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TITLE: A Risk Score To Predict the Incidence of Prolonged Air Leak after Video-Assisted Thoracoscopic Lobectomy: An Analysis from the European Society of Thoracic Surgeons Database.

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GLOSSARY OF ABBREVIATIONS

PAL: prolonged air leak

ESTS: European Society of Thoracic Surgeons

VATS: Videoassisted thoracoscopic surgery

FEV1: forced expiratory volume in 1 second

STS: Society of Thoracic Surgeons

BMI: body mass index

ECOG: Eastern Cooperative Oncology Group score

CAD: coronary artery disease

DLCO: carbon monoxide lung diffusion capacity

ABSTRACT

Objective: To develop an aggregate risk score for predicting the occurrence of prolonged air leak (PAL) after videoassisted thoracoscopic (VATS) lobectomy from patients registered in the European Society of Thoracic Surgeons (ESTS) database.

Methods: Five thousands and sixty-nine patients submitted to VATS lobectomy (July 2007-August 2015) were analyzed.

Exclusion criteria: sublobar resections or pneumonectomies, lung resection associated with chest wall or diaphragm resections, sleeve resections, need for postoperative assisted mechanical ventilation.

PAL was defined as an air leak longer than 5 days. Several baseline and surgical variables were tested for a possible association with PAL using univariable and logistic regression analyses, determined by bootstrap resampling. Predictors were proportionally weighed according to their regression estimates (assigning 1 point to the smallest coefficient).

Results: PAL was observed in 504 patients (9.9%). Three variables were found associated with PAL after logistic regression: male gender(p<0.0001,score=1),FEV1<80%(p<0.0001,score=1),body mass index<18.5kg/m^2 (p<0.0001,score=2).

The aggregate PAL risk score was calculated for each patient by summing the individual scores assigned to each variable (range 0-4). Patients were then grouped into 4 classes with an incremental risk of PAL (p<0.0001): class A (score 0 points,1,493 patients) 6.3% with PAL, class B (score 1 point,2,240 patients) 10% with PAL, class C (score 2 points,1,219 patients) 13% with PAL, class D (score>2 points,117 patients) 25% with PAL.

Conclusions: An aggregate risk-score was created to stratify the incidence of PAL after VATS lobectomy. The score can be used for patient counseling and to identify those patients who can benefit from additional intraoperative preventative measures.

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Perspective Statement

An aggregate risk score for prolonged air leak specific for VATS lobectomy has been developed. This score can be used to identify high-risk patients who may benefit of intraoperative preventative measures (sealants, buttressing material etc.) aimed at reducing the occurrence of this complication with a potential clinical and financial benefit.

Central Message

The risk score predicting prolonged air leak after VATS lobectomy can be used to implement preventative measures and for patient informed counseling.

Introduction

Previous papers have tried to identify risk factors for prolonged air leak (PAL) after lung surgery[1-3], however, there is no risk score for patients operated on through video-assisted thoracosopic surgery (VATS). Reliable information about the risk of these patients developing PAL after lung resection would help to inform the need for intraoperative preventative measures, such as pleural tenting, surgical sealants, etc. to minimize the occurrence of this complication. Also, this information can help set realistic expectations about the duration of chest tubes and hospital stay, which remains a main driver in patient satisfaction after minimally invasive operation.

Furthermore, the use of minimally invasive approaches has expanded the inclusion criteria for lung resection, with an increasing proportion of patients with poor lung function and advanced age being operated[4-8]. The change in the case mix of surgical candidates traditionally submitted to thoracotomy warrants, the development of a risk model.

Although video-assisted thoracoscopic lung resection is associated with a lower incidence of complications compared with thoracotomy[9], the frequency of PAL appears similar in the two groups of patients, as shown in the two recent case matched analyses from the European Society of Thoracic Surgeons[10] (ESTS) and the Society of Thoracic Surgeons[11] (STS) general thoracic surgery databases.

The objective of this study was to develop an aggregate risk score for predicting the occurrence of PAL after VATS lobectomy from a large cohort of patients registered in the ESTS database.

Methods

Data Source

The features and scope of the ESTS Database have been described elsewhere[10,12]. Briefly, the ESTS database is an online voluntary general thoracic surgery database, free and publicly available to all ESTS members. The ESTS database is compliant with the International data protection assurance regulation. No Ethical Committee review is required to submit data to the database. Data can be inputted into the database online by individual surgeons or data managers or institutional dataset can be imported annually through an automated procedure involving variable matching.

