

Thoracoscopic lobectomy for locally advanced-stage non-small cell lung cancer is a feasible and safe approach: analysis from multi-institutional national database

Alessandro Gonfiotti^{1*}, Stefano Bongiolatti^{1*}, Luca Bertolaccini², Domenico Viggiano¹, Piergiorgio Solli², Andrea Droghetti³, Alessandro Bertani⁴, Roberto Crisci⁵, Luca Voltolini¹; Italian VATS Group*

¹Thoracic Surgery Unit, Careggi University Hospital, Florence, Italy; ²Thoracic Surgery Unit, AUSL Romagna Teaching Hospital, Ravenna, Italy; ³Department of Thoracic Surgery, ASST Mantova, Mantova, Italy; ⁴Department of Thoracic Surgery, IRCCS ISMETT-UPMC, University of Pittsburgh, Palermo, Italy; ⁵Department of Thoracic Surgery, University of L'Aquila, L'Aquila, Italy

Contributions: (I) Conception and design: A Gonfiotti, L Voltolini, R Crisci; (II) Administrative support: None; (III) Provision of study materials or patients: R Crisci, A Droghetti, P Solli; (IV) Collection and assembly of data: A Droghetti, R Crisci, L Bertolaccini, P Solli; (V) Data analysis and interpretation: A Gonfiotti, L Bertolaccini, A Bertani, P Solli, A Droghetti; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Alessandro Gonfiotti, MD. Thoracic Surgery Unit, University Hospital Careggi, Largo Brambilla, 1, 50134 Florence, Italy. Email: agonfiotti@gmail.com.

Background: Video-assisted thoracoscopic lobectomy (VATS-L) is a well-established approach for early-stage non-small cell lung cancer (NSCLC) with functional and oncological outcomes similar to thoracotomy. The role of VATS-L in locally advanced stage of NSCLC has not been well standardized. The objective of this study was to evaluate the state of the art in Italy of VATS-L for NSCLC advanced stages using the data from the Italian VATS Group Database.

Methods: Between 1st January 2014 and 31st May 2017, 3,720 patients underwent VATS-L at VATS Group participating centres and included in the VATS Group database. Patients were divided into two groups: (A) early stages and (B) locally-advanced stages (tumours with dimension >5 cm (cT2b), cT3, cT4 and/or tumours that received neo-adjuvant chemotherapy). A retrospective study was performed, to evaluate the safety and the oncological adequacy of VATS-L comparing peri-operative outcomes and pathological data.

Results: A total of 3,266 (87.7%) patients were included into the group A, while 454 (13.3%) patients formed the group B. VATS-L for locally advanced-stage NSCLC is associated with a longer procedure, a higher estimated blood loss, an increased incidence of conversion (9.3% vs. 13.0%, $P=0.018$) and a significant higher number of total, hilar and mediastinal dissected lymph nodes. The mortality rate (1.6% vs. 1.5%), the proportion of patients who suffered any complication (24.8% vs. 29.1%) and the hospitalization were not statistically different between the two groups ($P=0.880$, 0.057 and 0.660 , respectively); the overall complication rate was statistically higher in group B (30.4% vs. 37.0%; $P=0.04$). Patients of group B who required conversion had a statistically significantly higher operative time ($P<0.01$), blood loss ($P<0.01$) and hospital stay ($P<0.01$), but not significantly higher overall morbidity rate (35.5% vs. 28.0%) compared with patients completely operated by VATS.

Conclusions: VATS-L for locally advanced-stage NSCLC in Italy is a safe and effective procedure when performed in appropriately selected patients, ensuring peri-operative results similar to those obtained in early-stage tumours.

Keywords: Video-assisted thoracic surgery (VATS); lobectomy; lung cancer; advanced-stage lung cancer

Received: 23 August 2017; Accepted: 05 September 2017; Published: 07 November 2017.

doi: 10.21037/jovs.2017.09.06

View this article at: <http://dx.doi.org/10.21037/jovs.2017.09.06>

Introduction

Video-assisted thoracoscopic lobectomy (VATS-L) is a well-established approach for early-stage non-small cell lung cancer (NSCLC) (1-3) and is associated with a shorter length of stay, less post-operative pain, preserved pulmonary function, fewer post-operative complications and better compliance with adjuvant chemotherapy than lobectomy via thoracotomy (4-6). Furthermore, several and authoritative authors demonstrated the efficacy of VATS lobectomy in terms of oncological results and validity of mediastinal intra-operative staging (7-10), but the use of VATS-L for locally advanced-stage NSCLC is not well established. Some preliminary and single-centre retrospective studies have shown that VATS-L is feasible, safe and effective with long-term oncologic outcomes comparable to lobectomy via thoracotomy (11-13).

