ag} Servicio de Cirugía Torácica, Hospital Universitario Gregorio Marañón, Madrid, Spain

ARTICLE INFO

Article history:

Received 8 December 2020

Accepted 29 January 2021

Available online 6 May 2022

Keywords:

Predictive risk model

Anatomic lung resection

Thoracic surgery

Minimally invasive surgery

Surgical risk

Post-surgical morbidity and mortality

ABSTRACT

Introduction: The aim of this study was to develop a surgical risk prediction model in patients undergoing anatomic lung resections from the registry of the Spanish Video-Assisted Thoracic Surgery Group (GEVATS).

Methods: Data were collected from 3533 patients undergoing anatomic lung resection for any diagnosis between December 20, 2016 and March 20, 2018.

We defined a combined outcome variable: death or Clavien–Dindo grade IV complication at 90 days after surgery. Univariate and multivariate analyses were performed by logistic regression. Internal validation of the model was performed using resampling techniques.

Results: The incidence of the outcome variable was 4.29% (95% CI 3.6–4.9). The variables remaining in the final logistic model were: age, sex, previous lung cancer resection, dyspnea (mMRC), right pneumonectomy, and ppo DLCO. The performance parameters of the model adjusted by resampling were: C-statistic 0.712 (95% CI 0.648–0.750), Brier score 0.042 and bootstrap shrinkage 0.854.

Conclusions: The risk prediction model obtained from the GEVATS database is a simple, valid, and reliable model that is a useful tool for establishing the risk of a patient undergoing anatomic lung resection.

© 2021 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Riesgo quirúrgico tras resección pulmonar anatómica en cirugía torácica. Modelo predictivo a partir de una base de datos nacional multicéntrica

RESUMEN

Introducción: El objetivo es obtener un modelo predictor de riesgo quirúrgico en pacientes sometidos a resecciones pulmonares anatómicas a partir del registro del Grupo Español de Cirugía Torácica Video-Asistida (GEVATS).

Métodos: Se recogen datos de 3.533 pacientes sometidos a resección pulmonar anatómica por cualquier diagnóstico entre el 20 de diciembre de 2016 y el 20 de marzo de 2018.

Definimos una variable resultado combinada: mortalidad o complicación Clavien-Dindo IV a 90 días tras intervención quirúrgica. Se realizó análisis univariable y multivariable por regresión logística. La validación interna del modelo se llevó a cabo por técnicas de remuestreo.

Resultados: La incidencia de la variable resultado fue del 4,29% (IC 95% 3,6–4,9). Las variables que permanecen en el modelo logístico final fueron: edad, sexo, resección pulmonar oncológica previa, disnea (mMRC), neumonectomía derecha y DLCOppo. Los parámetros de rendimiento del modelo, ajustados por remuestreo, fueron: C-statistic 0,712 (IC 95% 0,648–0,750), Brier score 0,042 y Bootstrap shrinkage 0,854.

Conclusiones: El modelo predictivo de riesgo obtenido a partir de la base de datos GEVATS es un modelo sencillo, válido y fiable, y constituye una herramienta muy útil a la hora de establecer el riesgo de un paciente que se va a someter a una resección pulmonar anatómica.

© 2021 SEPAR. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Palabras clave:

Modelo predictivo de riesgo

Resección pulmonar anatómica

Cirugía torácica

Cirugía mínimamente invasiva

Riesgo quirúrgico

Morbimortalidad posquirúrgica

Introduction

Post-surgical complications impact significantly on hospital stay, postoperative mortality, and costs per patient.¹

While many predictive models of surgical morbidity and mortality have been published for different types of intervention, in reality, none is used universally and routinely.

Thoracoscore, for example, was developed from a large French database for any type of chest surgery, including patients without lung cancer,² and despite being validated in a sample of U.S. patients,³ it was insufficiently accurate when tested in other European patient groups.^{4,5} The French Society of Thoracic Surgery has recently published 2 surgical risk models for patients undergoing surgery exclusively for lung cancer based on a broader database than Thoracoscore (Epithor).⁶

For its part, the European Society of Thoracic Surgeons has developed its own predictive model (ESOS.01),⁷ which is calculated from 2 variables (FEV1 and age), but studies analyzing the accuracy of this model have drawn mixed conclusions.^{5,8,9} This European database for anatomical pulmonary resections was subsequently updated and the morbidity and mortality models revised.¹⁰ The situation with other types of predictive models is similar.^{11,12}

A surgical risk model in thoracic surgery would help improve decision-making on the best therapeutic option for a given patient, and optimize the information we give to our patients.^{13,14}

Models of this type can also be used as a quality of care indicator that allows researchers to compare outcomes from different thoracic surgery units. Moreover, objective knowledge of the surgical risk is of particular interest now that alternatives to surgery are being proposed for certain types of patients.