The database was started in 2007 and currently collects data and information from more than 200 European hospitals.

All variables and outcomes in the database have been standardized and defined a priori. Definitions of variables are reported in the joint STS-ESTS paper on standardization of definition of variables in the respective registries[12].

The ESTS database is not systematically audited and only samples of data from participating centers eligible for the Institutional Accreditation Program are subject to audit. These represent only 10% of all centers participating to the database.

Study Cohort

This is a retrospective analysis performed on 5,069 VATS lobectomies (99 bilobectomies and 4970 lobectomies) registered in the ESTS database from

July 2007 to August 2015. With the aim to eliminate a learning curve effect, only patients operated on in units contributing more than 20 VATS lobectomies were used for this analysis (these represented 90% of the total VATS lobectomies in the ESTS database). The number of VATS lobectomies registered from each center varied from 21 to 360 (19 centers contributed more than 100 patients). They represent 13% of all lobectomies registered in the ESTS database during the same period (38,672 lobectomies in total). The ESTS database does not collect information about the modality of VATS approach (i.e. number of ports, anterior or posterior approach, fissureless technique etc.) nor the occurrence of conversion to thoracotomy. Furthermore, it does not distinguish between video-assisted and robotic-assisted procedures. A more specific portion of the database dedicated to minimally invasive lung resection has been only recently implemented to overcome these limitations.

For the purpose of this investigation, patients submitted to anatomic or non-anatomic sub-lobar resections or pneumonectomies were excluded from the analysis. Similarly, patients submitted to VATS lobectomies and additional extended procedures such as chest wall or diaphragm resections (31 patients), sleeve resections (25 patients) or needing postoperative mechanical ventilation (34 patients) were not included in the analysis, as these characteristics were thought to influence the occurrence and duration of air leak or to alter the pulmonary mechanics. Additionally, forty nine patients died in hospital or within 30 days from operation (30 days mortality rate 1%) and were excluded from the analysis.

Data Collection and Statistical Model

According to the definition in the database, prolonged air leak (PAL) was defined as an air leak longer than 5 days[12]. PAL represents the main endpoint of this analysis. The ESTS database does not collect at the moment the duration of air leak expressed as continuous numeric variable.

The following baseline and surgical variables were screened for a possible association with PAL: age, sex, forced expiratory volume in one second (FEV1%) expressed in percentage of predicted value, body mass index (BMI), Eastern Cooperative Oncology Group score (ECOG), diabetes, presence of coronary artery disease (CAD), neoadjuvant chemotherapy, side and site of lobectomy.

For the purpose of this analysis, cardiopulmonary complications were considered those occurring during the hospital stay or within 30 days from operation and included the followings: respiratory failure requiring mechanical ventilation for longer than 24 hours, pneumonia, atelectasis requiring bronchoscopy, pulmonary embolism, pulmonary edema, adult respiratory distress syndrome, acute myocardial infarction, atrial fibrillation requiring medical or electrical cardioversion, cardiac failure, stroke.

Missing data were imputed by averaging the non-missing numeric values, or choosing the most frequent value in the categorical variables. All variables used for this analysis had less than 10% missing data. Carbon monoxide lung diffusion capacity was present in only 30% of patients and could not be used for constructing the model.

The normal distribution of numeric variables was first assessed by the Shapiro Wilk normality test.

In order to develop a risk score for PAL, an initial screening of variables was performed before applying stepwise logistic regression. The variables were screened by univariable analysis and only those with a $p<0.05$ were used as independent predictors in the logistic regression model (dependent variable: PAL).

Normally distributed variables were compared across groups using the Student's t-test while those without normal distribution were tested by the Mann-Whitney test. Categorical variables were tested by the Chi-square test.

For the purpose of developing the aggregate score, a threshold effect was determined using Receiver Operating Characteristic (ROC) curves for those numeric variables to be included in the logistic regression. The logistic regression was validated by bootstrap analysis. Only predictors with a $p<0.05$ in more than 50% of 1,000 bootstrap samples with the same number of observations as the original dataset were retained in the final model[13-15].

Bootstrap is a technique of resampling with replacement through which new samples (1000 in our analysis) of patients are generated by randomly selecting individuals from the original database.