The objective of this retrospective multi-institutional study was to confirm the safety and feasibility of thoracoscopic lobectomy in locally advanced-stage NSCLC and to compare the peri-operative outcomes with early-stage tumours using a national multi-institutional database, the Italian VATS Group Database.

Methods

Data source

The Italian VATS Group Database is a multicentre, web-based data system for collecting and reporting clinical characteristics, patterns of care, and outcomes data on NSCLC patients treated with a VATS-L. The Italian VATS Group has maintained this prospective database since January 2014. At the time of the latest report, there were more than 54 participating centres (general thoracic surgery units or services, not individual surgeons) and about 4,000 collected cases. Harvested data are maintained by the VATS Group Board and collected on a standardized data form that includes information about patient demographics, medical history, surgical procedures, cancer staging, and outcome. Patients are reviewed and records are updated the first time at 30 days after surgery, then at 180 days. Next update is recorded at 6 months from surgery and every 6 months for the first 2 years of follow-up, and annually thereafter. The Institutional Review Board has provided approval for the data collection, transmission and storage, as well as analyses of the data (No. 81/2014/O/Oss). The current analysis was reviewed and approved for scientific merit and feasibility by the VATS Group Scientific Committee and presented at the

annual VATS Group meeting. The VATS Group Database implements rigorous quality assurance and safety procedures to maintain a high level of accuracy and security of data. These include real-time Web-based edit checking, quality assurance reports that are provided by the data managers and on-site audits of a random sample of source documents against the submitted data performed by a Quality Committee. Security features include firewall security, web authentication password protected access, and data encryption transmissions over the internet. To be included in the database, patients must meet the criterion of a VATS-L using a standard approach as it has been defined by VATS Group policy: surgery performed by monitor vision, access incision smaller than 6 cm without rib spreading, one to three additional 1-cm ports, individual dissection of hilar structures with associated lymphadenectomy, use of an endo-bag for specimen extraction.

Patient population and methods

The study population consists of patients who received VATS-L as the primary procedure for locally advanced clinical stage NSCLC as defined by: tumours with dimension >5 cm (cT2b, cT3), cT4 [based on the seventh classification of American Joint Committee on Cancer (AJCC) (14)] and/or tumours that received neoadjuvant chemotherapy at VATS Group participating centres and included in the VATS Group database between 1st January 2014 and 31st May 2017.

Patients with these characteristics were divided into two groups and compared according to the clinical stage: the first group identified as “early-stage group” (group A) comprising clinical stage IA, IB and IIA while the second group, identified as “locally advanced-stage group” (group B), comprising all other patients in clinical stage IIB, IIIA or more. All patients underwent conventional pre-operative examinations, including cardiopulmonary function tests, contrast enhanced thoracic and abdominal computed tomography (CT) scan, brain CT scan and positron emission tomography-CT (PET-CT) scan. In case of mediastinal lymph node CT enlargement or PET-CT scan hyperactivity, endobronchial ultrasound-guided fine-needle aspiration (EBUS-FNA) or mediastinoscopic biopsy was performed before surgery. Restaging was completed with thoracic and abdominal CT-scan, PET-CT scan and/or EBUS-FNA or mediastinoscopy.

To evaluate the safety of VATS-L in locally advanced-stage NSCLC, we compared mortality rate, overall complication rate, frequency and the type of complications.

Table 1 Pre-operative patients characteristics

Variables	Early-stage group A (n=3,266)	Locally advanced-stage group B (n=454)	P value
Age (mean ± SD) (years)	67.42±9.42	68.44±9.19	0.030
Sex [n (%)]			0.000
Male	1,921 (58.80)	314 (69.20)	
Female	1,345 (41.20)	140 (30.80)	
FEV1% (mean ± SD)	94.15±20.93	91.32±21.07	0.009
FVC% (mean ± SD)	101.14±22.90	98.93±19.63	0.057
Tiffenau index (mean ± SD)	75.22±12.46	73.80±13.61	0.029
DLCO/VA% (mean ± SD)	64.57±39.37	63.22±37.61	0.500
Side [n (%)]			0.360
Right	1,950 (59.70)	261 (57.70)	
Left	1,316 (40.30)	193 (42.30)	
Surgical procedure [n (%)]			0.000
Upper lobectomy	1,938 (59.30)	225 (49.60)	
Median lobectomy	226 (6.90)	21 (4.60)	
Lower lobectomy	1,096 (33.50)	205 (45.10)	
Upper bi-lobectomy	3 (0.15)	2 (0.50)	
Lower bi-lobectomy	3 (0.15)	1 (0.20)	
Pre-operative chemotherapy	0	113 (24.80)	0.000

SD, standard deviation.

