

# Cost and effectiveness of lung lobectomy by video-assisted thoracic surgery for lung cancer

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**Background:** Video-assisted thoracic surgery (VATS) emerged as a minimally invasive surgery for diseases in the field of thoracic surgery. We herein reviewed our experience on thoracoscopic lobectomy for early lung cancer and evaluated Health System use.

**Methods:** A cost-effectiveness study was performed comparing VATS vs. open thoracic surgery (OPEN) for lung cancer patients. Demographic data, tumor localization, dynamic pulmonary function tests [forced vital capacity (FVC), forced expiratory volume in one second (FEV1), diffusion capacity (DLCO) and maximal oxygen uptake (VO<sub>2</sub>max)], surgical approach, postoperative details, and complications were recorded and analyzed.

**Results:** One hundred seventeen patients underwent lung resection by VATS (n=42, 36%; age: 63±9 years old, 57% males) or OPEN (n=75, 64%; age: 61±11 years old, 73% males). Pulmonary function tests decreased just after surgery with a parallel increasing tendency during first 12 months. VATS group tended to recover FEV1 and FVC quicker with significantly less clinical and post-surgical complications (31% vs. 53%, P=0.015). Costs including surgery and associated hospital stay, complications and costs in the 12 months after surgery were significantly lower for VATS (P<0.05).

**Conclusions:** The VATS approach surgery allowed earlier recovery at a lower cost than OPEN with a better cost-effectiveness profile.

**Keywords:** Video-assisted thoracic surgery (VATS); open thoracic surgery; pulmonary function tests; surgery lobectomy; lung cancer

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## Introduction

Since the beginning of the 1990s, thoracoscopic surgery has acquired widespread favour with the rapid development of associated techniques and instrumentation (1-3). The American College of Chest Physicians, in its evidence-based clinical practice guidelines, suggests that “In patients with stage I non-small cell lung cancer (NSCLC) who

are considered appropriate candidates for thoracoscopic anatomic lung resection (lobectomy or segmentectomy), the use of video-assisted thoracic (VATS) surgery by surgeons experienced in these techniques is an acceptable alternative to open thoracotomy” (4). Nowadays, centers consider this to be the procedure of choice for the treatment of early-stage lung cancer (5,6).

The advent of VATS, as minimally invasive surgery, has

significantly altered thoracic surgical procedures (7,8) and remarkable benefits to patients such as reduced wound pain and shorter hospital stay (9,10). Furthermore, several studies reported that provides better long-term survival benefit in lung cancer patients (11,12), the leading cause of cancer-related deaths worldwide (13). However, VATS has higher equipment costs, increased operating room times, at least initially, and a learning curve for the team (14).

Here we present a cost-effectiveness study comparing lung lobectomy by VATS *vs.* open thoracic surgery (OPEN) in 117 patients who were diagnosed with NSCLC.

## Methods

### Patients

A total of 117 NSCLC patients from the Department of Thoracic Surgery of the University General Hospital of Alicante suffering lung lobectomies for lung cancer treatment were included in this study. They were divided into two categories: a prospective group (n=42) that underwent VATS technique from March 2013 to January 2015; and a retrospective group of a prospectively maintained patient's database (n=75) who underwent OPEN from September 2001 to June 2005. All patients followed standard treatment and received information on the design and purpose of the study. Institutional review board approval and participants' informed consents were obtained.

All patients received thorough examinations including conventional blood tests, CT scan, PET-CT and head CT or magnetic resonance imaging (MRI) to exclude distant metastasis. Mediastinoscope or endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed when chest CT scan or PET indicated N2 or N3 diseases. Indications for VATS lobectomy included: no ipsilateral thoracotomy history; no evidence of severe pleural adhesions; resectable lesions  $\leq 5$  cm; no clinical sign of N2 metastases. Surgeon experience and preference were also relative indications. Preoperative discussion of each case was mandatory. All patients' clinical data were presented to evaluate the safety and efficiency at the routine meetings.