At each step of the simulation every individual from the original database is again eligible to be selected, irrespective of whether he has already been sampled. Therefore, in each bootstrap sample some of the original individuals may not be represented and others may be represented more than once. We have previously shown that the use of the entire dataset to develop the risk model and the application of bootstrap for its internal validation was superior to the traditional training and testing method of randomly splitting the database in a development and validation set[15]. When applied to an external population the model developed using the entire database and validated by bootstrap performed better than several models obtained by the training and testing methods[15]. For this reason we chose to use the former approach in this analysis.

The significant variables were used to construct an aggregate model according to the methodology described in previous studies[16,17]. A score was assigned to each variable in the final model by proportionally weighting the regression coefficients and assigning 1 point to the smallest one (i.e. if the smallest coefficient is 1.5 and another variable has a coefficient of 3, 1 point is assigned to the first variable with smallest coefficient and 2 points to the other variable). A total score was then generated for each patient by summing the individual points assigned to each variable. The patients were finally grouped in risk classes according to their total scores and similar incidence of PAL within the group.

The risk score was then applied to a sample of 2,454 VATS lobectomy patients registered in the ESTS database from August 2015 until June 2016 with the aim to validate it in a population not used for its development.

All tests were performed using Stata 12.0 statistical software (Stata Corp., College Station, TX, USA).

Results

The characteristics of the patients included in this study are shown in table 1.

PAL was observed in 504 patients (9.9%). Patients with PAL also experienced a higher rate of cardiopulmonary complications compared to those without

PAL (12% vs. 8.5%, p=0.02). In patients with no other complications the presence of PAL prolonged the postoperative hospital stay by 5 days compared to those without PAL (11.3 days vs. 6.2 days, p<0.0001).

The results of the univariable analysis to test the association of several variables with PAL are shown in table 1.

In particular, patients with PAL after VATS lobectomy had lower FEV1 (p<0.0001), lower BMI (p<0.0001) and were more frequently males (p<0.0001).

For the purpose of this study, the numeric variables FEV1 and BMI were categorized by using ROC analysis and selecting the best cutoff associated with PAL. The best cutoff values were 80% for FEV1 and 18.5 kg/m^2 for BMI, respectively.

As a consequence, the variables used as independent predictors in the logistic regression analysis were FEV1<80% predicted value, BMI<18.5 kg/m^2 and male sex.

Two thousands and one hundred-thirty seven patients in this sample (35% of total) had a FEV1 lower than 80%. Their PAL incidence was 12%, while PAL occurrence in those with higher FEV1 was 7%. PAL incidence in patients with FEV1<70%, 60% and 50% were 13%, 14% and 17%, respectively.

One hundred and eighty patients (3.6% of the total) had a BMI lower than 18.5 kg/m^2. The PAL incidence in this group was 21%. The PAL incidences in patients with BMI between 18.5 and 25 kg/m^2 or greater than 25 kg/m^2 were 11.3% and 8.3%, respectively.

All three variables were found to be associated with PAL after logistic regression analysis (table 2).

The variables were proportionally scored according to their regression coefficients as follows: male sex, score=1; FEV1<80% score=1; body mass index<18.5kg/m^2 score=2 (table 3).

A PAL score was calculated for each patient by summing the individual scores assigned to each variable and ranged from 0 to 4.

According to their scores, patients were grouped into 4 classes with an incremental risk of PAL (Chi square test, p<0.0001): class A (score 0 point, 1,493 patients) 6.3%, class B (score 1 point, 2,240 patients) 9.9%, class C (score 2 points, 1,219 patients) 13%, class D (score>2 points, 117 patients) 25% (Figure 1). Table 3 shows the distribution of patients with the three factors associated with PAL within each class of risk.

As expected, patients in the higher risk classes had longer postoperative hospital stays (includes all patients in the analysis) (class A 6.4 days, class B 7.1 days, class C 8.4 days, class D 9.5 days; Kruskal-Wallis test, p=0.0001).

Dunn's pairwise comparison (with Bonferroni adjustment for multiple comparisons) of postoperative stay between risk groups, showed that all differences between groups had p values lower than 0.0001 except for the difference between group C and D, which had a p value of 0.02.

Bootstrap analysis showed that patients in classes A (lowest risk class) and D (highest risk class) had a PAL incidence less than 7% in 86% of samples and greater than 20% in 87% of samples, respectively.