The effectiveness and oncological adequacy of VATS-L was assessed comparing conversion rate, intra-operative data (operative time, estimated blood loss), resection status and number of dissected lymph nodes.

Statistical methods

Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Standard descriptive statistics have been used to summarize data, with respect to demographic and oncological characteristics. Continuous variables, expressed as mean value ± standard deviation (SD), were compared by unpaired Student's *t*-tests; categorical variables were analysed by means of Chi-square tests. A P value below 0.05 was considered as statistically significant.

Results

After exclusions, n=3,720 VATS-L were identified (male:

n=2,235, 60.0%, mean age: 67.93 years) among 50 VATS Group affiliated centres. Dividing the study cohort according to the clinical stage, 3,266 (87.8%) patients were included in group A, while 454 (12.2%) patients formed group B. Pre-operative characteristics are depicted in the *Table 1*. Patients of group B were more frequently male, older, with lower pulmonary reserve and with a tumour localized in the lower lobes.

Surgical approach and type of lymphadenectomy did not differ between the two groups, while total number of dissected lymph nodes and the number of dissected N1 and N2 lymph nodes were statistically different between the two groups (*Table 2*).

VATS-L for locally advanced-stage NSCLC was associated with a longer procedure, with a higher estimated blood loss (144.63 vs. 169.44 mL; P=0.017) and an increased incidence of conversion (9.3% vs. 13.0%, P=0.018). The most common causes of thoracotomy in group B were: bleeding (16/59, 27.1%), an unexpected tumour extension

Table 2 Intra-operative data

Variables	Early-stage group A (n=3,266)	Locally advanced-stage group B (n=454)	P value
Surgical approach [n (%)]			0.320
Copenhagen anterior approach	2,465 (75.6)	334 (73.7)	
Uniportal approach	263 (8.1)	37 (8.1)	
Others	538 (16.4)	83 (18.2)	
Operative time (mean ± SD) (min)	186.69±69.65	193.85±63.69	0.038
Estimated blood loss (mean ± SD) (mL)	144.63±186.73	169.44±241.79	0.017
Type of lymphadenectomy [n (%)]			0.570
Systematic lymph node dissection	2,340 (71.6)	331 (72.9)	
Sampling	926 (28.4)	123 (27.1)	
Number of total lymph nodes dissected (mean ± SD)	13.48±8.18	15.69±10.47	0.000
Number of N1 lymph nodes dissected (mean ± SD)	6.38±4.30	7.55±6.96	0.000
Number of N2 lymph nodes dissected (mean ± SD)	7.02±5.58	8.27±6.62	0.000
Conversions [n (%)]	305 (9.3)	59 (13.0)	0.018
Cause of conversion [n (%)]			0.000
Bleeding	102 (33.4)	16 (27.1)	
Hilar calcific lymph nodes	73 (23.9)	13 (22.0)	
Fissure fusion	49 (16.1)	6 (10.2)	
Adhesions	51 (16.7)	9 (15.3)	
Tumour extension	30 (9.8)	15 (25.4)	

SD, standard deviation.

precluding a safe thoracoscopic dissection (15/59, 25.4%) and a calcific hilar adenopathy (13/59, 22.0%).

Patients of group B requiring conversion, had a significantly higher operative time, blood loss, hospital stay and positive surgical margins, but not a higher overall morbidity rate (35.5% vs. 28.0%) compared with patients operated by VATS (Table 3).

The mortality rate (1.6% vs. 1.5%), the proportion of patients who suffered from any complication (24.8% vs. 29.1%) and the hospital stay (7.35 vs. 7.96 days) were not statistically different between the two groups (P=0.880, 0.057 and 0.660, respectively). The complication rate was significantly higher in group B (30.4% vs. 37.0%); particularly we observed a higher incidence of hemothorax (1.0% vs. 3.3%) (Table 4).