Inclusion criteria consisted of lung lobectomy surgery with curative intent and a definitive pre- or postoperative diagnosis of NSCLC not been treated with postoperative chemotherapy or radiotherapy. For OPEN group, criteria also included having a minimum of two postoperative pulmonary function tests performed correctly. Exclusion criteria were pneumonectomy or sublobar resection,

patients with unresectable disease, postoperative chemo- or radiotherapy, or rapid postoperative disease progression.

### Data and lung function tests

Demographic, clinical, surgical factors (incidence of complications and 30-day mortality) were evaluated.

Pulmonary function tests were carried out in the immediate preoperative period, and 1, 3 and 12 months after surgery (15) Following the American Thoracic and European Respiratory Society (ATS/ERS) 2005 international standards (14). Pulmonary function tests (PFTs), their reliability and the association with the general disease stage measured by the Brooke score. Dynamic PFTs [forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), diffusion capacity (DLCO) and maximal oxygen uptake (VO<sub>2</sub>max)] was measured by the single-breath method or by spirometry was performed after bronchodilator administration. DLCO, FVC, FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio were obtained and expressed as percentage of predicted for age, sex, and height according to the European Community for Steel and Coal prediction equations (16,17).

### Preoperative staging and follow up

Conventional blood tests, thoracic CT and brain, CT or brain MRI were done to establish absence of brain metastases when neurologic symptoms occurred. A standard follow-up was followed. Additionally, during 12 months, patients were monitored for PFTs at each time point.

Perioperative mortality was defined as death within 30 days of the operation or within the same hospital admission. Survival was recorded from day of the operation until date of death or last follow-up.

### Surgery methods

Thoracoscopic lobectomy, as previously reported, was performed under epidural catheter anaesthesia and general anaesthesia with dual-lumen endotracheal tubes in the absence of rib spreading (18). Postoperative chest pain was controlled by multimodal analgesia, including the provision of epidural or continuous intravenous analgesia and/or nonsteroidal anti-inflammatory drugs, which were titrated to maintain adequate pain control in order to achieve early mobilisation. The leading group made up of 4 most experienced surgeons in our department would authority

the surgery and applicable approach.

### Video-assisted thoracic surgery (VATS)

A 10 mm, 30° thoracoscope was introduced through the 7th intercostal space in the midaxillary line. A 5-cm access thoracotomy was usually placed in the 4th or 5th intercostal space in the anterior axillary line for upper/middle or lower lobectomy, respectively. When necessary a third opening was performed in the back of the chest, on the posterior axillary line, at the level of the 7th or 8th intercostal space. All structures to be resected were stapled with two types of linear machines: Endo-GIA Covidien, Autosuture Company Division (US Surgical Corporation, MA, USA) or ECHELON FLEX™ 60 Powered ENDOPATH® Stapler (Ethicon Endo-Surgery Inc., OH, USA).

### Open thoracotomy (OPEN)

Lobectomy via open thoracotomy was performed using a posterolateral incision, of variable length depending on the case, through the 4th or 5th intercostal space. The vascular and bronchial structures were individually dissected and divided using vascular Endo-GIA 45 mm Stapler, linear 60 or 100 mm Stapler for fissures and TA 60 mm Stapler for bronchus (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA).

### Histopathological examination

Pathological staging was performed according to the 7th International Staging System for Lung Cancer. Tumors were evaluated in size, location and anatomic relationships (T), the degree of lymphatic invasion node (N), and in the presence of metastatic (M) (19).

### Cost calculation

The total costs were calculated at the same time point for both groups and were calculated as the sum of: (I) cost of the length of surgery time (14.33 €/minute) and stapling loads (200–300 €/shot); (II) cost of the length of time at the intensive care unit (ICU) postoperatively (1,191.3 €/day); and (III) hospitalization cost plan (323 €/day). Since the charges were recorded in books of surgery that were already destroyed 10 years ago, stapling loading costs for retrospective OPEN group were calculated using the mean of the last 10 patients on surgery as fixed value (2,104.60 €/patient).

Incremental cost-effectiveness ratio (ICER) was calculated as the cost difference between the two interventions, divided by the difference on their effect. The following issues were

included in the effectiveness assessment: hospital stay for surgery, pathological stage and survival.