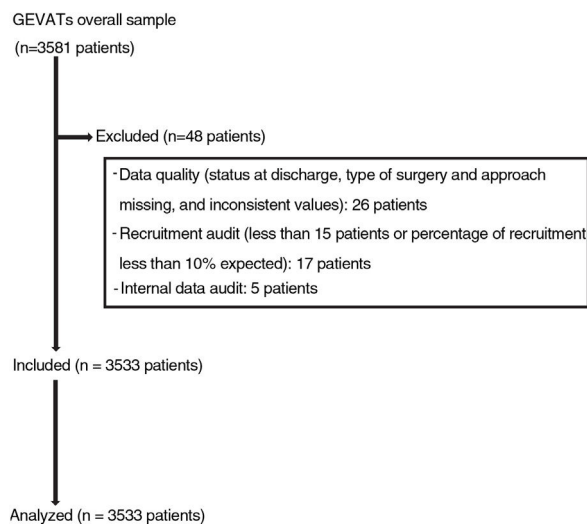


Fig. 1. Flow chart.

The aim of this study was to develop a surgical risk prediction model in patients undergoing anatomic lung resections using the database of the Spanish Video-Assisted Thoracic Surgery Group (GEVATS).¹⁵

Materials and methods

In 2015, the GEVATS database project was set up under the auspices of the Spanish Society of Thoracic Surgery, with the aim of analyzing the morbidity and mortality and oncological outcomes of lung resection surgery in Spain. An online database was developed that included patients undergoing anatomical pulmonary resection for any diagnosis and from any approach in all GEVATS thoracic surgery departments over a period of 15 consecutive months (December 20, 2016–March 20, 2018) (Fig. 1).

The project was approved by the Research Ethics Committee of all participating centers. All patients gave their informed consent for their clinical data to be used for scientific purposes.

Bilateral surgical procedures and patients under 18 years of age were excluded.

Demographic, functional, and comorbidity data were collected on the surgical procedure and on postoperative morbidity and mortality (at 90 days) (supplementary material).

All variables were defined according to the published guidelines of the Society of Thoracic Surgeons (STS) and the European Society of Thoracic Surgeons.¹⁶

Respiratory, cardiovascular and other complications were graded according to the Clavien-Dindo severity classification.¹⁷

Cases for whom no data were available on the type of pulmonary resection, type of surgical approach, and patient status at hospital discharge were excluded. Data from sites where recruitment was less than 10% of the expected rate or that recruited fewer than 15 patients during the study period were also excluded.

The quality of the data was ascertained by the members of the GEVATS scientific committee during an internal audit that consisted of comparing certain variables recorded in the database (date of surgery, type of resection, approach, hospital stay, grade IIIb–IV complications, and patient status at discharge) with the same variables recorded in the medical records of at least 20% of cases included by each of the participating centers.

Table 1
Patient demographics.

Men: 2464 (70.02%)
Women: 1056 (29.98%)
Age: 64.91 years (SD 10.06)

Statistical analysis

The descriptive analysis was performed by obtaining absolute and relative frequencies for categorical variables, and mean and standard deviation or median and percentiles 25 and 75 for numerical variables.

The outcome variable was defined as a composite variable, in which the presence of any Clavien-Dindo grade IV complication within 90 days of the intervention or mortality from any cause was the event of interest. The univariate analysis was performed by testing the hypothesis using Pearson's Chi-squared test or Fisher's exact statistic for categorical variables and Mann-Whitney tests for numerical variables.

The variables that were significant in the univariate analysis and other clinically relevant variables (although not statistically significant) were used to develop the multivariate logistic predictive model. A collinearity diagnosis was performed between the independent variables included in the model, and those that met the criteria were eliminated. An automatic regression modeling strategy was applied, by which variables with a significance level in the Wald test of $p > 0.05$ were successively removed from the model.

Internal validation of the model was performed using bootstrap resampling techniques with 100 replications, including measures of overall performance, calibration and discrimination. Calibration was evaluated using a calibration curve, discrimination using the C-statistic, and overall performance using the Brier score.^{18–21}

Finally, to facilitate the interpretation of the prognostic models, a nomogram with the results of the final model was generated using the “nomolog” patch in STATA.²²

The threshold for statistical significance was set at 0.05. The statistical analysis was carried out using the Stata/IC v.16 package (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

Results

Data on mortality and Clavien-Dindo grade IV complications from 3533 patients from 33 thoracic surgery departments were analyzed.

The characteristics of the sample and the variables analyzed are shown in Tables 1 and 2.

The incidence of the composite variable (mortality at 90 days + grade IV complications at 90 days) was 4.29% (95% CI: 3.6–4.9).

There were 2 cases of intraoperative mortality (0.06%). Mortality at discharge was 1.59%, at 90 days it was 2.93%, and the rate of readmissions was 6.96%.

Median hospital stay was 5 days (P25 4 days; P75 7 days).

More than half of the patients in the sample underwent minimally invasive procedures (54.26%). The reconversion rate was 15.85%.

The most frequent postoperative complications were respiratory (22.39%), of which prolonged air leak was the most common (52.97%). The second most frequent type of complications were cardiovascular (7.02%), 68.51% of which were arrhythmias.