In group B, we observed a larger amount of squamous cell carcinoma (SCC) (26.4%) compared to group A (14.8%). Due to selection bias, the pathological stages were different between the two groups with a higher incidence

of advanced stage in group B: 26.8% of patients in group B had metastatic hilar or mediastinal lymph nodes and also 3.7% of patients had positive margins. Furthermore, some adjuvant therapies were administered to 33.5% of patients in group B (Table 5).

Discussion

VATS-L is recognized to be associated with many advantages compared with lobectomy by thoracotomy. Recent analysis of post-operative outcomes performed on both single institutional series and official databases proposed VATS-L to be superior in terms of length of stay, post-operative pain, preserving pulmonary function, post-operative complications and compliance with adjuvant chemotherapy when compared to open lobectomy (1-6). Moreover, VATS-L has been recommended by National Comprehensive Cancer Network (NCCN) guidelines as the preferred approach for early-stage NSCLC (15).

Table 3 Analysis of patients who required conversion

Variables	No-converted patient early stage-group A (n=395)	Converted patient locally advanced-stage group B (n=59)	P value
Sex (male) [n (%)]	271 (59.7)	43 (72.8)	0.549
Mean age (mean ± SD) (years)	68.39±9.22	68.71±9.03	0.800
FEV1% (mean ± SD)	91.93±21.35	87.00±18.64	0.112
FVC% (mean ± SD)	99.60±19.93	94.26±16.76	0.061
DLCO (mean ± SD) (%)	63.74±36.91	59.65±42.35	0.456
Side [n (%)]			0.672
Right	229 (58.0)	32 (54.3)	
Left	166 (42.0)	27 (45.7)	
Surgical approach [n (%)]			0.880
Copenhagen anterior approach	295 (74.68)	39 (66.20)	
Uniportal	33 (8.35)	4 (6.70)	
Others	67 (16.96)	16 (27.10)	
Surgical procedure [n (%)]			0.466
Upper lobectomy	191 (49.36)	22 (37.28)	
Middle lobectomy	18 (4.81)	5 (8.47)	
Lower lobectomy	175 (44.30)	27 (45.76)	
Upper bilobectomy	5 (1.26)	1 (1.69)	
Lower bilobectomy	6 (1.51)	4 (6.77)	
Type of lymphadenectomy [n (%)]			0.765
Radical lymph node dissection	290 (73.4)	41 (69.4)	
Sampling	105 (26.6)	18 (30.6)	
EBL (mean ± SD) (mL)	144.91±157.97	366.25±538.10	0.000
Operative time (mean ± SD) (min)	189.70±61.12	221.63±73.51	0.000
Final pathological diagnosis [n (%)]			0.026
ADC	255 (64.50)	28 (47.45)	
SCC	97 (24.50)	23 (38.98)	
Others	43 (11.00)	8 (13.55)	
Pathological stage [n (%)]			0.067
2bN0	113 (28.60)	17 (28.81)	
3N0	115 (29.11)	13 (22.00)	
3N2	20 (5.00)	5 (8.47)	
2bN2	12 (3.00)	4 (6.77)	
3N1	18 (4.50)	3 (5.00)	

Table 3 (continued)

Table 3 (continued)

Variables	No-converted patient early stage-group A (n=395)	Converted patient locally advanced-stage group B (n=59)	P value
Pathological N status [n (%)]			0.113
N0	295 (74.6)	37 (62.7)	
N1	49 (12.4)	9 (15.3)	
N2	51 (12.9)	13 (22.0)	
Pathological resection status [n (%)]			0.000
R0	384 (97.2)	53 (89.9)	
R1	11 (2.8)	4 (6.8)	
R2	0	2 (3.3)	
Number of total lymph nodes dissected (mean ± SD)	15.95±10.72	13.95±8.47	0.171
Number of N1 lymph nodes dissected (mean ± SD)	7.71±7.66	6.49±4.30	0.210
Number of N2 lymph nodes dissected (mean ± SD)	8.39±6.61	7.42±6.68	0.290
Any complications [n (%)]	111 (28.0)	21 (35.5)	0.282
Hospital stay (mean ± SD) (days)	7.29±6.89	12.41±21.32	0.000
Adjuvant therapy [n (%)]	132 (33.4)	20 (33.9)	0.920

DLCO, diffusing capacity of the lung for carbon monoxide; SD, standard deviation; ADC, adenocarcinoma; SCC, squamous cell carcinoma; EBL, estimated blood loss.