All the costs were summed and expressed as euros (€). Various thresholds of willingness-to-pay (WTP) to calculate the net benefit (NB) when VATS was compared to OPEN were calculated by applying the following equation in which an intervention was considered cost-effective if it resulted in a positive NB:  $NB = \text{effectiveness} \times WTP - \text{cost}$  (20). Also, incremental cost and incremental effectiveness were calculated as the difference between both surgical procedures (OPEN and VATS).

WTP refers to the amount of money the payer is willing to pay for an outcome. The commonly cited WTP threshold, 50,000–100,000 USD/life year (LY), means that the payer is generally willing to pay this amount to gain a year of life and is usually considered as a threshold to decide whether an intervention is cost-effective or not (21,22). This WTP range also covers the WHO criteria (3 times gross domestic product per capita) regarding cost-effectiveness in Spain is around 101.505€ with a positive monetary net gain, so it is also cost-effective at this specific WTP level. When the incremental NB (INB) of an intervention is positive at a specific WTP level, this intervention is associated with a positive financial gain and, thus, is also cost-effective at this specific WTP level.

### Statistical analysis

All variables followed a normal distribution, thus, parametric tests were used. Continuous variables are presented as means and categorical variables are expressed as absolute numbers and/or percentages. *t*-test for independent samples and the Pearson  $\chi^2$  were used to assess variations in the study parameters between groups. A stepwise regression was used to cost with all clinical variables. Patients underwent lung tests at 1, 3 and 12 months postoperatively, and the data were compared with those gathered preoperatively. All statistical analyses were performed with the R (3.3.1) y R-Studio (0.99.892) for MAC-OSX.  $P < 0.05$  were considered to indicate significance for all parameters.

## Results

### Patient's preoperative data

Patient's demographic and clinical data are shown in *Tables 1* and *2*.

One hundred seventeen patients underwent anatomical

**Table 1** Clinical, demographic and preoperative data

Data	VATS (n=42)	OPEN (n=75)	P value
Age, mean $\pm$ SD	63.43 $\pm$ 9.11	61.24 $\pm$ 10.77	0.27
Male (%)	57.1%	88.0%	0.00
BMI, mean $\pm$ SD (min-max)	28.23 $\pm$ 5.84 (18.00–44.85)	26.27 $\pm$ 3.57 (16.40–34.57)	0.05
Smoking (pack year), mean (min-max)	42.29 (0–120)	48.6 (0–116)	0.26
Pathology, n (%)			0.006
Adenocarcinoma	31 (73.81%)	38 (50.67%)	
Epidermoid	8 (19.05%)	31 (41.33%)	
Pathological stage, n (%)			0.00
Non detected	1 (2.38%)	7 (9.33%)	
Ia	28 (66.67%)	22 (29.33%)	
Ib	10 (23.81%)	11 (14.66%)	
IIa	2 (4.76%)	21 (28.00%)	

VATS, video-assisted thoracic surgery; BMI, body mass index.

**Table 2** Tumor characteristics, pathological stage and postoperative clinical evolution

Data	VATS (n=42)	OPEN (n=75)	P value
Preoperative chemotherapy			
No	41 (97.62%)	55 (73.33%)	0.00
T stage, n (%)			
T1a	16 (30.09%)	18 (24.00%)	
T1b	12 (28.57%)	17 (22.67%)	0.005
T2a	10 (23.81%)	17 (22.67%)	
Radiological image, n (%)			0.02
Lung nodule	30 (71.43%)	27 (45.76%)	
Mass	9 (21.43%)	29 (49.15%)	
Lobar Atelectasia	3 (7.14%)	3 (5.08%)	
Surgery time (h, mean $\pm$ SD)	3.86 $\pm$ 0.9	4.11 $\pm$ 1.31	0.30
ICU admission (days, mean $\pm$ SD)	1.05 $\pm$ 0.31	1.72 $\pm$ 2.21	0.02
Hospital admission (days, mean $\pm$ SD)	5.57 $\pm$ 2.64	8.19 $\pm$ 4.48	0.00
Complications, n (%)	13 (30.9%)	40 (53.3%)	0.015