The incidence of more serious complications (Clavien-Dindo IV) in respiratory, cardiovascular and other organs and systems was 1.04%, 0.68% and 0.36%, respectively.

Table 2
Other population variables.

Variables	
Active smoker	980 (28.37%)
Alcohol use	224 (6.37%)
HBP	1561 (44.33%)
Diabetes mellitus	657 (28.66%)
Heart failure	82 (2.32%)
Ischemic heart disease	314 (8.92%)
Arrhythmia	277 (7.87%)
Peripheral vascular disease	318 (9%)
ACVA	180 (5.1%)
mMRC dyspnea	
0	2231 (63.45%)
1	1000 (28.44%)
2	252 (7.17%)
3	33 (0.94%)
Liver failure	33 (0.94%)
BMI	26.86 (SD 4.57)
Albumin (g/dl)	4.1(SD 0.54)
Creatinine (>2 mg/dl)	93 (2.64%)
Dementia	19 (0.54%)
ppo FEV1	69.96%(SD 18.26)
ppo DLCO	65.41% (SD 18.47)
ppo VO ₂ max (ml/kg/min)	13.83(SD 3.57)
ASA	
I	81 (2.30%)
II	1464 (41.69%)
III	1876 (53.42%)
IV	91 (2.59%)
Previous thoracic surgery (oncological)	130 (4.23%)
Previous cardiac surgery	63 (1.78%)
Surgeon's years of experience	
>20 years	834 (23.69%)
10–20 years	1108 (31.45%)
<10 years	1356 (44.92%)
House officer	222 (6.31%)
Surgeon's VATS experience	
>100 cases	981 (27.87%)
50–100 cases	1015 (28.84%)
<50% cases	1432 (40.68%)
No experience	92 (2.61%)
Approach	
Open	1616 (45.74%)
VATS	1917 (54.46%)
Site	
Central	1198 (39%)
Peripheral	1873 (61%)
Lymph node involvement on imaging (CT)	
cN1	230 (7.5%)
cN2	315 (10.26%)
cN3	18 (0.59%)
Neoadjuvance	
CT	245 (7.97%)
RT	74 (2.41%)
Diagnosis	
Lung cancer	3074 (87.33%)
Lung metastases	244 (6.93%)
Other	202 (5.74%)
Number of functioning segments resected	
0	62 (1.76%)
1–3	1632 (46.39%)
4–5	1584 (45.03%)
≥6	240 (6.82%)
Right pneumonectomy	90 (2.55%)
Reintervention	122 (3.46%)
Respiratory complications	
Persistent air leak	791 (22.39%)
Pneumonia	419 (11.86%)
Atelectasis	163 (4.61%)
Effusion	124 (3.51%)
	78 (2.21%)

Table 2 (Continued)

Variables	
Reintubation	53 (1.50%)
Empyema	44 (1.25%)
ARDS	44 (1.25%)
Bronchopleural fistula	27 (0.76%)
PET	13 (0.37%)
CD I	312 (39.44%)
CD II	208 (26.30%)
CD III	199 (23.89%)
CD IV	37 (4.68%)
CD V	45 (5.69%)
Cardiovascular complications	248 (7.02%)
Arrhythmias	170 (4.81%)
ACVA	5 (0.14%)
Heart failure	20 (0.57%)
AMI	3 (0.08%)
DVT	1 (0.03%)
CD I	33 (13.31%)
CD II	170 (68.55%)
CD III	12 (4.84%)
CD IV	24 (9.68%)
CD V	9 (3.63%)
Other complications	236 (6.74%)
Gastrointestinal	43 (1.22%)
Urologic	82 (2.32%)
Psychiatric	16 (0.45%)
CNS	19 (0.54%)
Hematology	18 (0.51%)
CD I	97 (40.76%)
CD II	98 (41.18%)
CD III	17 (7.14%)
CD IV	13 (5.46%)
CD V	13 (5.46%)
Surgical wound infection	50 (1.42%)
Survival at 90 days	97.07%
Survival on discharge	98.41%
Mean hospital stay	5 days (P25–75: 4–7 days)
Readmission	6.96%

ACVA: acute cardiovascular accident; AMI: acute myocardial infarction; ASA: American Society of Anesthesiology Physical Status; CD: Clavien-Dindo classification (I–V); cN1: pathological hilar or intrapulmonary adenopathies on imaging; cN2: pathological ipsilateral mediastinal adenopathies on imaging; cN3: contralateral or ipsilateral supraclavicular mediastinal adenopathies on imaging; CNS: central nervous system; CT, chemotherapy; DVT: deep vein thrombosis; mMRC: modified Medical Research Council dyspnea scale; ppo FEV1: predicted postoperative FEV1. Calculated automatically in the database from the number of functioning segments resected; ppo DLCO: predicted postoperative DLCO. Automatically calculated in the database from the number of functioning segments resected; ppo VO₂ max: predicted postoperative maximum O₂ consumption. Automatically calculated in the database from the number of functioning segments resected; PTE: pulmonary thromboembolism; RT, radiation therapy; SDRA: adult respiratory distress syndrome; VATS: video-assisted thoracoscopic surgery.