VATS major pulmonary resections are still considered complex and demanding procedures, characterized by the need of a fine dissection of delicate and vulnerable vascular structures at risk for potential severe and life-threatening bleedings; because of this VATS-L has been used mainly for early-stage NSCLC. With the continuous development of surgical skills and new technical facilities (such as high definition 2-dimension or 3-dimension cameras and displays, endoscopic flexible stapler and retraction instruments), intra-operative technical difficulties have been gradually overcome. However, the role of VATS-L for the treatment of the locally advanced stages of NSCLC is not clear and is not well established; in experienced VATS centres this minimally invasive approach is gaining acceptance even in multimodality treatment of NSCLC (11-13,16).

This study compared outcomes between patients who underwent VATS-L for early-stage and locally advanced-stage NSCLC, using data from the national Italian database (www.vatsgroup.org), and demonstrated that in Italy, VATS-L is a safe approach even for locally advanced-

stage NSCLC. In this large retrospective analysis, the two groups did not significantly differ in early outcomes, 30-day mortality (beyond the 2% in both groups) and proportion of patients who suffered from any complication (24.8% *vs.* 29.1%). The overall complication rate was statistically different between the two groups (30.4% *vs.* 37.0%) and this datum can be considered quite normal, based on the selection criteria of the two groups; however, the more common complications after thoracic surgery, such as atrial fibrillation, pneumonia, respiratory failure, bleeding requiring transfusion, and prolonged air leak were not statistically different between the two groups. Moreover, even if the overall hospital stay in group B was higher than group A (7.35 *vs.* 7.96 days), this datum was not statistically significant.

The incidence of surgical complications after resection for locally-advanced NSCLC and/or after neoadjuvant therapy has been reported in the literature to be variable. Hennon and co-authors (11), comparing the outcomes of locally-advanced NSCLC treated by VATS or thoracotomy,

Table 4 Complications in detail

Complications	Early-stage group A (n=3,266) [n (%)]	Locally advanced-stage group B (n=454) [n (%)]	P value
Atrial fibrillation	251 (7.6)	46 (10.1)	0.090
Acute myocardial infarction	8 (0.2)	0	0.290
Neurovascular complication	7 (0.2)	1 (0.2)	1.000
Cardiac arrest	2 (0.06)	1 (0.20)	0.260
Prolonged air leak	270 (8.2)	33 (7.2)	0.550
Pulmonary embolism	4 (0.1)	1 (0.2)	0.590
ARDS	17 (0.5)	3 (0.6)	0.700
Pneumonia	115 (3.5)	16 (3.5)	0.880
Mechanical ventilation	14 (0.4)	1 (0.2)	0.510
Atelectasis	68 (2.0)	15 (3.3)	0.150
Sputum retention	82 (2.5)	14 (3.0)	0.580
Hemothorax	33 (1.0)	15 (3.3)	<0.001
Broncho-pleural fistula	13 (0.3)	0	0.350
Phrenic nerve palsy	3 (0.09)	1 (0.20)	0.430
Recurrent laryngeal nerve palsy	18 (0.5)	3 (0.6)	0.770
Transfusions	73 (2.2)	15 (3.3)	0.170
Need of mechanical ventilation for >72 h	16 (0.4)	3 (0.6)	0.630
Total	994 (30.4)	168 (37.0)	0.040

ARDS, adult respiratory distress syndrome.

observed only one peri-operative death in the VATS group and had a complication rate of 38.9% and 36.8%, respectively. Other similar works about VATS-L versus open lobectomy (12,16-18) showed different complication rates ranging from 25% to 40%, but statistically not higher compared to the open approach. Gonzalez-Rivas *et al.*, comparing early stage (cT1 and cT2) and advanced stage NSCLC treated by uniportal VATS-L, obtained a complication rate of 17.2% and 14.0%, respectively (13). These results demonstrated that VATS-L, in appropriately selected patient operated in experienced centres, is a safe approach even after induction therapy and for locally advanced stage. In addition, VATS-L may hypothetically improve survival because it allows more patients (and more rapidly) to receive adjuvant therapy compared to patients who underwent lobectomy via thoracotomy (5,18).

In our series, 152 patients of group B (33.4%) received some kind of adjuvant treatments. This value can be interpreted with the fact that more complex procedures are not included in our database, often associated with an advanced pathological stage,

such as pneumonectomy or bronchial/vascular sleeve resections, planned and performed preferentially through thoracotomy. Hennon *et al.* (11) showed in his series a similar datum that was significantly higher when compared with the group of resection via thoracotomy (37.2% vs. 5.3%). On the other hand, Chen *et al.* demonstrated a similar proportion between the two approaches (70% vs. 65%) (16).