Finally, the score was applied to an independent sample of 2,454 VATS lobectomy patients registered in the ESTS database following the completion of the analysis (from August 2015 to June 2016). In this group of patients not used to develop the model, the different classes of risk showed an incremental incidence of PAL (p=0.001): class A (score 0 point, 440 patients) 7%, class B (score 1 point, 1,071 patients) 8.8%, class C (score 2 points, 869 patients) 12.1%, class D (score>2 points, 74 patients) 17.5% (Figure 1).

When the logistic model was applied to the validation set, the classification accuracy for a predicted probability of PAL equal or greater than 13% (corresponding to the incidence of PAL in class C of the derivation set) was 88%.

Discussion

Background and objective

The application of VATS has been shown to reduce the incidence of morbidity rates particularly in high risk patients[4-8,10] allowing for expansion of operability criteria in patients with early stage lung cancer[18]. The different case mix and some VATS-related technical modifications during the lobectomy procedure (i.e. different approach to the fissures, more extensive use of blunt dissection of hilar structures, more liberal use of endostaplers, etc.) may have an impact on the occurrence of PAL.

Hence there is a need to develop a specific risk model for this VATS cohort of patients, with the aim of selecting those at higher risk for PAL as potential candidates for the application of intraoperative preventative measures.

The aim of this study was to develop an aggregate risk score for predicting the occurrence of PAL after VATS lobectomy based on the patients registered in the ESTS database.

Database

The choice to use a societal multi-institutional database has pros and cons. Certainly, when performing aggregate analyses on relatively rare events (such as PAL after VATS lobectomy) the utilization of a population of thousands of patients allows the development of a more reliable predictive model. Moreover, the findings from analyses performed on large organizational databases (such as ESTS database) are widely generalizable to the “real world” and represent contemporary information[19]. On the other hand, the ESTS database was not designed for research purposes, but rather for quality improvement initiatives. As such, when performing specific analyses on selected outcomes many critical variables potentially associated with the outcome of interest may be missing in the dataset. Moreover, as in all multi-institutional retrospective analyses patient selection, surgical technique and postoperative management may be variable in the different participating centers introducing inherent biases into the analysis. However, the ESTS database include most of the common risk factors associated with PAL in previously published single center investigations and has a high data quality as shown in previous specific investigations evaluating the quality of data in this specific database[20].

Main Findings

In the present study PAL was observed in 504 patients (9.9%) of the total patients submitted to VATS lobectomies.

This result is in line with previous papers focusing on the comparison of VATS and open approaches[10-11,21-23].

PAL has already been demonstrated to be one of the most important factors contributing to increased hospitalization length and overall hospital costs[24]. In a recent paper, Farjah and colleagues found that 90-day costs after VATS lobectomy are associated with prolonged hospital stay rather than health care use after discharge[25]. One of the most important findings of the present analysis was that in patients with no other complications, the simple presence of PAL was associated with a postoperative hospital stay 5 days longer compared to those without PAL. In addition, patients in the highest class of risk remained in the hospital 3 days longer than those in the lowest class of risk. The use of intraoperative measures to reduce the incidence of PAL or the volume of air leak (hence favoring earlier discharge with domiciliary chest drainage systems) in high risk patients seems therefore warranted even from a financial point of view.

The added cost of these measures, such as buttress material or surgical sealants, may become negligible in higher PAL risk groups because the cost of the measures may be increasingly offset by avoided hospital stay. Formalized economic analyses evaluating such measures in different PAL risk groups will be important to conduct in the future for hospital decision-makers.

The main finding of this study was the development of a simple PAL risk score based on 3 weighted factors: male gender, FEV1<80%, body mass index<18.5 kg/m^2.

The score is seemingly effective at stratifying patients into 4 classes of risk. Patients with no risk factors had an incidence of PAL of 6% whereas patients in the highest classes of risk (classes C and D) had 2-fold and 4-fold increases in PAL occurrence, respectively. This, as stated above, translated into a longer hospital stay for those in the highest classes of risk. Although a detailed financial analysis was not possible due to different economic systems present across countries contributing to the database, hospital stay is reputedly the main driver of hospital costs and can be taken as an indirect financial estimator.