The variables associated with the composite outcome variable (mortality + Clavien-Dindo IV complication) are summarized in Table 3.

Albumin demonstrated a statistically significant association in the univariate analysis, but a high proportion of values were missing (53%). A missing-at-random pattern cannot be assumed, so this variable was eliminated from the definitive analysis.

Diabetes mellitus was added to the multivariate logistic regression analysis in addition to the variables that showed statistical significance, as this is associated with an increase in surgical morbidity and mortality in some series.^{23–25} Moderate-to-severe hepatic impairment and alcohol consumption showed a statistically strong association, but they were withdrawn from the final analysis because no specific alcohol consumption data or definition of the diagnosis or severity of liver failure were recorded in the database, preventing objective classification. The maximum model was built using age, sex, smoking habit, high blood pressure, ischemic heart disease, diabetes mellitus, previous lung cancer

Table 3
Univariate analysis.

Variables	Outcome 90 daysNo	Outcome 90 daysYes	p
Demographics			
Sex			<0.001
Female	1036 (30.7%)	20 (13.2%)	
Male	2333 (69.25%)	131 (86.65%)	
Age (years)	64.77 (SD 10.11)	68.14 (SD 8.40)	0.001
Comorbidities			
Smoking			0.001
Never	540 (16.3%)	8 (5.4%)	
Former smoker ≤ 12 months	1383 (41.8%)	76 (51.3%)	
Former smoker > 12 months	443 (13.4%)	26 (17.6%)	
Smoker	942 (28.5%)	38 (25.7%)	
Unknown	942 (28.5%)	38 (25.7%)	
Alcohol			<0.001
Yes	204 (6.1%)	20 (13.2%)	
No	3165 (93.94%)	131 (86.75%)	
Cardiovascular			0.045
HBP yes	1482 (44.03%)	79 (52.32%)	
HBP no	1884 (55.97%)	72 (47.62%)	
Diabetes mellitus			0.096
Yes	621 (18.44%)	36 (23.84%)	
No	2747 (81.56%)	115 (76.16%)	
Heart failure			0.171
Yes	76 (2.26%)	6 (3.97%)	
No	3292 (97.74%)	145 (96.03%)	
Ischemic heart disease			0.013
Yes	292 (8.67%)	22 (14.57%)	
No	3077 (91.33%)	129 (85.43%)	
Arrhythmias			0.973
Yes	265 (7.87%)	139 (92.05%)	
No	3102 (92.13%)	12 (7.95%)	
Peripheral vascular disease			0.330
Yes	301 (8.94%)	134 (88.74%)	
No	3067 (91.06%)	17 (11.26%)	
ACVA			0.216
Yes	169 (5.02%)	11 (7.28%)	
No	3199 (94.98%)	140 (92.72%)	
mMRC dyspnea grade			<0.001
0	2162 (64.25%)	69 (45.70%)	
1	940 (27.93%)	60 (39.74%)	
2	233 (6.92%)	19 (12.58%)	
3	30 (0.89%)	3 (1.99%)	
Liver failure			<0.001
Yes	27 (0.80%)	145 (96.03%)	
No	3342 (99.20%)	6 (3.97%)	
BMI	26.85 (SD 4.58)	26.96 (SD 4.39)	0.783
Albumin	4.11 (SD 0.53)	3.82 (0.71)	0.032
Creatinine (>2 mg/dl)			0.114
Yes	86 (2.55%)	7 (4.67%)	
No	3282 (97.45%)	143 (95.33%)	
Dementia			0.834
Yes	18 (0.53%)	1 (0.66%)	
No	3351 (99.47%)	159 (99.34%)	
Functional parameters			
ppo FEV1	70.40 (SD 18.18)	59.97 (SD 17.20)	0.001
ppo DLCO	65.85 (SD 18.36)	56.18 (SD 16.50)	0.001
ppo VO ₂ max	13.97 (SD 3.54)	12.34 (SD 3.65)	0.001
ASA			0.002
I	81 (2.41%)	0	
II	1417 (42.15%)	47 (31.33%)	
III	1781 (52.97%)	95 (63.33%)	
IV	83 (2.47%)	8 (5.33%)	
Surgical procedure			
Previous chest surgery (oncological)			0.007
Yes	118 (4.02%)	12 (8.76%)	
No	2815 (95.98%)	125 (91.24%)	
Previous cardiac surgery			0.285
Yes	62 (1.84%)	1 (0.66%)	
No	3307 (98.16%)	150 (99.34%)	
Surgeon's years of experience			0.216
>20 years	806 (23.92%)	28 (1.54%)	
10–20 years	1050 (31.17%)	58 (38.41%)	
>10 years	1299 (38.56%)	57 (37.75%)	
House officer	214 (6.35%)	8 (5.30%)	

Table 3 (Continued)