ICU, intensive care unit; VATS, video-assisted thoracic surgery.

lung resection for NSCLC, 42 of them by VATS (36%; age: 63.4 $\pm$ 9.1 years old, 57% males) and 75 by OPEN (64%; age: 61.2 $\pm$ 10.7 years old, 88% males). In OPEN, male frequency was significantly higher probably due to gender smoking habit (73.3%, P=0.00), less overweight (BMI 26.3 $\pm$ 3.6 kg/m<sup>2</sup>,

P=0.05), less adenocarcinoma and more epidermoid lung cancer (50.67% and 41.33%, respectively P=0.006).

Pathological tumor stage was mostly stage Ia for VATS (67%), meanwhile for OPEN was mostly stages Ia and IIa (29.3% and 28%, respectively). In OPEN group, preoperative

neoadjuvant chemotherapy was significantly higher than for VATS (OPEN: n=20, 26.7%; VATS: n=1, 2.4%, P=0.00). None of the patients received postoperative chemotherapy. In VATS, the most frequent lobectomies were of the right upper (12/42 patients, 28.6%) and left lower lobes (11/42 patients, 26.2%). In comparison, most frequent OPEN lobectomies were of the left (28/75 patients, 37.3%) and the right upper (25/75 patients, 33.3%) lobes.

A sub analysis was done with stage II non-small cell lung (tumor present in the lung that may have spread to local lymph nodes, but has not spread further, without any preoperative significant differences between OPEN and VATS group (data not shown).

### Patient's postoperative data

Number of complications was significantly higher in OPEN (53.3%) than VATS group (30.9%, P=0.015) mostly related to subcutaneous emphysema in VATS and for both, prolonged pulmonary air leak (Table 3). All cases recovered and no operative or 30 days after surgery deaths were registered. A total of 21 readmissions occurred along the 12 months of study (2 for VATS and 19 for OPEN, P=0.001) mostly due to tumor progression.

During the first year, in VATS group, 2 deaths due to massive pulmonary embolism and progression of neoplastic disease were recorded. In contrast, 43 patients died in OPEN group, 5 patients died in the first year, 14 in the second, 8 in the third, 7 during the fourth, 3 during the fifth, and the rest (6) at a later date. Because VATS inclusion finished in January 2015, survival at long term cannot be compared.

### Lung function tests

Table 4 and Figure 1 show the evolution of postoperative lung function parameters.

Preoperative functional lung test scores decreased right after surgery with an improving tendency during 12 months of follow-up: FEV<sub>1</sub> (preoperative vs. 12 months in VATS vs. OPEN: 8.85% vs. 13.31%, respectively, P=0.584), FVC (0.9% vs. 11.46%, P=0.074), DLCO (2.45% vs. 6.08%, P=0.490), and VO<sub>2</sub>max (7.62% vs. 2.98%, P=0.485).

Values for most of the parameters in VATS group were higher than in OPEN, except for VO<sub>2</sub>max, which was higher in the OPEN group maybe because they were performed with a treadmill (that usually gives higher values) instead of the cycle-ergometer that was used for VATS.

The mean postoperative values presented parallel patterns,

with lower values in OPEN patients. Patients from VATS group tended to recover FEV<sub>1</sub> and FVC quicker than patients from OPEN group. Similar PFT results were obtained when only stage II NSCLC patients were analyzed.

### Cost-effectiveness analysis

Cost-effectiveness analysis data is presented in Table 5. There were statistically significant differences between the two groups in the costs of surgical equipment, number of supplies, days of hospitalization and days of ICU (Table 5). Total cost for VATS was significantly lower than for OPEN (8,751±1,909 vs. 10,032±2,983€, respectively, P=0.02). This difference was mostly related to the cost of total hospitalization days. For the entire follow-up period, no significant differences in the survival rate were found between VATS and OPEN (data not shown).