As mentioned above, PAL scores have been already published for open lobectomies. A few years ago Brunelli and coll. developed a four factor weighted aggregate score from a single center database[3]. Some of the variables were similar to the ones included in the present score. For instance, they found that low FEV1 and low BMI were significantly associated with PAL. A reduced pulmonary function has been consistently reported as a risk factor for PAL[3, 26,27]. The association between PAL and impaired pulmonary function can be explained by the increased susceptibility of a more fragile lung parenchyma to tear during lung dissection or manipulation and by a slower healing process.

Similarly, a low BMI, a marker of malnutrition and reduced healing capacity, was found associated with increased risk of PAL by many authors[3,10,28,29].

Nutritional assessment should be included in the routine preoperative selection to identify patients who can benefit from nutritional support programs.

Male gender and low BMI along with 7 other variables have been found to be associated with PAL in a previous risk model developed from the French Society of Cardiovascular and Thoracic Surgery database[2]. These variables were also recently validated in a population of VATS lobectomy patients[1], however, a specific score for VATS patients was not generated. The association between male gender and PAL is not entirely clear. In the present study male gender likely represent a surrogate for other unaccounted for variables such as smoking history or chronic obstructive pulmonary disease, which were not available in the database at the time of this analysis.

Another factor consistently associated with PAL in previous studies was the presence of pleural adhesions[10,30]. Unfortunately this variable is currently not recorded in the ESTS database and could not be factored into the present analysis. However, this study focuses on VATS lobectomies only, and extensive pleural adhesions may be a contraindication to VATS in some centers.

The other important use of this risk score may be as an informational tool during the preoperative information-provision process. The risk score may inform preoperative patient counseling, and allow clinicians to discuss the risk of developing a PAL and the likelihood of having a chest tube in place for a longer time, or being discharged with a chest drain with the patient. Although we have shown that patient satisfaction is not directly related to postoperative complications[31], the importance of a tailored, informed, shared-decision making process may contribute to setting realistic expectations for VATS patients, and may have further implication in their overall satisfaction with care.

Finally, a PAL risk score specific to VATS lobectomies would also simplify the selection of patients for future efficacy studies on preventative interventions or chest tube management, making the interpretation of results across different investigations more consistent and reproducible, especially in the presence of paucity of randomized trials in this area.

Clinical Implications and future perspectives

The main clinical implication of this study is the possibility to apply this score to select VATS lobectomy patients at high risk of developing PAL. This may serve a clinical and investigational purpose:

- With a VATS approach the submersion test to verify air leak at the end of the procedure is sometime unreliable and the use of this risk score can help in selecting patients at increased risk of PAL who may benefit most of the application of sealants or other intraoperative preventative measures. A financial analysis should be performed in each local health care system to estimate whether the cost of applying preventative measures in all high risk patients would be off set by the reduction of PAL incidence and hospital stay costs in the 15%-25% of patients in whom PAL is expected to occur.
- The score can be used to select high risk patients to be included in future randomized trials investigating the cost effectiveness of sealants

or other measures aimed at reducing the incidence of air leak, improving the reliability and meaningfulness of these analyses.

Limitations of the study

This study has potential limitations.

As discussed above, all the results generated from multi-institutional databases should be interpreted taking into consideration the restrains and structural limitations of these datasets (such as the lack of specific variables of interest, variability in patient selection, surgical technique and postoperative management across participating centers).

For the purpose of this study we did not have access to information regarding specific VATS techniques or modalities, regarding for instance the rate of conversion, the approach to the fissures, etc. Furthermore, in the ESTS database at the moment there is no information regarding the number and type of endostaplers used or the use of energy devices to develop the fissures. Another important aspect that is missing from the ESTS database is the utilization of intraoperative measures to minimize air leakage, such as pleural tenting, the application of buttressed staple devices or the use of sealants. Similarly, the ESTS database does not contain any information regarding the type of chest drainage systems used (digital vs. traditional) nor the type of postoperative chest tube management (suction vs. no suction).

The future implementation of a specific section for minimally invasive procedures will likely obviate these problems.

Another limitation of the database is the absence of the duration of air leak expressed as numeric variable, which would have allowed to test different thresholds of prolonged air leak.

A low BMI was present in only 3.5% of patients. This may represent a critical factor as this predictor may be under-represented in certain population strata. In the current dataset, the value of 18.5 represented the best cut off, however, future analyses are warranted aimed at redefining this threshold to increase its representativeness.