Variables	Outcome 90 daysNo	Outcome 90 daysYes	p
Surgeon's VATS experience			
>100 cases	950 (28.20%)	31 (20.53%)	0.022
50–100 cases	962 (28.55%)	53 (35.10%)	
>50 cases	1373 (40.75%)	59 (39.07%)	
No experience	84 (2.49%)	8 (5.30%)	
Site			
Central	1130 (38.51%)	68 (49.64%)	0.009
Peripheral	1804 (61.49%)	69 (50.36%)	
Lymph node involvement (CT)			
cN0	2405 (82.03%)	101 (73.72%)	0.034
cN1	217 (7.40%)	13 (9.49%)	
cN2	292 (9.96%)	23 (16.79%)	
cN3	18 (0.61%)	0	
Neoadjuvant			
Yes	250 (8.51%)	12 (8.76%)	0.919
No	2687 (91.49%)	125 (91.24%)	
Diagnostic			
Lung cancer	2937 (87.18%)	137 (90.73%)	0.433
Lung metastases	236 (7.01%)	8 (5.30%)	
Others	196 (5.82%)	6 (3.97%)	
Functional segments resected			
0	56 (1.66%)	6 (3.97%)	<0.001
1–3	1568 (46.57%)	64 (42.38%)	
4–5	1529 (45.41%)	55 (36.42%)	
≥6	214 (6.36%)	26 (17.22%)	
Right pneumonectomy			
Yes	71 (2.11%)	19 (12.58%)	<0.001
No	3298 (98.89%)	132 (87.42%)	

ACVA: acute cardiovascular accident; ASA: American Society of Anesthesiology Physical Status; BMI: body mass index; cN1: pathological hilar or intrapulmonary adenopathies on imaging; cN2: pathological ipsilateral mediastinal adenopathies on imaging; cN3: contralateral or ipsilateral supraclavicular mediastinal adenopathies on imaging; mMRC: modified Medical Research Council dyspnea scale; ppo DLCO: predicted postoperative DLCO, automatically calculated in the database from the number of functioning segments resected; ppo FEV1: predicted postoperative FEV1, calculated automatically in the database from the number of functioning segments resected; ppo VO₂ max: predicted postoperative maximum O₂ consumption, automatically calculated in the database from the number of functioning segments resected; VATS, video-assisted thoracoscopic surgery.

Table 4
Multivariate analysis.

	OR (95% CI)	p-Value
Age	1.03 (1.00–1.05)	0.007
Sex (Female)	0.30 (0.16–0.57)	<0.001
Previous lung cancer	2.02 (1.00–4.10)	0.049
Dyspnea (mMRC)	1.87 (1.26–2.77)	0.002
Right pneumonectomy	4.06 (2.05–8.03)	<0.001
ppo DLCO	0.98 (0.01–0.39)	0.004

mMRC: modified Medical Research Council dyspnea scale; ppo DLCO: predicted postoperative DLCO, automatically calculated in the database from the number of functioning segments resected.

Table 5
Performance after resampling.

Performance after resampling (100 replications)	
C-statistic	0.712 (95% CI 0.648–0.750)
Brier score	0.042
Bootstrap shrinkage	0.854

surgery, dyspnea grade, ASA score, tumor size, right pneumonectomy, FEV1 predicted, ppo DLCO and surgeon's experience with VATS. After backward elimination, the variables age, sex, previous lung cancer surgery, dyspnea, right pneumonectomy, and ppo DLCO remained in the final model (Table 4).

One hundred subsamples were obtained by bootstrap resampling techniques, and the modeling strategy was repeated for each one. The performance parameters of the model, adjusted by boot-

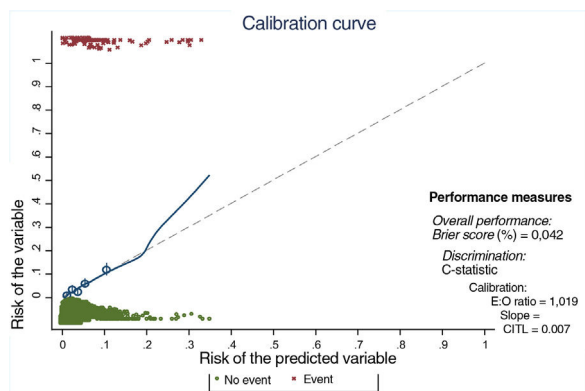


Fig. 2. Calibration curve. E:O ratio: ratio between the number of estimated cases and the number of observed cases; CITL: calibration in the large. The ideal calibration is shown in the curve by the dotted line and the match between expected and observed risk on the solid line. The line fits well in most quintiles (shown by circles), and only deviates when there are a small number of observations (after a predicted risk of 20%).

strapping, are shown in Table 5, and show good outcomes in performance, calibration (Fig. 2) and discrimination.

A nomogram was generated using the results of the final logistic regression analysis to graphically show the weight of each variable. The total score, obtained by adding the points corresponding to each of the variables in the final model, represents the predicted probability of experiencing an event, death or Clavien-Dindo \geq IV complication at 90 days (Fig. 3). For example, a male patient (3.5 points), 78 years of age (7 points), with dyspnea on moderate exertion (2 points), who underwent lung resection for previous adenocarcinoma (2 points), who has a ppo DLCO of 50% (6.5 points), who is a candidate for anatomical resection will have a total score of 22, corresponding to a 20% risk of 90-day postoperative mortality or major complications. The risk in the same patient, but with DLCO 100%, falls to 10%, and to 5% if it is his first lung resection.