The conversion rate was higher (13%), but this datum is easily understandable since the complexity of the performed procedures: large masses could determine a worse handling of the whole lung and often are associated with infiltration of anatomical structures or hilar adenopathy requiring the open approach. Furthermore, the anatomical alterations caused by induction therapies (as calcified lymph nodes or scarring fibrous tissue strongly tightened to pulmonary artery or bronchus) lead to more complex procedures such as a broncho-vascular sleeve resection or a pneumonectomy (9).

Our study demonstrated that the decision of conversion was caused mainly by (I) bleeding not manageable by VATS;

Table 5 Post-operative results and pathological findings

Variables	Early-stage group A (n=3,266)	Locally advanced-stage group B (n=454)	P value
30-day mortality [n (%)]	53 (1.6)	7 (1.5)	0.880
Hospital stay (mean ± SD) (days)	7.35±29.39	7.96±10.10	0.660
Patients who suffered any complications [n (%)]	810 (24.8)	132 (29.1)	0.057
Final pathology [n (%)]			0.000
ADC	2,349 (71.9)	283 (62.3)	
SCC	485 (14.8)	120 (26.4)	
Others	432 (13.2)	51 (11.2)	
Pathological stage [n (%)]			0.000
IA	1,937 (59.30)	28 (6.20)	
IB	887 (27.20)	16 (3.50)	
IIA	219 (6.70)	138 (30.40)	
IIB	0	151 (33.30)	
IIIA	206 (6.30)	100 (22.00)	
IIIB	0	5 (1.10)	
IVA	6 (0.18)	1 (0.20)	
IVB	11 (0.33)	15 (3.30)	
Pathological N status [n (%)]			0.000
N0	2,838 (86.9)	332 (73.1)	
N1	221 (6.8)	58 (12.8)	
N2	207 (6.3)	64 (14.1)	
Resection status [n (%)]			0.001
R0	3222 (98.6)	437 (96.3)	
R1	38 (1.2)	15 (3.3)	
R2	6 (0.2)	2 (0.4)	
Adjuvant therapy [n (%)]	362 (11.1)	152 (33.5)	0.000

ADC, adenocarcinoma; SCC, squamous cell carcinoma; SD, standard deviation.

(II) an unexpected tumour extension and (III) the presence of hilar calcific lymph nodes precluding a safe dissection. Despite longer procedures and a higher estimated blood loss, the post-operative mortality and complication rates of converted patients were not superior compared with patients operated by VATS, thus demonstrating the limited influence of conversion to open thoracotomy on the post-operative outcomes.

Even if the minimally invasive VATS approach is widely recommended for early-stage NSCLC (15), thoracotomy is still the preferred approach for large tumours and after induction therapies. Our study shows that a substantial

portion of patients (14%) with locally-advanced NSCLC can benefit from VATS-L. So, since the lack of specific guidelines, what are the best candidates for minimally invasive resection in case of locally-advanced NSCLC? Our cohort is wide and heterogeneous, but clinical peripheral T2b and T3 tumours without lymph node involvement (stage IIA and IIB) show post-operative outcomes similar to early stages and seem to be the best candidates for VATS-L. Almost 25% of patients had chemotherapy before surgery, but in this cohort, we included different cases that could be differently evaluated on the basis of the clinical experience of the recruiting centre.

The initial doubts about VATS-L oncological adequacy for early-stage NSCLC have been overcome, as demonstrated by several authoritative papers (1-10); the minimally invasive technique and the traditional open technique have proven to be equivalent in terms of overall survival and disease free-survival also for locally advanced NSCLC (10-13). Unfortunately, our study lacks of mid- and long-term survival results; however, we have some valid oncological data such as the extent of lymphadenectomy and the resection margin status. It is well known that an incomplete mediastinal lymph node dissection in NSCLC may result in an incorrect staging and patients would be denied adjuvant treatments and subsequently overall survival may be affected. Our data showed an increased number of lymph nodes dissected for patients with locally-advanced NSCLC, indicating a tendency to a more invasive, aggressive and accurate mediastinal staging in this group. Other authors showed similar results with conventional three-port approach (16) and uniportal approach in single institution series (13).

Finally, this study has several limitations. The database is large and multi-institutional, but the cohort of patients is heterogeneous and non-randomized; it is limited to Italy and the practice patterns may not be representative of other centres outside Italy.