Finally, the ESTS database is a voluntary database. Although more than 200 European Hospitals contribute data into the registry, they represent less than 30% of all centers practicing thoracic surgery in Europe. This may introduce some problems of representativeness and generalizability of the data used for the analysis.

Strengths of the study

The study is based on a large multicenter organizational database, which ensures that the findings are contemporary and reflect the real clinical world. In addition, we performed an external validation using a sample of patients not used to develop the original model. This validation confirmed the generalizability of the risk score.

The model developed and validated in this study includes only three readily available variables making it very user-friendly and easy to implement in the clinical practice.

Conclusions

We created an aggregate risk-score to stratify the incidence of PAL after VATS lobectomy. The score can be used for patient counseling and to identify those patients who can benefit of additional intraoperative preventative measures.

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Table 1: Characteristics of the patients included in the analysis and comparison of baseline and surgical variables between those with and without PAL after VATS lobectomies

Variables	Entire cohort (n=5,069)	With PAL (504 patients)	Without PAL (4,565 patients)	Odds ratio (95% CI)	p-value (between patients with and without PAL)
Age	64 (57-71)	65.0 (58-72)	64.0 (57-71)		0.2
Sex male (n,%)	2,862 (56%)	332 (66%)	2530 (55%)	1.55 (1.3-1.9)	<0.0001
BMI (kg/m^2)	25.5 (22.5-28)	24.3 (21.5-26.0)	25.6 (22.7-28.2)		<0.0001
BMI<18.5 (n,%)	180 (3.6%)	37 (7.3%)	143 (3.1%)	2.45 (1.6-3.6)	<0.0001
FEV1%	84.4 (72.9-96)	81 (66.8-93.1)	84.4 (73-96)		<0.0001
FEV1<80% (n,%)	1,838 (36%)	234 (46%)	1604 (35%)	1.6 (1.3-1.9)	<0.0001

CAD (n,%)	417 (8.2%)	48 (9.5%)	369 (8.1%)	1.2 (0.9-1.6)	0.3
ECOG score	0 (0-1)	0 (0-1)	0 (0-1)		0.4
Diabetes (n,%)	188 (3.7%)	18 (3.5%)	170 (3.7%)	0.95 (0.5-1.6)	0.9
Side right (n,%)	3,035 (60%)	307 (61%)	2,728 (60%)	1.04 (0.9-1.3)	0.6
Site upper (n,%)	3,215 (63%)	315 (63%)	2,900 (64%)	0.96 (0.8-1.2)	0.7

Results are expressed as medians and interquartile ranges for numeric variables and numbers and percentages of patients within the group for categorical variables. CAD: coronary artery disease; ECOG: Eastern Cooperative Oncology Group score; BMI: body mass index; FEV1: forced expiratory volume in one second.

Table 2: **Results of the regression analysis (dependent variable: PAL)**

Predictors	Coefficients	SE	p-value	Bootstrap frequency	Score
Intercept	-2.7	0.09			
Male sex	0.44	0.2	<0.0001	99.7%	1
FEV1<80%	0.4	0.1	<0.0001	99%	1
BMI<18.5	0.96	0.2	<0.001	99%	2

BMI: body mass index; FEV1: forced expiratory volume in one second. Bootstrap frequency: percentage of samples in which the variable resulted with $p<0.05$

Table 3: Breakdown of patient characteristics leading to class assignment

Variables	Class A n=1,493	Class B n=2,240	Class C n=1,219	Class D n=117
Male sex (n,%)	0	1,647 (74%)	1,156 (95%)	59 (50%)
FEV1<80% (n,%)	0	593 (26%)	1,156 (95%)	89 (76%)
BMI<18.5 kg/m^2 (n,%)	0	0	63 (5.2%)	117 (100%)

Results are expressed as numbers and percentages of the total number of patients in that class of risk. BMI: body mass index; FEV1: forced expiratory volume in one second.

Figure Legend:

Figure 1: Incidence of prolonged air leak after video assisted thoracoscopic lobectomy according to the class of risk in the derivation and validation sets. Numbers in the Y axis indicate percentage of patients with prolonged air leak.

Video Legend:

Dr. Alessandro Brunelli, senior author and consultant thoracic surgeon in Leeds, UK, describes the rationale, main finding and implications of this study.

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