Discussion

A tool to anticipate which patients may develop significant complications after surgery is essential for making decisions about the best treatment available in each situation, and for comparing the performances of the different units providing a service – in this case, anatomical lung resections.

The morbidity and mortality outcomes in our series are comparable to those of other large published series.^{2,10,12} However, while the evidence suggests that approximately 15% of patients requiring anatomical resection undergo minimally invasive surgery, it is interesting to note that in our series the percentage of patients undergoing video-assisted thoracoscopic surgery was significantly higher (54.26%). This may be explained by the more rapid implementation of minimally invasive techniques in Spain than in neighboring countries, and possibly by the high percentage of procedures performed by thoracic surgery specialists.

Certain functional parameters and comorbidities are known to be associated with an increase in perioperative risk in patients undergoing lung resections, and various predictive models of morbidity and mortality have been designed, mainly based on national databases.^{1,2,10,11} However, none of these models is used universally.

This low uptake may be due to several reasons. Sometimes, genetic characteristics and health and social welfare conditions that are applicable in one population are not applicable in another. For example, Thorascor, a surgical risk model developed from a French database, does not perform well in the U.S. population. Furthermore, many of these models are complex to apply on a

day-to-day basis, and use variables that are not available during consultation with the patient to inform them of their options (extended resections, type of approach, and disease staging).

Our aim with this model is to predict the surgical risk of a patient using the variables immediately available during the visit. It is not uncommon, given preoperative findings or even the judgment of the surgeon, for the complexity of the proposed intervention to be overestimated. In addition, interventions that are not necessarily technically difficult (e.g., intrapericardial pneumonectomy or partial resection of the diaphragm, chest wall, pericardium, etc.) are classed as extended surgeries in many publications.^{10,12}

Age and sex are variables that are persistently associated with increased surgical risk. Similarly, the dyspnea grade indicates a patient's cardiorespiratory status and has been shown in many studies to have a prognostic impact in patients with respiratory disease.^{2,10,12}

Among the current recommendations for a comprehensive study on the operability of a patient undergoing lung anatomical resection, predicted postoperative DLCO (ppo DLCO) is accepted as the most reliable indicator of the patient's functional reserve, to a greater extent even than FEV1.²⁶ However, the models available to date do not include ppo DLCO, mainly because it is not widely performed. We did not include FEV1 as a predictor in our model, but we did include ppo DLCO, in line with the available scientific evidence.

Right pneumonectomy consistently appears as a negative prognostic factor in published series,²⁷ and our analysis confirmed its impact on the morbidity and mortality of patients.

It is interesting to note the predictive value of a previous history of lung cancer. This variable is not included in any of the models described so far, except for the latest revision of Ephitor.⁶ It is estimated that about 6% of patients who undergo lung cancer resection will develop a second primary tumor, and now, thanks to screening CT scans, it is now increasingly common to detect resectable lesions in the earliest stages even on more than 1 occasion, permitting a more conservative approach. Establishing the added risk of a second intervention in a given patient can often guide the decision between a surgical approach or other therapeutic options.

The reliability parameters of our model are acceptable, especially for low scores. The model tends to overestimate higher risk scores, probably because the number of events is small compared to the number of predictor variables included in the model.

This study has some limitations:

- First of all, it is based on a voluntary database. This may result in significant selection bias. However, it should be noted that patients from sites with low recruitment rates were excluded (median overall recruitment was 99% [p25–p75: 76–100%]), and an internal audit of data quality was carried out, revealing a degree of concordance of 98%.¹⁵
- Blood albumin levels, which in several studies have shown a prognostic impact on patients undergoing surgery, could not be analyzed because of the high percentage of patients for whom these data were missing. Other variables that might be of interest in assessing a patient's surgical risk, such as advanced liver disease or alcohol consumption, were collected in the database, but the lack of a clear definition meant that they had to be excluded from the analysis.
- In our analysis, we included all patients undergoing anatomical lung resection, regardless of their diagnosis. Most series include only patients with a lung cancer diagnosis without considering the type of lung resection performed.^{6,12} The diagnosis obviously has prognostic implications for the patient, but it seems logical to believe that complications in the immediate postoperative period will be more closely related to the type of resection performed and to the patient's current clinical situation (operability). The gold