FEV<sub>1</sub> within one year after surgery was lower for VATS vs. OPEN (0.9115 vs. 0.8669 L, respectively). Incremental cost was -1,281€ (VATS - OPEN cost = 8,751€ - 10,032€) and incremental effectiveness 0.0446(=0.9115-0.8669 L) FEV<sub>1</sub>, the NB if WTP equals €100,000/LY would be positive 3,179€ [=0.0446×100,000-(-1,281)]. The ICER when VATS was compared to OPEN was -28,722€ (= -1,281/0.0446 €/FEV<sub>1</sub>).

Thus, VATS is potentially more cost-effective than OPEN at short-term (1 year) within the common WTP levels from a payer's perspective since VATS estimated ICER (-28,722 €/LY) was below the WHO common criteria (100,000 €/LY).

### Discussion

As it is well known, VATS lobectomy has been accepted as one of the surgical therapeutic methods for lung cancer resection by the National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology mainly because presents a tendency of less damage to respiratory function, in the same way in early tumor stages, less complications being the cost of this technique lower. The results of the present study are in line with previous preliminary estimates (14,23,24).

Jiao *et al.* set at 6 months the time-point to evaluate the permanent lung functional loss after VATS lobectomy. Usually, there is no further significant improvement in pulmonary function tests in the follow-up period (25). However, in our data, although must be confirmed, there was a tendency for lung function recovery at 12 months after VATS lobectomy. Meanwhile, in accordance with previous studies of Bolliger *et al.* (26) and Nezu *et al.* (27),

**Table 3** Postoperative readmission causes and complications

Readmission causes and complications	VATS (n=42)	OPEN (n=75)
Readmission etiology		
Lung abscess	0	1
Tumor progression	0	15
Pulmonary embolism	0	3
Emphysema	1	0
Pleural invasion	1	0
Complications	13 (30.95%)	40 (53.33%)*
Persistent air leak	2 (15.38%)	6 (15%)
Subcutaneous emphysema	3 (23.08%)	1 (2.5%)
Surgical wound infection	1 (7.69%)	4 (10%)
Paralytic abdominal ileus	1 (7.69%)	3 (7.5%)
Transfusion for bleeding	0	4 (10%)
Pleural effusion requiring new drainage	0	4 (10%)
Reoperation for bleeding	0	2 (5%)
Atrial fibrillation	0	3 (7.5%)
Lobar atelectasis	2 (15.38%)	2 (5%)
Atrial flutter	1 (7.69%)	0
Residual space	0	2 (5%)
Respiratory distress	0	2 (5%)
Left recurrent nerve paralysis	1 (7.69%)	1 (2.5%)
Heart failure	0	1 (2.5%)
Urinary infection	0	1 (2.5%)
Hypertensive crisis	1 (7.69%)	0
Pleural space requiring new drainage	1 (7.69%)	0
Angina	0	1 (2.5%)
Postoperative pleural emphysema	0	1 (2.5%)
Renal failure	0	1 (2.5%)
Rectal bleeding	0	1 (2.5%)

\*, P=0.015. VATS, video-assisted thoracic surgery.

we found that OPEN led to a 10% permanent loss in pulmonary function. Several reports suggested that lobectomy patients suffered a significant reduction (15%) of functional reserve at 6 months postoperatively, with almost equal deterioration between lung function and exercise capacity (28,29). Also, for many patients, the risk of impaired quality-of-life after surgery is an important

consideration. Several reports suggested that pulmonary resection has a negative influence on the quality-of-life with a subsequent partial recovery over time (30-32).

It is believed that metastases occur most frequently during the perioperative period, when injury and repair are more prominent and stress can elaborate various humoral substances that potentiate the growth of carcinomas. Thus,

**Table 4** Changes of FEV<sub>1</sub>, FVC, DLCO, and VO<sub>2</sub>max (percentage loss) from preoperative values to the different follow-up times

Pulmonary function tests	Postoperative time (months)	
	1	12
%FEV <sub>1</sub>		
VATS	20.59	8.85
OPEN	24.66	13.31
P value	0.640	0.584
%FVC		
VATS	18.48	0.90
OPEN	26.57	11.46
P value	0.357	0.074
%DLCO		
VATS	17.32	2.45
OPEN	25.79	6.08
P value	0.338	0.490
%VO <sub>2</sub> max		
VATS	18.33	7.62
OPEN	nd	2.98
P value	nd	0.485

FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; DLCO, diffusion capacity; VO<sub>2</sub>max, maximal oxygen uptake; VATS, video-assisted thoracic surgery; nd, non determined.