Moreover, our analysis does not include long-term disease-free or overall survival, which are needed to evaluate VATS-L oncological adequacy also for locally advanced NSCLC. Another limitation of our study is the absence of a comparative analysis with an open approach group, since our data comes from a VATS national database.

Concluding, VATS-L for locally advanced-stage NSCLC in Italy seems to be a safe and effective procedure when performed in appropriately selected patients, ensuring peri-operative results similar to those obtained in early-stage tumours. Although conversion rate is higher than in early stage, its influence on post-operative outcomes is limited. Further analyses are needed to compare mid- and long-term survival and confirm the oncological adequacy of minimally invasive approach for locally advanced NSCLC.

Acknowledgements

None.

Footnote

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

*, List of collaborators of the Italian VATS Group: Carlo Curcio, MD (Monaldi Hospital, Napoli); Dario Amore, MD (Monaldi Hospital, Napoli); Giuseppe Marulli, MD (University of Padova); Samuele Nicotra, MD (University of Padova); Andrea De Negri, MD (San Martino Hospital, Genova); Paola Maineri, MD (San Martino Hospital, Genova); Gaetano di Rienzo (Vito Fazzi Hospital, Lecce); Camillo Lopez, MD (Vito Fazzi Hospital, Lecce); Angelo Morelli, MD (S. Maria delle Misericordia Hospital, Udine); Francesco Londero, MD (S. Maria delle Misericordia Hospital, Udine); Lorenzo Spaggiari, MD (IEO Hospital, Milano); Roberto Gasparri, MD (IEO Hospital, Milano); Guido Baietto, MD (Maggiore della Carità Hospital, Novara); Caterina Casadio, MD (Maggiore della Carità Hospital, Novara); Maurizio Infante, MD (Borgo Trento Hospital, Verona); Cristiano Benato, MD (Borgo Trento Hospital, Verona); Marco Alloisio, MD (IRCCS Humanitas, Milano); Edoardo Bottoni, MD (IRCCS Humanitas, Milano); Giuseppe Cardillo, MD (Forlanini Hospital, Roma); Francesco Carleo, MD (Forlanini Hospital, Roma); Franco Stella, MD (S. Orsola Hospital, Bologna); Giampiero Dolci, MD (S. Orsola Hospital, Bologna); Francesco Puma, MD (University of Perugia); Damiano Vinci, MD (University of Perugia); Giorgio Cavallesco, MD (University of Ferrara); Pio Maniscalco, MD (University of Ferrara); Luca Ampollini, MD (University of Parma); Paolo Carbognani, MD (University of Parma); Alberto Terzi, MD (Negrar Hospital, Verona); Andrea Viti, MD (Negrar Hospital, Verona); Giampiero Negri, MD (S. Raffaele Hospital, Milano); Alessandro Bandiera, MD (S. Raffaele Hospital, Milano); Reinhold Perkmann, MD (Bolzano Hospital, Bolzano); Francesco Zaraca, MD (Bolzano Hospital, Bolzano); Claudio Andretti, MD (S. Andrea Hospital, Roma); Camilla Poggi, MD (S. Andrea Hospital, Roma); Felice Mucilli, MD (S. Maria Annunziata Hospital, Chieti); Pierpaolo Camplese, MD (S. Maria Annunziata Hospital, Chieti); Luca Luzzi, MD (University of Siena); Marco Ghisalberti, MD (University of Siena); Andrea Imperatori, MD (University of Varese); Nicola Rotolo, MD (University of Varese); Luigi Bortolotti, MD (Humanitas Gavazzeni Hospital, Bergamo); Giovanna Rizzardi, MD (Humanitas Gavazzeni Hospital, Bergamo); Massimo Torre, MD (Niguarda Hospital, Milano); Alessandro Rinaldo, MD (Niguarda Hospital, Milano); Armando Sabbatini, MD (Ospedali Riuniti, Ancona); Majed Refai, MD (Ospedali Riuniti, Ancona); Mauro Roberto Benvenuti, MD (Spedali Civili, Brescia); Diego Benetti, MD (Spedali Civili, Brescia); Alessandro Stefani, MD (Ospedale Policlinico, Modena);

Pamela Natali, MD (Ospedale Policlinico, Modena); Paolo Lausi, MD (Ospedale Molinette, Torino); Francesco Guerrera, MD (Ospedale Molinette, Torino).