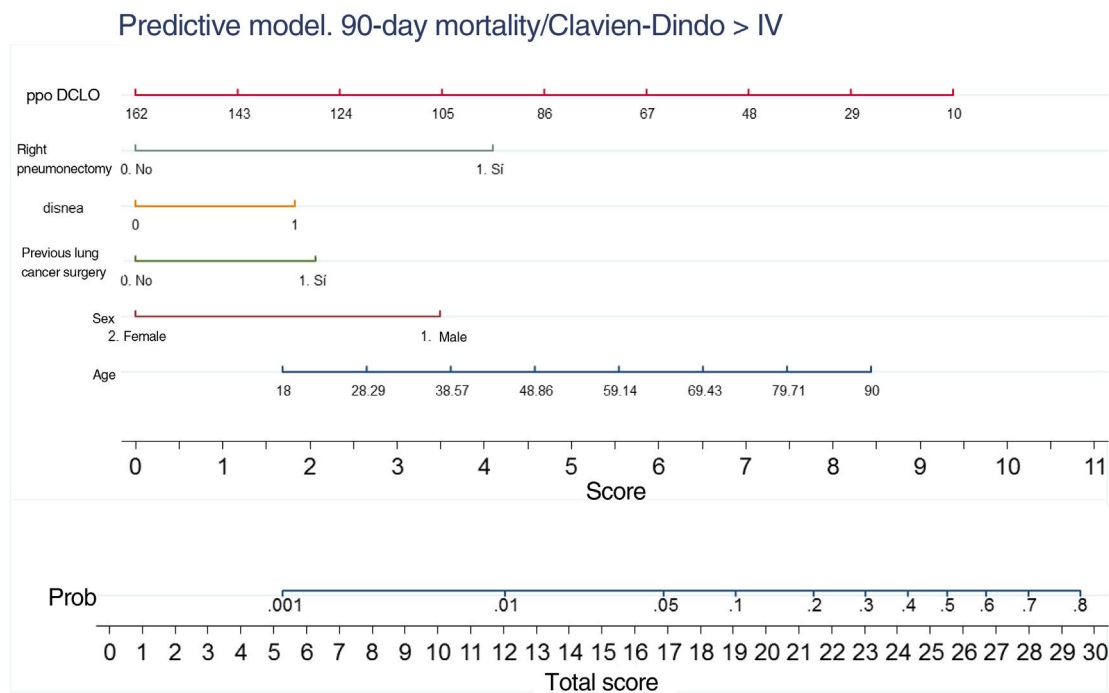


Fig. 3. Normogram.

standard in the surgical treatment of lung cancer is lobectomy, and in some very specific cases, anatomical sublobar resection. In our opinion, the GEVATS series is more representative of patients who are candidates for surgical treatment with curative intent for any diagnosis than other larger series.

We conclude that the predictive risk model obtained from this database is a simple, reliable model that constitutes a highly useful tool in classifying patients undergoing anatomical lung resection, and one that helps empower patients when making decisions about their treatment.

Funding

The costs of setting up and maintaining the GEVATS database were covered by Ethicon, Johnson & Johnson. The authors have had absolute freedom and control in all aspects of the design, methodology, analysis and writing of the study.

GEVATS received a research grant from the Spanish Society of Thoracic Surgery in 2015.

Conflict of interests

The authors state that they have no conflicts of interest.

Acknowledgments

We thank Johnson & Johnson for their collaboration in the development of the GEVATS database. We also thank all the clinical documentation staff at the participating centers for their collaboration in the audit.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbres.2021.01.039.

References

1. Wright CD, Gaissert HA, Grab JD, O'Brien SM, Peterson ED, Allen MS. Predictors of prolonged length of stay after lobectomy for lung cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database risk-adjustment model. *Ann Thorac Surg.* 2008;85:1857–65.
2. Falcoz PE, Conti M, Brouchet L, Chocron L, Puyraveau M, Mercier M, et al. The thoracic scoring system (Thoracoscore): risk model for in hospital death in 15,183 patients requiring thoracic surgery. *J Thorac Cardiovasc Surg.* 2007;133:325–32.
3. Chamogeorgakis T, Toumpoulis I, Tomos P, Ieromonachos C, Angouras D, Georgiannakis E, et al. External validation in the modified Thoracoscore in a new thoracic surgery program: prediction of in-hospital mortality. *Interact Cardiovasc Thorac Surg.* 2009;9:463–6.
4. Qadri SS, Jarvis M, Ariyaratnam P, Chaudry MA, Cale AR, Griffin S, et al. Could Thoracoscore predict postoperative mortality in patients undergoing pneumonectomy? *Eur J Cardiothorac Surg.* 2014;14:556–9.
5. Poullis M, McShane J, Shaw M, Wolley S, Shackcloth M, Page R, et al. Prediction in-hospital mortality following pulmonary resections: improving on current risk models. *Eur J Cardiothorac Surg.* 2013;44:238–43.
6. Bernard A, Rivera C, Pages PB, Falcoz PE, Vicaut E, Dahan M. Risk model of in-hospital mortality after pulmonary resection for cancer: a national database of the French Society of Thoracic and Cardiovascular Surgery (Epithor). *J Thorac Cardiovasc Surg.* 2011;141:449–58.
7. Berrisford R, Brunelli A, Rocco G, Tressure T, Utleay M, Audit and guidelines committee of the European Society of Thoracic Surgeons; European Association of Cardiothoracic Surgeons. The European Thoracic Surgery Database project. Modelling the risk of in-hospital death following lung resection. *Eur J Cardiothorac Surg.* 2005;28:301–11.
8. Barua A, Handagala SD, Socci L, Barua B, Malik M, Johnstone N, et al. Accuracy of two scoring systems for risk stratification in thoracic surgery. *Interact Cardiovasc Thorac Surg.* 2012;14:556–9.
9. Sharkey A, Ariyaratnam P, Anikin V, Belcher E, Kendall S, Lim E, et al. Thoracoscore and European Society Objective Score fail to predict mortality in the UK. *World J Oncol.* 2015;6:270–5.
10. Brunelli A, Cicconi S, Decaluwe H, Szanto Z, Falcoz PE. Parsimonious Eurolung risk models to predict cardiopulmonary morbidity and mortality following anatomic lung resections: an updated analysis from the European Society of Thoracic Surgeons database. *Eur J Cardiothorac Surg.* 2019;1–7. <http://dx.doi.org/10.1093/ejcts/ezz272>.
11. Rich AL, Tata LJ, Stanley RA, Free CM, Peake MD, Baldwin DR, et al. Lung cancer in England: Information from the National Lung Cancer Audit (LUCADA). *Lung Cancer.* 2011;72:16–22.
12. Kozower BD, Sheng S, O'Brien SM, Liptay MJ, Lau CL, Jones DR, et al. STS database risk models: predictors of mortality and major morbidity for lung cancer resection. *Ann Thorac Surg.* 2010;90:875–81.
13. Cykert S. Risk acceptance and risk aversion: patients' perspectives on lung surgery. *Thorac Surg Clin.* 2004;14:287–93.