Lewis *et al.* (33) proposed that VATS minimal invasive surgical procedures performed with small incisions could account for improved long-term survival. Furthermore, in VATS, fewer malignant cells would be disseminated and passed into blood vessels or lymphatics, which could occur from the extensive mechanical stress through palpation and compression common to the OPEN technique (33,34).

Moreover, VATS would potentially avoid complications, eliminate disruptions from anaesthetic induction, and shorten hospital stay, providing a more cost-effective approach (35). In the study of Paul *et al.* (12), 73.8% of patients who underwent VATS presented no complications, while 65.3% of patients that underwent OPEN had no complications. They also found that patients that underwent VATS had a lower incidence of arrhythmias, reintubation, blood transfusion, shorter hospital stay, and chest tube duration (12). In addition, to these early functional advantages, VATS lobectomy has been shown to have similar long-term outcomes compared to OPEN (36,37).

Swanson *et al.* compared hospital costs and perioperative outcomes for VATS (n=1,054) and OPEN (n=2907), in the United States using the premier prospective length of stay was 7.83 days for OPEN *vs.* 6.15 days for VATS. As in our study, surgery duration was shorter for VATS *vs.* OPEN procedures (3.75 *vs.* 4.09 hours). Also, the risk of adverse events was significantly lower in VATS group (P=0.019) and hospital costs were higher for OPEN *vs.* VATS [\$21,016 *vs.* \$20,316 (P=0.027)]. Higher costs for OPEN surgery were confirmed in several studies (38,39). In addition, our results show that VATS is potentially more cost-effective than OPEN within the common WTP levels.

However, our study presented some limitations. The main limitations were: (I) the different period of study; (II) different diagnostic and staging methods; (III) different surgeons performing the procedures. In addition, there is always concern in potential unobserved confounding bias especially being VATS prospective and OPEN retrospective, taking into account the gender differences. Secondly, although the long term outcome of early stage NSCLC was quite good, the duration of our study (1 year) might not be long enough to fully capture the cost-effectiveness, and, probably longer follow-up might make VATS more favourable given the slightly improved survival and similar cost at the end of our follow-up period. Furthermore, the number of patients in our study is relatively low and further studies with larger groups should be performed. In addition, similar tumor stages should be compared in order to estimate survival and cost-effectiveness and OPEN costs were calculated from the last 10 surgeries. Another possible bias of the VATS technique could be that smaller tumors without affecting the pulmonary hilum or nearby structures will be operated.