References

1. Onaitis MW, Petersen RP, Balderson SS, et al. Thoracoscopic lobectomy is a safe and versatile procedure: experience with 500 consecutive patients. *Ann Surg* 2006;244:420-5.
2. Swanson SJ, Herndon JE 2nd, D'Amico TA, et al. Video-assisted thoracic surgery lobectomy: report of CALGB 39802--a prospective, multi-institution feasibility study. *J Clin Oncol* 2007;25:4993-7.
3. Whitson BA, Andrade RS, Boettcher A, et al. Video-assisted thoracoscopic surgery is more favorable than thoracotomy for resection of clinical stage I non-small cell lung cancer. *Ann Thorac Surg* 2007;83:1965-70.
4. Laursen LØ, Petersen RH, Hansen HJ, et al. Video-assisted thoracoscopic surgery lobectomy for lung cancer is associated with a lower 30-day morbidity compared with lobectomy by thoracotomy. *Eur J Cardiothorac Surg* 2016;49:870-5.
5. Petersen RP, Pham D, Burfeind WR, et al. Thoracoscopic lobectomy facilitates the delivery of chemotherapy after resection for lung cancer. *Ann Thorac Surg* 2007;83:1245-9; discussion 1250.
6. Stephens N, Rice D, Correa A, et al. Thoracoscopic lobectomy is associated with improved short-term and equivalent oncological outcomes compared with open lobectomy for clinical Stage I non-small-cell lung cancer: a propensity-matched analysis of 963 cases. *Eur J Cardiothorac Surg* 2014;46:607-13.
7. Gonfiotti A, Bongiolatti S, Borgianni S, et al. Development of a video-assisted thoracoscopic lobectomy program in a single institution: results before and after completion of the learning curve. *J Cardiothorac Surg* 2016;11:130.
8. Watanabe A, Koyanagi T, Ohsawa H, et al. Systematic node dissection by VATS is not inferior to that through an open thoracotomy: a comparative clinicopathologic retrospective study. *Surgery* 2005;138:510-7.
9. Gonfiotti A, Bongiolatti S, Viggiano D, et al. Does videomediastinoscopy with frozen sections improve mediastinal staging during video-assisted thoracic surgery pulmonary resections? *J Thorac Dis* 2016;8:3496-504.
10. Villamizar NR, Darrabie M, Hanna J, et al. Impact of T status and N status on perioperative outcomes after thoracoscopic lobectomy for lung cancer. *J Thorac Cardiovasc Surg* 2013;145:514-20; discussion 520-1.
11. Hennon M, Sahai RK, Yendamuri S, et al. Safety of thoracoscopic lobectomy in locally advanced lung cancer. *Ann Surg Oncol* 2011;18:3732-6.
12. Yang CF, Meyerhoff RR, Mayne NR, et al. Long-term survival following open versus thoracoscopic lobectomy after preoperative chemotherapy for non-small cell lung cancer. *Eur J Cardiothorac Surg* 2016;49:1615-23.
13. Gonzalez-Rivas D, Fieira E, Delgado M, et al. Is uniportal thoracoscopic surgery a feasible approach for advanced stages of non-small cell lung cancer? *J Thorac Dis* 2014;6:641-8.
14. Sobin LH, Gospodarowicz MK, Wittekind C. editors. *TNM Classification of Malignant Tumours, 7th Edition*. Wiley-Blackwell, 2011.
15. National Comprehensive Cancer Network. *Non-Small Cell Lung Cancer (Version 8.2017)*. Available online: https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
16. Chen K, Wang X, Yang F, et al. Propensity-matched comparison of video-assisted thoracoscopic with thoracotomy lobectomy for locally advanced non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2017;153:967-76.e2.
17. Nakanishi R, Fujino Y, Yamashita T, et al. Thoracoscopic anatomic pulmonary resection for locally advanced non-small cell lung cancer. *Ann Thorac Surg* 2014;97:980-5.
18. Nagahiro I, Andou A, Aoe M, et al. Pulmonary function, postoperative pain, and serum cytokine level after lobectomy: a comparison of VATS and conventional procedure. *Ann Thorac Surg* 2001;72:362-5.

doi: 10.21037/jovs.2017.09.06

Cite this article as: Gonfiotti A, Bongiolatti S, Bertolaccini L, Viggiano D, Solli P, Droghetti A, Bertani A, Crisci R, Voltolini L; Italian VATS Group. Thoracoscopic lobectomy for locally advanced-stage non-small cell lung cancer is a feasible and safe approach: analysis from multi-institutional national database. *J Vis Surg* 2017;3:160.