14. Cykert S, Kissling G, Hansen CJ. Patient preferences regarding possible outcomes of lung resection: what outcomes should preoperative evaluations target? *Chest*. 2000;117:1551–9.
15. Embun R, Royo-Crespo I, Recuero Díaz JL, Bolufer S, Call S, Congregado M, et al. Spanish video-assisted thoracic surgery group: method auditing, and initial results from a national prospective cohort of patients receiving anatomical lung resections. *Arch Bronconeumol*. 2020;56:718–24. <http://dx.doi.org/10.1016/j.arbres.2020.01.005>. English, Spanish. Epub 2020 Feb 22; PMID: 32098728.
16. Fernandez FG, Falcoz PE, Kozower BD, Salati M, Wright CD, Brunelli A. The Society of Thoracic Surgeons and the European Society of Thoracic Surgeons general surgery databases: joint standardization of variable definitions and terminology. *An Thorac Surg*. 2015;99:368–76.
17. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *An Surg*. 2004;240:205–13.
18. Moons KG, Altman DG, Reitsma JB, Ioannidis JP, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): explanation and elaboration. *Ann Intern Med*. 2015;162:W1. <http://dx.doi.org/10.7326/M14-0698>.
19. Van Houwelingen JC, Le Cessie S. Predictive value of statistical models. *Stat Med*. 1990;9:1303–25. <http://dx.doi.org/10.1002/sim.4780091109>.
20. Steyerberg EW. Validation of prediction models. In: Steyerberg EW, editor. *Clinical prediction models: a practical approach to development. Validation and updating*. Cham: Springer; 2019. p. 329–44. <http://dx.doi.org/10.1007/978-3-030-16399-0>.
21. Harrell FE. *Regression modeling strategies: with applications to linear models, logistic and ordinal regression and survival analysis*. 2nd ed. Springer; 2015.
22. Zlotnik A, Abaira V. A general-purpose nomogram generator for predictive logistic regression models. *Stata J*. 2015;15:537–46. <http://dx.doi.org/10.1177/1536867X1501500212>.
23. Sirbu H, Busch T, Aleksic I, Schreiner W, Oster O, Dalichau H. Bronchopleural fistula in the surgery of non-small cell lung cancer: incidence, risk factors, and management. *Ann Thorac Cardiovasc Surg*. 2001;7:330–6.
24. Mammana M, Marulli G, Zuin A, Perissinotto E, Comacchio GM, de Franceschi E, et al. Postpneumonectomy bronchopleural fistula: analysis of risk factors and the role of bronchial stump coverage. *Surg Today*. 2020;50:114–22. <http://dx.doi.org/10.1007/s00595-019-01871-0>.
25. Haraguchi S, Koizumi K, Hioki M, Hirata T, Hirai K, Mikami I, et al. Analysis of risk factors for postpneumonectomy bronchopleural fistulas in patients with lung cancer. *J Nippon Med Sch*. 2006;73:314–9. <http://dx.doi.org/10.1272/jnms.73.314>.
26. Brunelli A, Charloux A, Bolliger CT, Rocco G, Sculier JP, Varela G, et al. ERS/EST clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J*. 2009;34:17–41.
27. Kim AW, Boffa DJ, Wang Z, Detterbeck FC. An analysis, systematic review, and meta-analysis of the perioperative mortality after neoadjuvant therapy and pneumonectomy for non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2012;143:55–63. <http://dx.doi.org/10.1016/j.jtcvs.2011.09.002>. Epub 2011 Nov 4 PMID: 22056364.