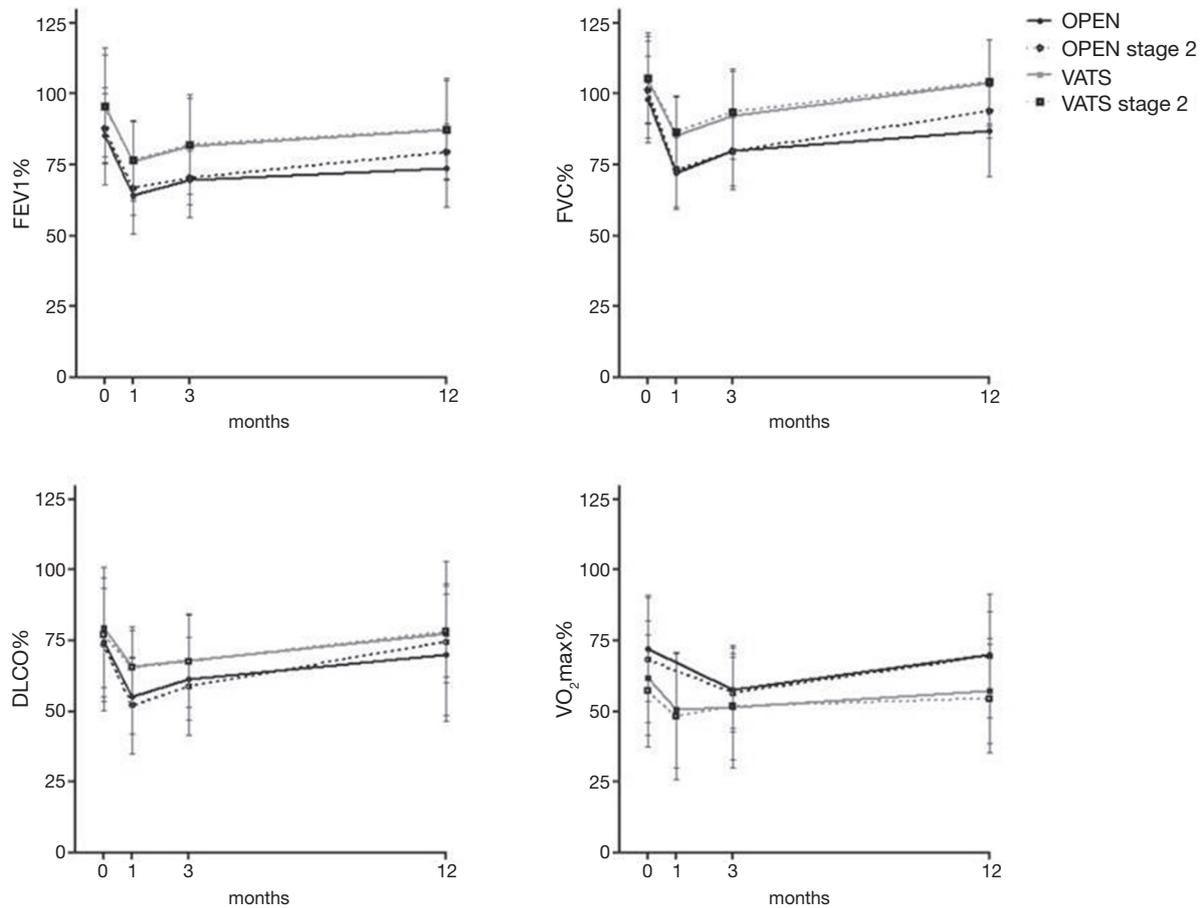
We provided evidence that VATS is a safe and feasible technique and, when compared to OPEN, it was potentially more cost-effective at short term (1 year) within the common WTP levels from payer's perspective in Spain. Further studies would be helpful to see the long-term cost-effectiveness results and whether the same results could be obtained in other health care systems.

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### Footnote

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



**Figure 1** Lung function tests for preoperative (0) and postoperative at 1, 3, and 12 months for VATS (grey solid line) and OPEN (black solid line) groups, as well as for stage 2 tumors (grey and black dashed lines respectively). Data represented is mean  $\pm$  standard deviation. VATS, video-assisted thoracic surgery.

**Table 5** Cost-effectiveness analysis

Cost (€)	VATS	OPEN	P value
Staple-line sutures	2,361.5 $\pm$ 890.45	2,104.600 $\pm$ 0	nd
Surgery	3,322.11 $\pm$ 781.90	3,527.38 $\pm$ 1,129.11	0.304
ICU admission	1,248.03 $\pm$ 367.64	2,049.74 $\pm$ 2,626.56	0.016
Hospital admission	1,799.57 $\pm$ 853.51	2,646.33 $\pm$ 1,447.64	0.000
Total cost	8,750.96 $\pm$ 1,908.89	10,031.59 $\pm$ 2,982.66	0.020
Effectiveness (FEV <sub>1</sub> -year)	0.912	0.867	
Incremental cost	-1,281	Reference	
Incremental effectiveness	0.046	Reference	
ICER	28,722	Reference	
INB (at WTP 100,000 €)	5,741	Reference	

VATS, video-assisted thoracic surgery; nd, non determined; ICU, intensive care unit; FEV<sub>1</sub>, forced expiratory volume in one second; ICER, Incremental cost-effectiveness ratio; INB, incremental net benefit; WTB, willingness-to-pay.

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